Docket: T1340/7008

CANADIAN HUMAN RIGHTS TRIBUNAL

B E T W E E N:

FIRST NATIONS CHILD AND FAMILY CARING SOCIETY OF CANADA and ASSEMBLY OF FIRST NATIONS

Complainants

- and -

CANADIAN HUMAN RIGHTS COMMISSION

Commission

- and -

ATTORNEY GENERAL OF CANADA
(representing the Minister of Indigenous Services Canada)

Respondent

- and -

CHIEFS OF ONTARIO,
AMNESTY INTERNATIONAL and
NISHNAWBE ASKI NATION

AFFIDAVIT OF SIDNEY SEGALOWITZ

I, Sidney Segalowitz, of the City of St. Catharines, Regional Municipality of Niagara, in the Province of Ontario, **SOLEMNLY AFFIRM THAT:**

1. I am a professor at Brock University's Psychology Department, the Director of the Cognitive and Affective Neuroscience Laboratory and the Director of The Jack and Nora Walker Centre for Lifespan Development Research. I hold a doctorate in Psychology

(Human Development) from Cornell University, and a Bachelor of Arts in Psychology from McGill University.

2. I have been a professor in the Department of Psychology at Brock University since 1974. I have taught undergraduate and graduate courses in and worked in the field of developmental psychology, brain development and neuropsychology for over forty years. I served as Editor-in-Chief of the refereed journal *Brain and Cognition* from 2002-2014. I have published sixteen books and collections in these fields and authored or co-authored over six hundred other articles, chapters, abstracts and presentations on these subjects. As such, I have personal knowledge of the matters hereinafter deposed to, save and except for those matters stated to be on information and belief and where so stated, I believe them to be true.

3. A complete copy of my curriculum vitae is attached hereto as **Exhibit "A"**.

Background

4. I am aware that the First Nations Child and Family Caring Society (the "**Caring Society**") and the Assembly of First Nation (the "**AFN**") are the complainants in an ongoing human rights complaint before the Canadian Human Rights Tribunal (the "**Tribunal**") against Canada in relation to child welfare services on-reserve and in the Yukon, as well as Jordan's Principle.

5. I am further aware that in September 2019, the Tribunal ordered that the victims of Canada's discriminatory conduct are entitled to financial compensation under the *Canadian Human Rights Act* (the "**Compensation Entitlement Order**"). I understand that some of the victims who may be entitled to this compensation are currently children and youth under the age of 18.

6. Following the release of the Compensation Entitlement Order, I was contacted by Dr. Cindy Blackstock of the Caring Society. She asked me to provide the Tribunal and the parties with information regarding brain development and the physiological and

anatomical markers of continued brain maturation in youth and adolescents into their twenties. In response to this request, I prepared a paper entitled: *When Does the Adolescent Brain Reach Adult Maturity*. A copy of the paper is attached hereto as **Exhibit "B"**.

7. Consistent with ethical research guidelines, human neurological research is occasionally informed by animal studies. As a result, some of the research referenced in my paper at Exhibit "B" includes comparative studies involving animals and humans.

8. I am further attaching the available abstracts referenced in my paper as **Exhibit "C"**.

Overall Conclusions of the Research

9. It is generally accepted that the age of majority (18 years) does not represent a transition to full adulthood, although obviously some aspects of adulthood are adequately reached. While some studies refer to adolescence as being a period that continues on to 25, there is a growing consensus among researchers to refer to the period from 18 to 25 years as 'emerging adulthood'.

10. Studies of brain anatomy and function (referred to collectively here as brain physiology or neurophysiology) demonstrate that there are continued developments well into the third decade after birth.

11. There is a growing consensus that, for many important functions, the *average* age at which brain development in a healthy individual nears completion is approximately 25 years. However, there will a sizable group whose trajectory is behind this schedule as well as some who are ahead of it. As a professional with over forty years of experience in the fields of brain development and neuropsychology it is my opinion that the research conducted to date on this question supports these conclusions.

12. I recognize that I am swearing this affidavit as an expert witness, and it is on this same basis that I have prepared the paper that is attached as Exhibit "B". As an expert, I

understand that it is my duty to the Tribunal to provide opinion evidence that is fair, objective and non-partisan, to provide opinion evidence that is related only to matters that are within my area of expertise, and to provide such additional assistance as the Tribunal may reasonably require to determine a matter in issue. I acknowledge that these duties prevail over any obligation that I may owe to any party by whom or on whose behalf I am engaged.

AFFIRMED BEFORE ME this 9th day of January, 2020 in the Regional Municipality of Niagara, in the Province of Ontario.

Commissioner for taking affidavits

SIDNEY SEGALOWITZ

Spenser Wesley Alexander Chalmers,
a Commissioner etc. Province of
Ontario for Clarke Child and Family Law.
Expires September 4, 2021.

This is Exhibit "A" to the affidavit of Sidney Segalowitz, affirmed before me this 9th day of January, 2020

A Commissioner for taking Affidavits etc.

Spenser Wesley Alexander Chalmers, a Commissioner etc. Province of Ontario for Clarke Child and Family Law. Expires September 4, 2021.

CURRICULUM VITAE

NAME: **Sidney J. Segalowitz**
Country of citizenship: Canada
DATE Nov 30, 2019
MAILING ADDRESS:
Office: Department of Psychology
Brock University
St. Catharines, Ontario L2S 3A1
Telephone: 905-688-5550, off: ext 5446; lab: 3451; admin assistant: 5050
Fax: 905-688-6922
E-mail: sid.segalowitz@brocku.ca

EDUCATIONAL HISTORY

B.A. McGill University, June 1970 Field: Psychology
Ph.D. Cornell University, January 1975 Field: Psychology (Human Development)

PROFESSIONAL HISTORY

Brock University
Department of Psychology

Assistant Professor	July 1974
Associate Professor	July 1979
Professor	July 1986
Director, Child Studies Programme	1983 - 1987
Director, Institute of Applied Human Development	1990 - 1992
Graduate Faculty, Fac. of Education, Brock University	1990 - 2012
Director, Brock Institute for Electrophysiological Research	Sept 2001- June 2014
Chair, Dept of Psychology	July 2000 - 2003
Editor-in-Chief, *Brain and Cognition* (published by Elsevier)	Sept 2002 – Jan 2014
Centre de recherche de l'Institut universitaire de gériatrie de Montréal (Université de Montréal), Chercheur associé,	2005 - 2020
Director, Jack and Nora Walker Canadian Centre for Lifespan Development Research, Brock University	2007 – present
Scientific Advisor, Pathstone Mental Health Research Institute	2012 – present
Member, Scientific Advisory Committee, ARiEAL (Centre for Advanced Research in Experimental and Applied Linguistics, McMaster University)	2018 – 2020

PUBLICATION HISTORY

Books and Collections

1. Segalowitz, S.J. & Luciana, M. (2014). Reward and regulatory processes in adolescence. Special issue of *Brain and Cognition, 89*(1), 1-126.
2. Jetha, M.K. & Segalowitz, S.J. (2012). *Adolescent Brain Development: Implications for Behavior.* San Diego: Academic Press.
3. Schmidt, L.A. & Segalowitz, S.J. (2008). *Developmental psychophysiology.* Cambridge: Cambridge University Press.
4. Ridderinkhof, K.R., van den Wildenberg, W.P.M., Segalowitz, S.J. & Carter, C.S. (2004). Neurocognitive mechanisms of performance monitoring and inhibitory control. Special Issue of *Brain and Cognition, 56*(2), 129-277.
5. Segalowitz, S.J. & Rapin, I. (2003). *Handbook of Child Neuropsychology*, second edition. Vol 8, Part 2, in F. Boller & J. Grafman (series eds.) *Handbook of Neuropsychology.* Amsterdam: Elsevier.
6. Segalowitz, S.J. & Rapin, I. (2002). *Handbook of Child Neuropsychology,* second edition. Vol 8, Part 1, in F. Boller & J. Grafman (series eds.) *Handbook of Neuropsychology.* Amsterdam: Elsevier.
7. Band, G., Ridderinkhof, R. & Segalowitz, S.J. (Eds.) (2002). Neuropsychology of aging. Special issue of *Brain and Cognition, 49*, 259-435.
8. Segalowitz, S.J. & Burgess, C. (Eds.) (2000). Neuropsychology in the New Millennium. Special issue of *Brain and Cognition, 42*(1), 1-169.
9. Segalowitz, S.J. & Rose-Krasnor, L. (Eds.) (1992). The role of frontal lobe maturation in cognitive and social development. Special issue for *Brain and Cognition, 20*(1), 1-213.
10. Rapin, I. & Segalowitz, S.J. (Volume Eds.) (1992). *Child Neuropsychology: Part I.* F. Boller & J. Grafman (series eds.) *Handbook of Neuropsychology, vol 6.* Amsterdam: Elsevier.
11. Segalowitz, S.J. & Rapin, I. (Volume Eds.) (1992). *Child Neuropsychology: Part II.* F. Boller & J. Grafman (series eds.) *Handbook of Neuropsychology, vol 7.* Amsterdam: Elsevier.
12. Molfese, D.M. & Segalowitz, S.J. (Eds.) (1988). *Brain lateralization in children: Developmental implications.* New York: Guilford Press.
13. Young, G., Segalowitz, S.J., Corter, C. & Trehub, S. (Eds.) (1983). *Manual specialization and the developing brain.* New York: Academic.
14. Segalowitz, S.J. (Ed.) (1983). *Language functions and brain organization.* New York: Academic.
15. Segalowitz, S.J. (1983). *Two sides of the brain.* Englewood Cliffs, NJ: Prentice Hall.
16. Segalowitz, S.J. & Gruber, F.A. (Eds.) (1977). *Language development and neurological theory.* New York: Academic Press.

Refereed Journal Articles

1. Willner, C.J., Jetha, M.K., Segalowitz, S.J., & Gatzke-Kopp, L.M. (in press). Neurophysiological evidence for distinct biases in emotional face processing associated with internalizing and externalizing symptoms in children. *Biological Psychology.* (Accepted Nov 27, 2019, BIOPSY_2018_646R3)
2. Hafer, C.L., Drolet, C.E., Davis, E.E., Segalowitz, S.J., & Shulman, E.P. (in press). Evidence of a Processing Advantage for Deservingness-Relevant Information. *Social Psychology. (*Accepted July 9, 2019, SoPsy-MS-877R1)
3. Milligan, K., Sibalis, A., McKeough, T., Lackner, C, Schmidt, L.A., & Segalowitz, S.J. (in press). Mindfulness enhances neural indices of attention in youth with learning disabilities and co-occurring mental health challenges. *Mindfulness,* accepted Feb 25, 2019 (MIFU-D-18-00398R1).
4. Klymkiw, D.F., Milligan, K., Lackner, C., Phillips, M., Schmidt, L.A., and Segalowitz, S.J. (in press). Does Anxiety Enhance or Hinder Attentional and Impulse Control in Youth With ADHD? An ERP Analysis. *Journal of Attention Disorders.* DOI: 10.1177/1087054717707297

5. Milligan, K., Sibalis, A., McKeough, T., Lackner, C. Schmidt, K.A., Pun, C., & Segalowitz, S.J. (2019). Impact of Mindfulness Martial Arts Training on Neural and Behavioral Indices of Attention in Youth with Learning Disabilities and Co-occurring Mental Health Challenges. *Mindfulness, 10*, 2152–2164.
6. Sibalis, A., Milligan, K., Pun,C., McKeough, T., Schmidt, L.A., & Segalowitz, S.J. (2019). An EEG Investigation of the Attention-Related Impact of Mindfulness Training in Youth With ADHD: Outcomes and Methodological Considerations. *J Attention Disorders, 23*(7), 733-743. DOI: 10.1177/1087054717719.
7. Mulligan, B., Smart, C., & Segalowitz, S.J. (2019). Neuropsychological and resting-state electroencephalographic markers of older adult neurocognitive adaptability. *The Clinical Neuropsychologist, 33*(2), 390-418
8. Davis, C. P., Libben, G., & Segalowitz, S. J. (2019). Compounding matters: Event-related potential evidence for early semantic access to compound words. *Cognition, 184*(1), 44-52.
9. Campopiano, A., van Noordt, S., & Segalowitz, S.J. (2018). STATSLAB: An open-source toolbox for computing single-subject effects using robust statistics. *Behavioural Brain Research, 347*, 425-435.
10. Lackner, C.L., Santesso, D. L., Dywan, J., O'Leary, D., Wade, T.J., & Segalowitz, S.J. (2018). Adverse Childhood Experiences are Associated with Self-Regulation and the Magnitude of the Error-Related Negativity Difference. *Biological Psychology, 132*, 244-251.
11. Mulligan, Bryce P., Smart, Colette M., Segalowitz, Sidney J., & MacDonald, Stuart W.S. (2018). Characteristics of healthy older adults that influence self-rated cognitive function. *Journal of the International Neuropsychological Society, 24*(1), 57-66.
12. Smart, C. & Segalowitz, S.J. (2017). Respond, Don't React: The Influence of Mindfulness Training on Performance Monitoring in Older Adults. *Cognitive, Affective and Behavioral Neuroscience, 17*, 1151–1163.
13. Segalowitz, S. J., Sternin, A., Lewis, T. L., Dywan, J., & Maurer, D. (2017). Electrophysiological evidence of altered visual processing in adults who experienced visual deprivation during infancy. *Dev Psychobiol, 59*(3), 375-389. doi: 10.1002/dev.21502
14. Van Noordt, S.J.R., Desjardins, J.A., Gogo, C., Tekok-Kilic, A., Segalowitz, S.J. (2017). Cognitive control in the eye of the beholder: Electrocortical theta and alpha modulation during response preparation in a cued saccade task. *Neuroimage, 145*(Pt A), 82-95.
15. Tang, A., Santesso, D., Segalowitz, S., Schulkin, J., & Schmidt, L. (2016). Distinguishing shyness and sociability in adults: An event-related electrocortical-neuroendocrine study. *Biological Psychology, 199*, 200-209.
16. Van Noordt, S., Campopiano, A., & Segalowitz, S.J. (2016). A functional classification of medial frontal negativity event-related potentials: Theta oscillations and single subject effects. *Psychophysiology, 53*(9), 1317-1334.
17. Smart, C.M., Segalowitz, S.J., Mulligan, B.P., Koudys, J., & Gawryluk, J.R. (2016). Mindfulness Training for Older Adults with Subjective Cognitive Decline: Results from a Pilot Randomized Controlled Trial. *Journal of Alzheimer's Disease, 52*, 757-774. DOI 10.3233/JAD-150992
18. Segalowitz, S.J. Exercise and Pediatric Brain Development: a Call to Action. (2016). *Pediatric Exercise Science, 28*, 217-225, http://dx.doi.org/10.1123/pes.2016-0028.
19. Tang, A., Santesso, D.L., Segalowitz, S.J., & Schmidt, L.A. (2016). Distinguishing Shyness and Sociability in Children: An ERP Study. *Journal of Experimental Child Psychology, 142*, 291-311.
20. Gatzke-Kopp, L. M., Willner, C. J., Jetha, M., K., Abenavoli, R. M., DuPuis, D., & Segalowitz, S. J. (2015). How does Reactivity to Frustrative Non-Reward Increase Risk for Externalizing Symptoms? *International Journal of Psychophysiology, 98*, 300-309. doi:10.1016/j.ijpsycho.2015.04.018

21. Van Noordt, S., Desjardins, J., & Segalowitz, S.J. (2015). Watch Out! Medial frontal cortex is activated by cues signaling potential changes in response demands. *NeuroImage, 114,* 356-370. *http*://dx.doi.org/10.1016/j.neuroimage.2015.04.021.
22. Willner, C.J., Gatzke-Kopp, L.M., Bierman, K., Greenberg, M., & Segalowitz S.J. (2015). Relevance of a neurophysiological marker of selective attention for children's learning-related behaviors and academic performance. *Developmental Psychology, 51*(8), 1148-1162.
23. DuPuis, D., Ram, N., Willner, C.J., Karalunas, S., Segalowitz, S.J., Gatzke-Kopp, L.M. (2015). Implications of Ongoing Neural Development for the Measurement of the Error-Related Negativity in Childhood. *Developmental Science, 18*(3), 452-468. DOI: 10.1111/desc. 12229.
24. Marshall, W.J., Lackner, C.L., Marriott, P., Santesso, D.L., & Segalowitz, S.J. (2014). Using Phase Shift Granger Causality to Measure Effective Connectivity in EEG Recordings. *Brain Connectivity, 4*(10), 826-841, doi:10.1089/brain.2014.0241
25. Smart, C.M., Segalowitz, S.J., Mulligan, B.P., & MacDonald, S.W. (2014). Attention capacity and self-report of subjective cognitive decline: a P3 ERP study. *Biol Psychol, 103*, 144-151. doi: 10.1016/j.biopsycho.2014.08.016 S0301-0511(14)00201-4
26. Capuana, L. J., Dywan. J., Tays, W. J., Elmers, J. L., Witherspoon, R., & Segalowitz, S. J. (2014). Factors influencing the role of autonomic regulation in the service of cognitive control. *Biological Psychology, 102*, 88-97.
27. Aniyan, A. Kumar, Sajeeth N. P., Samar, V.J., Desjardins, J., & Segalowitz, S.J. (2014). A wavelet based algorithm for the identification of event-related potential components. *Neuroscience Methods*, 233C, 63-72. doi: 10.1016/j.jneumeth.2014.06.004
28. Lackner, C.L., Santesso, D.L., Dywan, J., Wade, T.J., Segalowitz, S.J. (2014). Event-related Potentials Elicited to Performance Feedback in High- and Low-Shy Adolescents. *Infant and Child Development,* 23, 283-294. doi: 10.1002/icd.1865.
29. Zheng, X., & Segalowitz, S. J. (2014). Putting a face in its place: In- and out-group membership alters the N170 response. *Soc Cogn Affect Neurosci*, 9(7), 961-968. doi:10.1093/scan/nst069.
30. Gatzke-Kopp, L. M., Jetha, M. K., & Segalowitz, S. J. (2014). The role of resting frontal EEG asymmetry in psychopathology: Afferent or efferent filter? *Developmental Psychobiology, 56*, 73–85.
31. Lackner, C.L., Marshall, W.J., Santesso, D. L., Dywan, J., Wade, T., & Segalowitz, S.J. (2014). Adolescent Anxiety and Aggression can be Differentially Predicted by Electrocortical Phase Reset Variables. *Brain and Cognition,* 89(1), 90-98. http://dx.doi.org/10.1016/j.bandc.2013.10.004.
32. Jetha, M.K., Zheng, X., Goldberg, J.O., Segalowitz, S.J., & Schmidt, L.A. (2013). Shyness and Emotional Face Processing in Schizophrenia: An ERP study. *Biological Psychology, 94,* 562–574.
33. Weissflog, M., Choma, B., van Noordt, S., Dywan, J., & Segalowitz, S.J. (2013). The Political (and Physiological) Divide: Political Orientation, Performance Monitoring, and the Anterior Cingulate Response. *Social Neuroscience, 8*(5), 434-447.
34. Desjardins, J.A., & Segalowitz, S.J. (2013). The timing and consistency of event-related potential responses when processing faces: Deconstructing the P100-N170 complex using ICA and robust estimation. *Journal of Vision,* 13(5):22, 1–18. http://www.journalofvision.org/content/13/5/22, doi:10.1167/13.5.22.
35. Mondloch, C. J., Segalowitz, S.J., Lewis, T.L., Dywan, J., Le Grand, R., Levin, A.V., & Maurer, D. (2013). The effect of early visual deprivation on the development of face detection. *Developmental Science, 16*(5), 728-742. DOI: 10.1111/desc.12065
36. Lackner, C.L., Santesso, D.L., Dywan, J., Wade, T.J., Segalowitz, S.J. (2013). Electrocortical indices of selective attention predict adolescent executive functioning. *Biological Psychology, 93*, 325-333, DOI: 10.1016/j.biopsycho.2013.03.001

37. van Noordt, S. & Segalowitz, S.J. (2012). Performance monitoring and the medial prefrontal cortex: a review of individual differences and context effects as a window on self-regulation. *Frontiers in Human Neuroscience, 6,* article 197. http://www.frontiersin.org/Human_Neuroscience/10.3389/fnhum.2012.00197/full
38. Choma, B., Hafer, C.L., Dywan, J., Segalowitz, S.J., Busseri, M. (2012). Political liberalism and political conservatism: functionally independent? *Pers Indiv Diff, 53*(4), 431-436.
39. Capuana, L., Dywan, J., Tays, W.J., & Segalowitz, S.J. (2012). Cardiac workload and inhibitory control in younger and older adults. *Biological Psychology, 90,* 60-70.
40. Zheng, X., Mondloch, C.J., & Segalowitz, S.J. (2012). The timing of individual face recognition in the brain. *Neuropsychologia, 50*(7), 1451-1461. doi:10.1016/j.neuropsychologia.2012.02.030
41. Segalowitz, S.J., Santesso, D.L., Willoughby, T., Reker, D.L., Campbell, K., Chalmers, H., & Rose-Krasnor, L. (2012). Adolescent peer interaction and trait surgency weaken medial prefrontal cortex responses to failure. *Social, Cognitive, and Affective Neuroscience. 7*(1), 115-124.
42. Jetha, M.K., Zheng, X., Schmidt, L.A., & Segalowitz, S.J. (2012). Shyness and the first 100 milliseconds of emotional face processing. *Social Neuroscience, 7*(1), 74-89. http://dx.doi.org/10.1080/17470919.2011.581539.
43. Masaki, H., Murphy, T.I., Desjardins, J.A., & Segalowitz, S.J. (2012). The error-related negativity associated with different strength of stimulus-response interference. *Clinical Neurophysiology, 123,* 689–699. doi:10.1016/j.clinph.2011.07.043
44. Zheng, X., Mondloch, C.J., Nishimura, M., Vida, M.D., Segalowitz, S.J. (2011). Telling one face from another: Electrocortical correlates of facial characteristics among individual female faces. *Neuropsychologia, 49,* 3254–3264.
45. Santesso, D.L., Dzyundzak, A., Segalowitz, S.J. (2011). Age, sex and individual differences in punishment sensitivity: Factors influencing the feedback-related negativity. *Psychophysiology,* 48(11), 1481-1488.
46. Mathewson, K.J., Dywan, J., Snyder, P.J, Tays, W.J., & Segalowitz, S.J. (2011). Autonomic regulation and maze-learning performance in older and younger adults. *Biological Psychology, 88,* 20-27.
47. Tays, W.J., Dywan, J., Capuana, L.J., & Segalowitz, S.J. (2011). Age-related differences during simple working memory decisions: ERP indices of early recognition and compensation failure. *Brain Research, 1393,* 62-72.
48. Mathewson, K.J., Drmic, I.E., Jetha, M.K., Bryson, S.E., Goldberg, J.O., Hall, G.B., Santesso, D.L., Segalowitz, S.J., & Schmidt, L.A. (2011). Behavioral and cardiac responses to emotional Stroop in adults with autism spectrum disorders: Influence of medication. *Autism Research,* 4, 98-108.
49. Santesso, D. L., Drmic, I. E., Jetha, M. K., Bryson, S. E., Goldberg, J. O., Hall, G. B., Mathewson, K. J., Segalowitz, S. J., & Schmidt, L. A. (2011). An event-related source localization study of response monitoring and social impairments in autism spectrum disorder. *Psychophysiology, 48,* 241-251.
50. Mathewson, K.J., Jetha, M.K., Drmic, I.E., Bryson, S.E., Goldberg, J.O., Hall, G.B., Santesso, D.L., Segalowitz. S.J., & Schmidt, L.A. (2010). Autonomic predictors of Stroop performance in young and middle-aged adults. *International Journal of Psychophysiology, 76,* 123-129.
51. Segalowitz, S.J., Santesso, D., Chantziantoniou, D., Murphy, T.I., Homan, D., Khan, S. (2010). Retest reliability of medial frontal negativities during performance monitoring. *Psychophysiology, 47,* 260-270.
52. Segalowitz, S. J., Santesso, D. L., & Jetha, M. K. (2010). Electrophysiological changes during adolescence: A review. *Brain and Cognition, 72*(1), 86-100.
53. Tays, W.J., Dywan, J., & Segalowitz, S.J. (2009). General proactive interference and the N450 effect. *Neuroscience Letters, 462,* 239-243.
54. Segalowitz, S.J. & Dywan, J. (2009). Individual differences and developmental change in the ERN response: implications for models of ACC function. *Psychological Research, 73,* 857-870.
55. Segalowitz, S.J. & Zheng, X. (2009). An ERP study of category priming: Evidence of early lexical semantic access. *Biological Psychology, 80,* 122-129.

56. Santesso, D., & Segalowitz, S.J. (2009). The error-related negativity is related to risk-taking and empathy in young men. *Psychophysiology, 46*, 143-152.
57. Mathewson, K.J., Dywan, J., Snyder, P.J., Tays, W.J., & Segalowitz, S.J. (2008). Aging and electrocortical response to error feedback during a spatial learning task. *Psychophysiology, 45*, 936-948.
58. Santesso, D.L., Segalowitz, S.J., Ashbaugh, A.R., Antony, M. M., McCabe, R.E., & Schmidt, L.A. (2008). Frontal EEG asymmetry and sensation seeking in young adults. *Biological Psychology, 78*, 164–172.
59. Tays, W. J., Dywan, J., Mathewson, K. J., & Segalowitz, S. J. (2008). Age differences in target detection and interference resolution in working memory. *Journal of Cognitive Neuroscience, 20*, 2250-2262.
60. Dywan, J., Mathewson, K. J., Choma, B. L., Rosenfeld, B., & Segalowitz, S. J. (2008). Autonomic and electrophysiological correlates of emotional intensity in older and younger adults. *Psychophysiology, 45*, 389–397.
61. Santesso, D.L. & Segalowitz, S.J. (2008). Development of error-related ERPs in middle to late adolescent males. *Developmental Psychology, 44,* 205-217.
62. Schmidt, L.A., Santesso, D.L., Schulkin, J., Segalowitz, S.J. (2007). Shyness is a necessary but not sufficient condition for high salivary cortisol in typically developing 10 year-old children. *Personality and Individual Differences, 43*, 1541-1551.
63. Munro, G., Dywan, J., Harris, G.T., McKee, S., Unsal, A., & Segalowitz, S.J. (2007). ERN varies with degree of psychopathy in an emotion discrimination task. *Biological Psychology, 76*, 31-42.
64. Stemmer, B., Segalowitz, S. J., Dywan, J., Panisset, M., & Melmed, C. (2007). The error negativity in nonmedicated and medicated patients with Parkinson's disease. *Clinical Neurophysiology, 118,* 1223-1229.
65. Segalowitz, S.J., Mahaney, P., Santesso, D.L., MacGregor, L., Muir, C., Dywan, J. & Willer, B. (2007). Retest reliability in adolescents of a computerized neuropsychological battery used to assess recovery from concussion. *NeuroRehabilitation, 22,* 1-9.
66. Munro, G. Dywan, J., Harris, G. T., McKee, S., Unsal, A. & Segalowitz, S. J. (2007). Response inhibition in psychopathy: The frontal N2 and P3. *Neuroscience Letters, 418,* 149–153.
67. Stieben, J., Lewis, M.D., Granic, I., Zelazo, P.D., Segalowitz, S.J., & Pepler, D. (2007). Neurophysiological mechanisms of emotion regulation for subtypes of externalizing children. *Development & Psychopathology, 19,* 455-480.
68. Beaton, E.A. , Schmidt, L.A. , Ashbaugh, A.R., Santesso, D.L., Antony, M.M. , McCabe, R.E., Segalowitz, S.J., Schulkin, J. (2006). Low Salivary Cortisol Levels among Socially Anxious Young Adults: Preliminary Evidence from a Selected and a Non-selected Sample. *Personality and Individual Differences, 41,* 1217-1228.
69. Santesso, D., Segalowitz, S.J. & Schmidt, L.A. (2006). Error-related electrocortical responses in 10-year-old children and young adults. *Developmental Science, 9(5),* 473-481.
70. Murphy, T.I., Richard, M., Masaki, H. & Segalowitz S.J. (2006). The Effect of Sleepiness on Performance Monitoring: I know what I am doing, but do I care? *Journal of Sleep Research, 15,* 15-21.
71. Lewis, M.D., Lamm, C., Segalowitz, S.J., Stieben, J. & Zelazo, P.D. (2006). Neurophysiological Correlates of Emotion Regulation in Children and Adolescents. *Journal of Cognitive Neuroscience, 18(3),* 430-443.
72. Santesso, D., Segalowitz, S.J. & Schmidt, L.A. (2006). Error-Related Electrocortical Responses are Enhanced in Children With Obsessive-Compulsive Behaviors. *Developmental Neuropsychology, 29(3),* 431-445.
73. Santesso, D., Reker, D. L., Schmidt, L.A., & Segalowitz, S.J. (2006). Frontal electroencephalogram activation asymmetry, emotional intelligence, and externalizing behaviors in 10-year-old children. *Child Psychiatry and Human Development, 36(3),* 311-328.

74. Mathewson, K., Dywan, J. & Segalowitz, S.J. (2005). Brain bases of error-related ERPs as influenced by age and task. *Biological Psychology, 70,* 88-104.
75. Santesso, D., Segalowitz, S.J. & Schmidt, L.A. (2005). ERP Correlates of Error Monitoring in 10 Year Olds are Related to Socialization. *Biological Psychology, 70,* 79-87.
76. Leclerc, C., Segalowitz, S.J., Desjardins, J., Lassonde, M. & Lepore, F. (2005). EEG coherence in early-blind humans during sound localization. *Neuroscience Letters, 376,* 154-159.
77. Segalowitz, S.J. & Lane, K. (2004). Perceptual fluency and lexical access for function versus content words. *Behavioral and Brain Sciences, 27,* 307-308.
78. Ridderinkhof, K.R., van den Wildenberg, W.P.M., Segalowitz, S.J. & Carter, C.S. (2004). Neurocognitive mechanisms of cognitive control: The role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. *Brain and Cognition, 56(2),* 129-140.
79. Pailing, P.I. & Segalowitz, S.J. (2004). The effects of uncertainty in error monitoring on associated ERPs. *Brain and Cognition, 56,* 215-233.
80. Davies, P.L., Segalowitz, S.J. & Gavin, W.J. (2004). Development of Error Monitoring ERPs in Adolescents. *Annals of the New York Academy of Sciences, 1021,* 324-328.
81. Murphy, T.I. & Segalowitz, S.J. (2004). Eliminating the P300 rebound in short oddball paradigms. *International Journal of Psychophysiology, 53(3),* 233-238.
82. Davies, P.L., Segalowitz, S.J., Gavin, W.J. (2004). Development of Response-Monitoring ERPs in 7- to 25-Year-Olds. *Developmental Neuropsychology, 25(3),* 355-376.
83. Segalowitz, S.J. & Davies, P.L. (2004). Charting the maturation of the frontal lobe: an electrophysiological strategy. *Brain and Cognition, 55,* 116-133.
84. Pailing, P.E. & Segalowitz, S.J. (2004). The error-related negativity (ERN/Ne) as a state and trait measure: motivation, personality and ERPs in response to errors. *Psychophysiology, 41,* 84-95.
85. McNeely, H., Dywan, J., & Segalowitz, S.J. (2004). ERP indices of emotionality and semantic cohesiveness during recognition judgements. *Psychophysiology, 41,* 117-129.
86. Stemmer, B., Segalowitz, S.J., Witzke, W., & Schoenle, P.W. (2003). Error detection in patients with lesions to the medial prefrontal cortex: An ERP study. *Neuropsychologia, 42,* 118-130.
87. Band, G. P., Ridderinkhof, K. R., & Segalowitz, S. (2002). Explaining neurocognitive aging: is one factor enough? *Brain and Cognition, 49(3),* 259-267.
88. Dywan, J. Segalowitz, S.J. & Arsenault, A. (2002). Electrophysiological response during source memory decisions in older and younger adults. *Brain and Cognition, 49,* 322-340.
89. Hopkins, M. J., Dywan, J., & Segalowitz, S. J. (2002). Altered electrodermal response to facial expression after closed head injury. *Brain Injury, 16,* 245-257.
90. Pailing, P.E., Segalowitz, S.J., Dywan, J. & Davies, P.L. (2002). Error Negativity (Ne/ERN) and Response Control. *Psychophysiology, 39,* 198-206.
91. Segalowitz, S.J., Wintink, A.J., & Cudmore, L.J. (2001). P300 topographical change with task familiarization and task complexity. *Cognitive Brain Research, 12,* 451-457.
92. Baker, K., Segalowitz, S.J., & Ferlisi, M-C. (2001). The effect of differing scoring methods for the Tower of London Task on developmental patterns of performance. *The Clinical Neuropsychologist, 15,* 309-313.
93. Davies, P.L., Segalowitz, S.J., Dywan, J., & Pailing, P.E. (2001). Error-related negativity and positivity as they relate to other ERP indices of attentional control and stimulus processing. *Biological Psychology, 56,* 191-206.
94. McNeely, H.E., Dywan, J., & Segalowitz, S.J. (2001). ERP evidence for age differences in susceptibility to emotional distraction in a source monitoring task. *Brain and Cognition, 47,* 165-169 (short communication).
95. Segalowitz, S.J., Bernstein, D.M., & Lawson, S. (2001). P300 event-related potential decrements in well-functioning university students with mild head injury. *Brain and Cognition, 45,* 342-356.

96. Dywan, J., Segalowitz, S. J., Webster, L., Hendry, K., & Harding, J. (2001). ERP evidence for age-related differences in attentional allocation during a source monitoring task. *Developmental Neuropsychology, 19,* 99-120.
97. Baker, K., Segalowitz, S.J., & Ferlisi, M-C. (2001). The relation between performance on the Wisconsin Card Sorting Test and working memory, inhibition and complex attention in children and adults. *Brain and Cognition, 47,* 186-189 (short communication).
98. Chevalier, H., Metz-Lutz, M-N., & Segalowitz, S.J. (2000). Impulsivity and control of inhibition in benign focal childhood epilepsy. Brain and Cognition, 43, 86-90 (short communication).
99. Ross, P. & Segalowitz, S.J. (2000). An EEG coherence test of the frontal dorsal-versus-ventral hypothesis in n-back working memory. *Brain and Cognition, 43,* 375-379 (short communication).
100. Cudmore, L.J., & Segalowitz, S.J. (2000). Signal-to-noise ratio sensitivity in ERPs to stimulus and task complexity: different effects for early and late components. *Brain and Cognition, 43,* 130-134 (short communication).
101. Segalowitz, S.J. & Lane, K. (2000). Lexical access of function versus content words. *Brain and Language, 75,* 376-389.
102. Segalowitz, S.J. (2000). Predicting child language impairment from too many variables: Overinterpreting stepwise discriminant function analysis. *Brain and Language, 71,* 337-343.
103. Cudmore, L.J., Segalowitz, S.J., & Dywan, J. (2000). EEG Coherence Shows Altered Frontal-Parietal Communication in TBI During a Dual-Task. *Brain and Cognition, 44,* 86-90 (short communication).
104. Segalowitz, S.J. (2000). Dynamics and variability of brain activation: Searching for neural correlates of skill acquisition. *Brain and Cognition, 42,* 163-165.
105. Segalowitz, S.J. (1999). Why twin studies don't really tell us much about human heritability. *Behavioral and Brain Sciences, 22,* 904-905.
106. Segalowitz, N.S., Poulsen, C., & Segalowitz, S.J. (1999). RT coefficient of variation is differentially sensitive to executive control involvement in an attention switching task. *Brain and Cognition, 40,* 255-258.
107. Dywan, J., Segalowitz, S.J., & Webster, L. (1998). Source monitoring: ERP evidence for greater reactivity to non-target information in older adults. *Brain and Cognition, 36,* 390-430.
108. Segalowitz, S.J., Segalowitz, N.S., & Wood, A. (1998). Assessing the development of automaticity in second language word recognition. *Applied Psycholinguistics, 19,* 53-67.
109. Storrie-Baker, H.J., Segalowitz, S.J., Black, S.E., McLean, J.A.G., & Sullivan, N. (1997). Improvement of hemispatial neglect with cold-water calorics: An electrophysiological test of the arousal hypothesis of neglect in a case study. *Journal of the International Neuropsychological Society, 3,* 394-402.
110. Segalowitz, S.J., Van Roon, P., & Dywan, J. (1997). The ERP late positivity: A graduated response to stimulus repetition. *NeuroReport, 8,* 757-760.
111. Segalowitz, S.J., Dywan, J. & Unsal, A. (1997). Attentional factors in response time variability after traumatic brain injury: An ERP study. *Journal of the International Neuropsychological Society, 3,* 95-107.
112. Dywan, J. & Segalowitz, S.J. (1996). Self- and family ratings of adaptive behavior after traumatic brain injury: Psychometric scores and frontally generated ERPs. *Journal of Head Trauma Rehabilitation, 11,* 79-95.
113. Dywan, J., Segalowitz, S.J., DiMatteo, L., & Murphy, W. (1996). Late slow potential indices of face recognition in prosopagnosia. *Brain and Cognition, 30,* 408-411 (short communication).
114. Segalowitz, N.S., Watson, V., & Segalowitz, S.J. (1995). Vocabulary skill: Single case assessment of automaticity of word recognition in a timed lexical decision task. *Second Language Research, 11,* 121-136.

115. Segalowitz, S.J. & Lawson, S. (1995). Subtle symptoms associated with self-reported mild head injury. *Journal of Learning Disabilities, 28,* 309-319.
116. Unsal, A. & Segalowitz, S.J. (1995). Sources of P300 attenuation after head injury: Single trial amplitude, latency jitter, and EEG power. *Psychophysiology, 32(3),* 249-256.
117. Dywan, J., Segalowitz, S.J., & Williamson, L. (1994). Memory for source and frontal lobe function in older adults: Psychometric and electrophysiological (CNV) correlates. *Psychology and Aging, 9,* 568-577.
118. Segalowitz, S.J., Berge, B.E., Lawson, S., & Brown, D. (1994). If you can replicate the handedness-immune disorder effect, the more power to you. *Brain and Cognition, 26,* 217-227.
119. Weber, A.M., Segalowitz, S.J., Levine, M.L., & Cooper, D.C. (1994). Attentional capacity in children with learning disabilities. *Assessment in Rehab. and Exceptionality, 1,* 235-250.
120. Segalowitz, S.J. & Barnes, K.L. (1993). The reliability of ERP components in the auditory oddball paradigm. *Psychophysiology, 30*(5), 451-459.
121. Segalowitz, N.S. & Segalowitz, S.J. (1993). Skilled performance, practice and the differentiation of speed-up from automatization effects: Evidence from second language word recognition. *Applied Psycholinguistics, 14,* 369-385.
122. Benjafield, J. & Segalowitz, S.J. (1993). Left and right in Leonardo's drawings of faces. *Empirical Studies of the Arts, 11,* 25-32.
123. Dywan, J., Segalowitz, S.J., Henderson, L., & Jacoby, L. (1993). Memory for source in traumatic brain injury. *Brain and Cognition, 21,* 20-43.
124. Dywan, J., Segalowitz, S.J. & Unsal, A. (1992). Speed of information processing, health and cognitive performance in older adults. *Developmental Neuropsychology, 8,* 473-490.
125. Segalowitz, S.J. & Rose-Krasnor, L. (1992). The construct of brain maturation in theories of child development. *Brain and Cognition, 20,* 1-7.
126. Segalowitz, S.J., Wagner, W.J. & Menna, R. (1992). Lateral versus Frontal ERP Predictors of Reading Skill. *Brain and Cognition, 20,* 85-103.
127. Segalowitz, S.J., Unsal, A., & Dywan, J. (1992). Cleverness and wisdom in 12-year-olds: Electrophysiological evidence for late maturation of the frontal lobe. *Developmental Neuropsychology, 8,* 279-298.
128. Segalowitz, S., Unsal, A. & Dywan, J. (1992). CNV Evidence for the Distinctiveness of Frontal and Posterior Neural Processes in a Traumatic Brain Injured (TBI) population. *Journal of Clinical and Experimental Neuropsychology, 14,* 108-128.
129. Segalowitz, S.J. & Brown, D. (1991). Mild head injury as a source of developmental disabilities. *Journal of Learning Disabilities, 24,* 551-559.
130. Stewart, J.L. & Segalowitz, S.J. (1991). Differences in the given names of good and poor readers. *Canadian Journal of Education, 16,* 103-105.
131. Segalowitz, S.J. & Graves, R. (1990). Suitability of the IBM PC/AT/PS2 keyboard, mouse and game port as response devices in reaction time paradigms. *Behavior Research Methods, Instruments, & Computers, 22,* 283-289.
132. Weber, M.A. & Segalowitz, S.J. (1990). A measure of children's attentional capacity. *Developmental Neuropsychology, 6,* 13-23.
133. Segalowitz, S.J. & Cohen, H. (1989). Right hemisphere EEG sensitivity to speech. Brain and Language, 37, 220-231.
134. Segalowitz, S.J. (1988). IBM PC tachistoscope II: Assembly subroutines. *Behavior Research Methods, Instruments, & Computers, 20,* 432.
135. Archer, L. A., Campbell, D. & Segalowitz, S.J. (1988). A prospective study of language development and hand preference in 18 to 30 month olds. I. Hand preference. *Developmental Neuropsychology, 4,* 85-92.

136. Archer, L.A., Segalowitz, S.J. & Campbell, D. (1988). A prospective study of language development and hand preference in 18 to 30 month olds. II Relations between hand preference and language development. *Developmental Neuropsychology, 4,* 93-102.
137. Segalowitz, S.J. (1987). IBM PC Tachistoscope: Text stimuli. *Behavior Research Methods, Instruments, & Computers, 19,* 383-388.
138. Segalowitz, S.J. & Plantery, P. (1985). Music draws attention to the left and speech draws attention to the right. *Brain and Cognition 4,* 1-6.
139. Lederman, S.J., Jones, B. & Segalowitz, S.J. (1984). Lateral symmetry in the tactual perception of roughness. *Canadian Journal of Psychology, 38,* 599-609.
140. Chapman, J.S. & Segalowitz, S.J. (1983). Birth stress, lateral preference and cognitive functioning in prematurely born five year olds. *Nursing Papers (suppl.),* 373-386.
141. Segalowitz, S.J. & Chapman, J.S. (1980). Cerebral asymmetry for speech in neonates: a behavioral measure. *Brain and Language, 9,* 281-288.
142. Segalowitz, S.J. (1980). Piaget's Achilles' Heel: a safe soft spot? *Human Development, 23,* 137-140.
143. Bebout, L.J., Segalowitz, S.J. & White, G.J. (1980) Children's comprehension of instructions containing causal constructions with Because and So. *Child Development, 51,* 565-568.
144. Petrie, B.F. & Segalowitz, S.J. (1980) Use of fetal heart rate, other perinatal and maternal factors as predictors of sex. *Perceptual and Motor Skills, 50,* 871-874.
145. Segalowitz, S.J., Bebout, L.J. & Lederman, S.J. (1979) Lateralization for reading musical chords: disentangling symbolic, analytic and phonological aspects of reading. *Brain and Language, 8,* 315-323.
146. Segalowitz, S.J. & Stewart, C. (1979) Left and right lateralization for letter matching: strategy and sex differences. *Neuropsychologia, 17,* 521-525.

Chapters in books

1. Lackner, C.L. & Segalowitz, S.J. (2014). Culture and Context Modify Neural Correlates of Adolescent Risk-Taking Behavior. In J.A. Burack & L.A. Schmidt (eds). *Cultural and contextual perspectives on development at-risk and well-being*. Cambridge UP.
2. Segalowitz, S.J. (2007). The role of neuroscience in historical and contemporary theories of human development. In C. Coch, K.W. Fischer & G. Dawson (eds.) *Human behavior, learning, and the developing brain* (pp 3-29). New York: Guilford.
3. Segalowitz, S.J. (2007). Whose free will is it anyway? Or, The illusion of determinism. In H. Cohen & B. Stemmer (eds.), *Cognition and consciousness: Fragments of mind and brain* (pp. 163-170). Amsterdam: Elsevier.
4. Segalowitz, S.J. & Schmidt, L.A. (2007). Capturing the dynamic endophenotype: A developmental psychophysiological manifesto. In L.A. Schmidt & S.J. Segalowitz (eds.), *Developmental psychophysiology* (pp. 1-12). Cambridge: Cambridge University Press.
5. Masaki, H. & Segalowitz, S.J. (2004). Error negativity: A test of the response conflict versus error detection hypotheses, in M. Ullsperger & M. Falkenstein (eds), *Errors, Conflicts, and the Brain: Current Opinions on Performance Monitoring* (pp 76-83). Leipzig: Max Planck Institute for Cognition and Neurosciences.
6. Segalowitz, S.J., Davies, P.L., Santesso, D., Gavin, W.J., & Schmidt, L.A. (2004). The development of the error negativity in children and adolescents, in M. Ullsperger & M. Falkenstein (eds), *Errors, Conflicts, and the Brain: Current Opinions on Performance Monitoring* (pp 177-184). Leipzig: Max Planck Institute for Cognition and Neurosciences.
7. Dywan, J., Mathewson, K., & Segalowitz, S.J. (2004). "Error-related ERP Components and Source Monitoring in Older and Younger Adults", in M. Ullsperger & M. Falkenstein (eds), *Errors,*

Conflicts, and the Brain: Current Opinions on Performance Monitoring (pp 184-192). Leipzig: Max Planck Institute for Cognition and Neurosciences.

8. Segalowitz, S.J. & Schmidt, L.A. (2003). Developmental psychology and the neurosciences. In J. Valsiner & K.J. Connolly (Eds.), *Handbook of Developmental Psychology* (pp. 48-71). London: Sage
9. Segalowitz, S.J. & Hiscock, M. (2002). The neuropsychology of normal development: rapprochement between developmental neuroscience and psychology in a new Constructivism. In S.J. Segalowitz & I. Rapin (Eds.), *Child Neuropsychology,* vol 8 (pp. 7-28) in F. Boller & J. Grafman (series editors), Handbook of Neuropsychology. Amsterdam: Elsevier.
10. Rapin, I. & Segalowitz, S.J. (2002). On the nature and scope of child neuropsychology. In S.J. Segalowitz & I. Rapin (Eds.), *Child Neuropsychology,* vol 8 (pp. 1-6) in F. Boller & J. Grafman (series editors), Handbook of Neuropsychology. Amsterdam: Elsevier.
11. Segalowitz, S.J. & Hiscock, M. (1998, reprinted in Spanish). The emergence of a neuropsychology of normal development: Rapprochement between neuroscience and developmental psychology. In V. Feld & M.T. Rodriguez (ed.) *Neuropsicologia Infanti* (pp 71-115). Universidad Nacional de Lujan.
12. Segalowitz, S.J. & Chevalier, H. (1997). Event-Related Potential (ERP) Research in Neurolinguistics: I. Techniques and Investigations of Lexical Access. In B. Stemmer & H.A. Whitaker (Eds.), *Handbook of Neurolinguistics* (pp 95-109), Academic Press.
13. Segalowitz, S.J. & Chevalier, H. (1997). Event-Related Potential (ERP) Research in Neurolinguistics: II. Language processing and acquisition. In B. Stemmer & H.A. Whitaker (Eds.), *Handbook of Neurolinguistics* (pp 111-123), Academic Press.
14. Segalowitz, S.J., & Bernstein, D.M. (1997). Neural Networks and Neuroscience: What are connectionist simulations good for? In D. Johnson (ed.), *The future of the cognitive revolution* (pp 283-292). Oxford University Press.
15. Segalowitz, S.J. (1994). Los PRE y los progresos en neurolingüística. In F. Ostrosky-Solís & A. Ardila (Eds.), *Cerebro y lenguaje* (pp. 77-100). Mexico: Trillas. (translated and reprinted from "ERPs and research in neurolinguistics", 1989).
16. Segalowitz, S.J. (1994). Human behavior and brain development: An historical framework. In G. Dawson & K. Fischer (Eds.) *Human behavior and brain development* (pp 67-92). New York: Guilford Press.
17. Segalowitz, S.J., Velikonja, D., & Storrie-Baker, J. (1994). Attentional allocation and capacity in waking arousal. In J. Harsh & R.D. Ogilvie (Eds.), *Sleep onset mechanisms* (pp. 351-368). Washington, D.C.: APA.
18. Segalowitz, S.J. (1993). Les potentiels évoqués et les développements en neurolinguistique. In H. Cohen (Ed.), *Neuropsychologie expérimentale et clinique: processus spécialization et dysfunctionnement* (pp. 93-119). Montréal: Gaetan Morin. (translated and reprinted from "ERPs and research in neurolinguistics", 1989).
19. Rapin, I. & Segalowitz, S. (1992). Child neuropsychology: nature and scope. In I. Rapin & S.J. Segalowitz (Eds.) *Child neuropsychology.* Vol 6 (pp. 3-7) in F. Boller & J. Grafman (series editors) Handbook of neuropsychology. Amsterdam: Elsevier.
20. Segalowitz, S.J. & Hiscock, M. (1992). The emergence of a neuropsychology of normal development: Rapprochement between neuroscience and developmental psychology. In I. Rapin & S.J. Segalowitz (Eds.) *Child neuropsychology.* Vol 6 (pp. 45-71) in F. Boller & J. Grafman (series editors) *Handbook of neuropsychology*. Amsterdam: Elsevier.
21. Segalowitz, S.J. & Berge, B.E. (1995). Functional asymmetries in infancy and early childhood: A review of electrophysiological studies and their implications. In R.J. Davidson & K. Hugdahl (Eds.), *Brain asymmetry* (pp 579-616). Cambridge, MA: MIT.
22. Segalowitz, S.J. (1995). Brain growth and the child's mental development. In K. Covell (Ed), *Readings in child development.* Toronto: Nelson.

23. Segalowitz, S.J., Ogilvie, R.D & Simons, I.A. (1990). An ERP State Measure of Arousal Based on Behavioral Criteria. In J. Horne (Ed.), *Sleep '90: Selected Proceedings of the European Sleep Research Society* (pp. 23-25). Boston: Birkauer.
24. Segalowitz, S.J. (1989). ERPs and research in neurolinguistics. In A. Ardila & F. Ostrowsky (Eds.) Brain organization of language and cognitive processes. New York: Plenum Press (pp. 61-82).
25. Segalowitz, S.J. (1987). Individual differences in hemispheric specialization: Sources and measurement. In A. Glass (Ed.) *Individual differences in hemispheric specialization* (pp. 17-29). New York: Plenum Press.
26. Gibson, C. & Segalowitz, S.J. (1986). The impact of visual-spatial information on the development of reading proficiency in deaf children. In P. Perron, J.-L. Nespoulous & A.-R. Lecours (eds.) *Biological foundations of gestures: motor and semiotic aspects*. Hillsdale, NJ: Lawrence Erlbaum.
27. Segalowitz, S.J. (1986). Some notes on the implications of lateralization for developmental psychology. In P. Perron, J.-L. Nespoulous & A.-R. Lecours (eds.) *Biological foundations of gestures: motor and semiotic aspects.* Hillsdale, NJ: Lawrence Erlbaum.
28. Segalowitz, S.J. (1986). Validity and reliability of noninvasive measures of brain lateralization. In J. Obrzut & D. Hines (Eds.) *Child Neuropsychology: Empirical Issues* (pp. 191-208). New York: Academic Press.
29. Dywan, J. & Segalowitz, S.J. (1986). The role of the case study in neuropsychological research. In J. Valsiner (Ed.) *The role of the individual subject in scientific psychology.* New York: Plenum.
30. Segalowitz, S.J. & Bryden, M.P. (1983) Individual differences in hemispheric representation of language. In Segalowitz (ed.) *Language functions and brain organization* (pp. 341-372). New York: Academic Press.
31. Segalowitz, S.J. (1983). Cerebral asymmetries for speech in infancy. In Segalowitz (ed.) *Language functions and brain organization.* New York: Academic Press.
32. Segalowitz, S.J. (1983). On the requirements of a developmental theory of lateralization. In Segalowitz (ed.) *Language functions and brain organization.* New York: Academic Press.
33. Segalowitz, S.J. (1983). How many lateralities are there? In Young, Segalowitz, Corter & Trehub (eds.) *Manual specialization and the developing brain.* New York: Academic Press.
34. Young, G., Segalowitz, S.J., Misek, P., Alp, I. & Boulet, R. (1983). Is early reaching left-handed? A review of manual specialization research. In Young, Segalowitz, Corter & Trehub (eds.) *Manual specialization and the developing brain.* New York: Academic Press, 1983.
35. Young, G., Corter, C.M., Segalowitz, S.J., & Trehub, S.E. (1983). Manual specialization and the developing brain: an overview. In Young, Segalowitz, Corter & Trehub (eds.) *Manual specialization and the developing brain.* New York: Academic Press.
36. Gruber, F.A. & Segalowitz, S.J. (1977) Some issues and methods in the neuropsychology of language. In S. Segalowitz & F. Gruber (Eds.) *Language development and neurological theory.* New York: Academic Press.
37. Segalowitz, S.J. (1977) (i) What is it that is lateralized? (ii) Why is language lateralized to the left? In S. Segalowitz & F. Gruber (Eds.) *Language development and neurological theory*. New York: Academic Press.

Invited reports (nonrefereed) and book reviews

1. Jetha, M.K. & Segalowitz, S.J. (Oct 18, 2016). "The Impact of Stress during Middle Childhood". Report to the Ontario Ministry of Child and Youth Services. (65 pages).
2. Jetha, M.K. & Segalowitz, S.J. (2011). "Brain development from pre-adolescence to young adulthood and the implications for behaviour". Report to the Ontario Ministry of Child and Youth Services. (100 pages). Revised and Updated, June 2016 (135 pages).
3. Segalowitz, S.J. (1997). Parallels between cognitive development and brain growth. In F. Capra (ed.) *Computers and cognitive development.* Berkeley, CA: Center for Ecoliteracy.

4. Segalowitz, S.J. (1993). The brain controlling itself: Attentional control and the development of thinking. *Television and the Preparation of the Mind for Learning* (pp. 111-119). Washington, D.C.: U.S. Dept of Health and Human Services, Administration for Children and Families.
5. Segalowitz, S.J. (1991). An introduction to neurometrics. Review of E.R. John et al *Neurometric evaluation of brain functions*. Contemporary Psychology, 36, 230-231.
6. Segalowitz, S.J. (1990). The musical brain. The Clarinet, 17(4), 32-35.
7. Segalowitz, S.J. & Benjafield, J. (1987). Review of SIGSTAT for the IBM PC. *Canadian Journal of Mass Spectroscopy* 32, 40A.
8. Segalowitz, S.J. (1982). Return from dichotomania. *Contemporary Psychology, 27,* 372-373.
9. Segalowitz,S.J. (1980). Review of The Integrated Mind. *Brain and Language*, 11, 225-228.

ABSTRACTS (refereed)

1. Viczko1, Jeremy, Segalowitz, Sidney J., Smart, Colette (2018). On the nature of wakefulness: examining the relationship between self-report and electrophysiological markers of arousal in long-term Vajrayana Buddhist meditators. *Psychophysiology, 55,* S36.
2. Smart, Colette & Segalowitz, Sidney J. (2018). Learning to put the brakes on: attention control differences in long-term practitioners of somatic meditation. *Psychophysiology, 55,* S38.
3. Coy, A., Tekok-Kilic, A., Libben, G., & Segalowitz, S.J. (2018). When is a threat less of a threat? ERP support for differentiating threat levels in the IAPS pictures. *Psychophysiology, 55,* S43.
4. Chattha, O., Libben, G., & Segalowitz, S.J. (2018). An ERP investigation of present/past tense verb production and morphological regularity. *Psychophysiology, 55,* S85.
5. Segalowitz, S.J., Samar, V.J., Desjardins, J.A., & Weissflog, M. (2018). Childhood socioeconomic status affects adult medial frontal negativity (MFN) demonstrated by independent component analysis (ICA). *Psychophysiology, 55,* S88.
6. Weissflog, M., Segalowitz, S.J., & Dywan, J. (2017). Factor 1 and Factor 2 Psychopathic Trait Severity Dissociated in Early Visual ERPs. *Psychophysiology, 54,* S60.
7. Balakumar, S., Murphy, T. & Segalowitz, S.J. (2017). The Effect of Sleep Deprivation on Inter-Trial Coherence of the P100, ERN and CRN. *Psychophysiology, 54,* S104.
8. Lackner, C., Santesso, D., Dywan, J., O'Leary, D., Wade, T. & Segalowitz, S.J. (2017). Adverse Childhood Experiences are Associated with the Magnitude of The ERN Difference. *Psychophysiology, 54,* S124.
9. Segalowitz, S.J., Callegari, J., Chattha, O. & Smith, B. (2017). Is the Early Visual ERP Sensitive to Low-Level Visual Stimulus Properties? A Test of Luminance vs. Cognitive Factors. *Psychophysiology, 54,* S133.
10. Matsuhashi, T., Segalowitz, S.J., Nagano, Y. & Masaki, H. (2016). Error-related negativity predicts improvement of a sequence motor learning. *Psychophysiology, 53.*
11. Gogo, Cody E., van Noordt, Stefon J., Desjardins, James A., Segalowitz, Sidney J. & Tekok-Kilic, Ayda (2015). Cognitive control is in the eye of the beholder: Spectral EEG analysis of a cued pro-saccade/anti-saccade task. *Psychophysiology, 52.*
12. Gavin, William J., Taylor, Brittany K., Segalowitz, Sidney J. & Davies, Patricia L. (2014). A trial-by-trial distribution-based, outlier-rejection approach to creating averaged ERPs for contingent negative variation paradigms. *Psychophysiology, 51,* S17.
13. Willner, Cynthia J., Jetha, Michelle K., Segalowitz, Sidney J. & Gatzke-Kopp, Lisa M. (2014). Emotional face processing biases and children's social withdrawal and externalizing behaviors in school. *Psychophysiology, 51,* S19.
14. Sternin, Avital, Segalowitz, Sidney J., Lewis, Terri L., Dywan, Jane & Maurer, Daphne (2014). Electrophysiological evidence of altered visual processing in adults with blocked pattern vision during infancy. *Psychophysiology, 51,* S34.
15. Davis, Charles P., Libben, Gary & Segalowitz, Sidney J. (2014). Compounding matters: the P1 as an

index of semantic access to compound words. *Psychophysiology, 51*, S34.
16. Dzyundzyak, Angela, Santesso, Diane L. & Segalowitz, Sidney J. (2014). Problem gambling and the FRN. *Psychophysiology, 51*, S34.
17. Capuana, Lesley J., Dywan, Jane, Gibson, Raechelle M. & Segalowitz, Sidney J. (2014). Cardiac autonomic regulation and cognitive control in older and younger adults. *Psychophysiology, 51*, S34.
18. Lackner, C.L., Milligan, K., Wilkins, L., Spiroiu, F., Badali, P., Schmidt, L.A. & Segalowitz, S.J. (2014). Mindfulness martial arts training maintains intertrial coherence indices of selective attention in adolescents with ADHD and/or learning disabilities over repeated task administration. *Psychophysiology, 51*, S35.
19. Milligan, K., Wilkins, L., Sibalis, A., Spiroiu, F., Badali, P., Schmidt, L., & Segalowitz, S.J. (2014). Mindfulness treatment for boys with ADHD improves ERP indices of attention. *Psychophysiology, 51*, S34.
20. Campopiano, A. & Segalowitz, S.J. (2013). Understanding the Regularization Parameter in sLoreta: A Simulation Study. *Psychophysiology, 50*, S88.
21. Mulligan, B. P., Smart, C. M., MacDonald, S. W. S., & Segalowitz, S. J. (2013). Utility of neural and behavioral markers of intra-individual variability in the discrimination of healthy older adults from those with subjective cognitive impairment. Journal of the International Neuropsychological Society, 19 (Suppl. 1), 101.
22. Smart, C. M., Segalowitz, S. J., Mulligan, B.P., & MacDonald, S. W. S. (2013). Mindfulness Training Increases Error Processing in Older Adults With and Without Subjective Cognitive Impairment. Journal of the International Neuropsychological Society, 19 (Suppl. 1), 74.
23. Dzyundzyak, A., Santesso, D.L., & Segalowitz. (2013) Influences of Expectation and Sense of Control on the Feedback-Related Negativity. *Psychophysiology, 50*, S87-88.
24. Segalowitz, S.J., Marshall, W.J., & Lackner, C.L. (2012). Phase Shifting Granger Causality: A measure of directed coherence (symposium talk). *Psychophysiology, 49*, S8.
25. Jetha, M.K., Gatzke-Kopp, L.M., & Segalowitz, S.J. (2012). The prefrontal cortex is a moving target in early childhood: Implications for ongoing neural maturation for ERP research in longitudinal studies (symposium talk). *Psychophysiology, 49*, S16.
26. Zheng, X. & Segalowitz, S.J. (2012). Putting a face in its place: in- and out-group membership alters the N170 response. *Psychophysiology, 49*, S54.
27. Weissflog, M.W., Munro, G.E., Wirz, L.M., Segalowitz, S.J., & Dywan, J. (2012). Callous affect and the early visual processing of fearful faces. *Psychophysiology, 49*, S54.
28. van Noordt, S.J.R., Desjardins, J.A. , & Segalowitz, S.J. (2012). It's time for a change: Examining anterior cingulate cortex activation to cues signaling switches in response context. *Psychophysiology, 49*, S54.
29. Marshall, W.J., Lackner, C.L., Marriott, P., Santesso, D.L., & Segalowitz, S.J. (2012). Using phase shifting and granger causality to measure effective connectivity in EEG recordings. *Psychophysiology, 49*, S55.
30. Jetha, M.K., Gatzke-Kopp, L.M, & Segalowitz, S.J. (2012) The stability of visual ERP components in young children. *Psychophysiology, 49*, S55.
31. Lackner, C. L., Marshall, W., Santesso, D. L., & Segalowitz, S. J. (2011). Phase reset variables are differentially associated with anxiety and aggression in a typically developing adolescent sample. *Psychophysiology, 48*, S46.
32. Zheng, X., & Segalowitz, S. J. (2011). The N170 face inversion effect is both face-specific and domain-general: separate amplitude and latency effects. *Psychophysiology, 48*, S46.
33. Desjardins, J. A. & Segalowitz, S. J. (2011). Time course and robustness of the N170 face effect at the scalp and in independent components: separating the N170 and P100 face effects. *Psychophysiology, 48*, S46.

34. van Noordt, S. J.R. & Segalowitz, S. J. (2011). Error-related brain potentials are associated with transient increases in spectral power and phase alignment of on-going EEG oscillations *Psychophysiology, 48*, S98.
35. Dzyundzyak, A., MacLean, M. H., & Segalowitz, S. J. (2011). Influence of reward information on anticipatory processes: CNV and alpha event-related desynchrony study. *Psychophysiology, 48*, S97.
36. Capuana, L. J., Gibson, R.M., Tays, W. J., Segalowitz, S. J., & Dywan, J. (2011). Cortical and cardiac associations with performance monitoring and accuracy of response. *Psychophysiology, 48*, S97.
37. Weissflog, M. J., Dywan, J., & Segalowitz, S. J. (2011). Manipulation of spatial attention while viewing emotional faces delays electrophysiological indices of early visual processing. *Psychophysiology, 48*, S98.
38. Santesso, D. L., Segalowitz, S. J., Dywan, J., Wade, T. L., & Pizzagalli, D. A. (2011). Enhanced ACC responses to negative feedback are related to depressive symptoms in adults and adolescents. *Psychophysiology, 48*, S13.
39. Segalowitz, S. J., Santesso, D. L., & Lackner, C. L. (2011). Individual differences in the role of the medial frontal cortex in adolescent self-regulation. *Psychophysiology, 48*, S17.
40. Santesso, D. L., Dywan, J., Wade, T. J., & Segalowitz, S. J. (2010). Enhanced feedback-related ACC activity in relation to negative emotionality during adolescence. *Psychophysiology, 47*, S23.
41. Lackner, C. L., Santesso, D. L., Dywan, J., Wade, T. J., & Segalowitz, S. J. (2010). Medial prefrontal NoGo activation during an emotion Go/NoGo Task is related to worrying in adolescence. *Psychophysiology, 47*, S23.
42. Weissflog, M. J., van Noordt, S. J. R., Choma, B. L., Dywan, J., & Segalowitz, S. J. (2010). Machiavellianism, sociopolitical ideology, and the ERN. *Psychophysiology, 47*, S24.
43. Tays, W. J., Witherspoon, R. L., Capuana, L. J., Segalowitz, S. J., & Dywan, J. (2010). Resolving interference one component at a time: Dissociation between N2 and N450 in a modified Stroop paradigm. *Psychophysiology, 47*, S24.
44. Capuana, L. J., Elmers, J. L., Tays, W. J., Segalowitz, S. J., & Dywan, J. (2010). Autonomic correlations of response control in the context of memory-based interference and reward contingencies. *Psychophysiology, 47*, S24.
45. Jetha, M.K., Segalowitz, S.J., Gatzke-Kopp, Lisa & Ly, D. (2010). The Nogo-N2 effect predicts externalizing behavior in 5-6 year old children at risk for reduced inhibitory control. *Psychophysiology, 47*, S13
46. Dzyundzyak, A., & Segalowitz, S.J. (2010). Anticipating wins and losses: CNVs appear to be similar but reflect different traits. *Psychophysiology, 47*, S23.
47. Desjardins, J., Lackner, C.L., & Segalowitz, S.J. (2010). Perfecting the P50 gating paradigm: The benefits of using ICA and bootstrapping techniques. *Psychophysiology, 47*, S24.
48. Desjardins, J. & Segalowitz, S. J. (2009). Deconstructing the P1 and N170 Face-Effect Using Independent Component Analysis. *Psychophysiology, 46,* S24.
49. Zheng, X., Vida, M.D., Mondloch, C.J. & Segalowitz, S.J. (2009). The N170 ERP Relates to Both Featural and Configural Information Important for Face Processing. *Psychophysiology, 46,* S24.
50. Santesso, D.L., Dzyundzyak, A. & Segalowitz, S.J. (2009). The Relation of Punishment Sensitivity to ACC Activation in an ERP Gambling Paradigm is Greater in Younger Adolescents. *Psychophysiology, 46,* S27.
51. Segalowitz, S.J. & Santesso, D.L. (2009). ERN, FRN, and Stressors: ACC Activation Patterns as Related to the Comfort of Losing. *Psychophysiology, 46,* S16.
52. Santesso, D.L., Drmic, I.E., Jetha, M.K., Mathewson, K.J., Bryson, S.E., Goldberg, J.O., Hall, G.B., Segalowitz, S.J., & Schmidt, L.A. (2009). An ERP Source Localization Study of Performance Monitoring in Autism Spectrum Disorder. *Psychophysiology, 46,* S34.
53. Mathewson, K.J., Drmic, I.E., Jetha, M.K., Santesso, D.L., Bryson, S.E., Goldberg, J.O., Hall, G.B., Segalowitz, S.J. & Schmidt, L.A. (2009). Cardiac Responses to Affective Auditory and Visual Stimuli in Adults with Autism Spectrum Disorder (ASD). *Psychophysiology, 46,* S34.

54. Desjardins, J. & Segalowitz, S.J. (2009). EEG Dynamics Underlying the P1 and N170 Face Effect. *Psychophysiology, 46,* S96.
55. Capuana, L.J., Dywan, J., Tays, W.J., & Segalowitz, S.J. (2009). Cardiac Autonomic Function and Response Control Deficits in Older Adults. *Psychophysiology, 46,* S104.
56. Zheng, X., Vida, M.D., Mondloch, C.J., & Segalowitz, S.J. (2009). N170 is Sensitive to Several Factors Important for Differentiating Individual Faces. *Psychophysiology, 46,* S104.
57. Weissflog, Meghan J., Segalowitz, Sidney J., Munro, Gillian E. S. & Dywan, Jane (2009). ERP Correlates of Emotional Face Processing in Psychopathy. *Psychophysiology, 46,* S105.
58. Dzyundzyak, A., Santesso, D.L. & Segalowitz, S.J. (2009). Processing Reward Magnitude and Valence: Dissociations and Individual Differences in the FRB and P300. *Psychophysiology, 46,* S105.
59. Tays, William J., Dywan, Jane & Segalowitz, Sidney J. (2009). Identifying the Functional Role of the Interference-Elicited Medial Frontal Negativity. *Psychophysiology, 46,* S105.
60. Jetha, M.K., Segalowitz, S.J. & Gatzke-Kopp, L. (2009). Frontal EEG Asymmetry in Highly Aggressive 56 Year Old Girls. *Psychophysiology, 46,* S105.
61. Zheng, X. & Segalowitz, S.J. (2008). ERP evidence of early semantic access with a randomized semantic priming paradigm. *Psychophysiology, 45,* S21.
62. Mathewson, K.J., Dywan J., Tays, W.J. & Segalowitz, S.J. (2008). Aging decline in cardiac vagal regulation: Implications for complex cognition? *Psychophysiology, 45,* S21.
63. Munro, G.E.S., Dywan, J., Lim, W., & Segalowitz, S.J. (2008). Subclinical levels of psychopathy associated with an affect-specific processing deficit. *Psychophysiology, 45,* S21.
64. Masaki, H., Murphy, T.I., Desjardins, J., & Segalowitz, S.J. (2008). A test of the response-onflict hypothesis in the production of error-related negativity. *Psychophysiology, 45,* S21.
65. Capuana, L., Tays, W.J., Mathewson, K., Segalowitz, S.J., & Dywan, J. (2007). Respiratory Sinus Arrhythmia (RSA) and the N450 in Younger and Older Adults. *Psychophysiology, 44,* S52.
66. Mathewson,, K.J. Dywan, J., Tays, W.J., Snyder, P.J. & Segalowitz, S.J. (2007) Heart Rate Variability and Maze-Learning Performance in Older and Younger Adults. *Psychophysiology, 44,* S52.
67. Munro, G.E.S., Dywan, J., & Segalowitz, S.J. (2007). Subclinical Psychopathy (SRP-III) and ERP Responses to a Visual Oddball Task. *Psychophysiology, 44,* S52.
68. Tays, W.J., Dywan, J. Capuana, L., & Segalowitz, S.J. (2007). General Proactive Interference and the N450 Response. *Psychophysiology, 44,* S52.
69. Zheng, X, & Segalowitz, SJ. (2007) A High-Density ERP Study on Word Frequency and Neighborhood: Lexical Status Effects in the P100. *Psychophysiology, 44,* S53.
70. Gavin, W.J., Segalowitz, S.J., & Davies, P.L. (2007). ERP Measures of Efficiency During Error Processing in Children. *Psychophysiology, 44,* S53.
71. Segalowitz, S.J. & Dipoce, M. (2007). Eliciting Early VEP Components: A Comparison of Paradigms. *Psychophysiology, 44,* S53.
72. Munro, G.E., Dywan, J., Segalowitz, S.J., Harris, G.T., McKee, S., and Unsal, A. (2006). Frontal N2, Response Inhibition and Psychopathy. *Psychophysiology, 43,* S70.
73. Murphy, T.I., Coons, M.J., and Segalowitz, S.J. (2006). You May Respond when Sleepy but your Frontal Lobe may not: The Effect of Sleep Deprivation and Incentive on the Contingent Negative Variation. *Psychophysiology, 43,* S70.
74. Santesso, D.L. and Segalowitz, S.J. (2006). Poor Error Monitoring Response is Related to Lack of Empathy. *Psychophysiology, 43,* S86.
75. Segalowitz, S.J. and Santesso, D.L. (2006). A Lack of Inhibitory Components in the Nogo N2 and the ERN. *Psychophysiology, 43,* S89.
76. Martel, G., Stemmer, B., and Segalowitz, S.J. (2006). ERP Responses to French Phrase Structure Violations. *Psychophysiology, 43,* S62.

77. Sanichara, S., Segalowitz, S.J., Davies, P.L., Gavin, W.J., & Dywan, J. (2005). EEG gamma responses in the auditory modality: investigating stimulus, topographical and developmental effects. *Psychophysiology, 42,* S110.
78. Stemmer, B., Segalowitz, S.J., Dywan, J., Panisset, M. (2005). Dopaminergic medication and the ERN in Parkinson's Disease. *Psychophysiology, 42,* S119.
79. Munro, G.E., Dywan, J., Harris, G.T., Mckee, S., Unsal, A., Segalowitz, S.J. (2005). Source modeling of the error-related negativity in criminal psychopaths. *Psychophysiology, 42,* S93.
80. Murphy, T.I., Pine, M., Segalowitz, S.J. (2005). P300 latency is dangerously lengthened for dual-task when sleepy. *Psychophysiology, 42,* S94.
81. Martel, G., Stemmer, B., Segalowitz, S.J. (2005). Processing French visual phrase structure violations: an ERP study on the ELAN. *Psychophysiology, 42,* S84.
82. Tays, W.J., Dywan, J., Mathewson, K.J., Segalowitz, S.J. (2005). Age-related change in ERPs associated with context-based vs response-based interference. *Psychophysiology, 42,* S121.
83. Santesso, D.L., Segalowitz, S.J., Dyke, S.I. (2005). "Sensation seeking and reward sensitivity are related to poor performance monitoring (ERN) and decision-making (IGT). *Psychophysiology, 42,* S111.
84. Davies, P.L., Segalowitz, S.J., Gavin, W.J. (2005). Relationship of error-related negativity to cognitive skills from 7 to 18 years. *Psychophysiology, 42,* S48.
85. Masaki, H., Murphy, T.I., Desjardins, J., Segalowitz, S.J. (2005). ERN characteristics on partial versus complete errors. *Psychophysiology, 42,* S85.
86. Segalowitz, S.J., Santesso, D., Dywan, J. (2005). The ERN and the emotional modulation to events. *Psychophysiology, 42,* S19.
87. Mathewson, K.J., Dywan, J., Tays, W. J., Segalowitz, S.J., & Snyder, P.J. (2005). ERPs to error-related feedback during a spatial memory task in older and younger adults. *Psychophysiology, 42,* S86.
88. Schmidt, L.A., Santesso, D.L. & Segalowitz, S.J. (in press). Psychophysiological correlates of atypical social behavior in children. *Brain and Cognition.*
89. Mozolic, B.E., Davies, P.L., Segalowitz, S.J., & Gavin, W.J. (2004). Contingent negative variation and attention in children. *Psychophysiology, 41*, S30.
90. Folino, A., Desjardins, J., & Segalowitz, S.J. (2004). The attentional model of induced EEG gamma: A manipulation comparison with P300. *Psychophysiology, 41,* S29.
91. Santesso, D.L., Segalowitz, S.J. & Dywan, J. (2004). Stability and reliability of the error-related negativity (ERN). *Psychophysiology, 41,* S29.
92. Munro, G.E., Dywan, J., Harris, G.T., McKee, S., Unsal, A., & Segalowitz, S.J. (2004). Emotional specificity of ERN and error monitoring deficits associated with psychopathy. *Psychophysiology, 41,* S29.
93. Anum, A., Segalowitz, S.J.& Dywan, J. (2003). Information Processing Consistency in Event-Related Potentials (ERP): Effects of Aging and Attention Demands. *Psychophysiology, 40,* S23.
94. Masaki, H., Desjardins, J.A., Murphy, T.I., & Segalowitz, S.J. (2003). A Test of Functional Origins of the Error-Related Negativity. *Psychophysiology, 40,* S57.
95. Mathewson, K., Dywan, J. Segalowitz, S.J. (2003). Error-monitoring, Aging and Heart Rate Variability. *Psychophysiology, 40,* S58.
96. Murphy, T.I., Richard, M., Masaki, H., & Segalowitz, S.J. (2003). Whoops, DARN, who cares: The Effect of Sleepiness on the Error-Related Negativity. *Psychophysiology, 40,* S62.
97. Tays, W.J., Folino, A., Dywan, J. & Segalowitz, S.J. (2003). EEG Gamma Relates to Clarity of Thinking and Source Monitoring ERPs after Mild Head Injury. *Psychophysiology, 40,* S84.
98. Santesso, D., Segalowitz, S.J., & Schmidt, L.A. (2003). Diminished Error-Related Negativity in 10-Year-Old Children with Poor Social Behavior. *Psychophysiology, 40,* S75
99. Pailing, P.E., & Segalowitz, S.J. (2003). The Role of Uncertainty in Error Monitoring: An ERP Investigation. *Psychophysiology, 40,* S65.

100. Segalowitz, S.J., Folino, A., Dywan, J. (2003). Reductions in gamma band EEG and cognitive performance associated with post-concussive symptoms. *Acta Neurobiologiae Experimentalis, 63(3),* 249.
101. Dywan, J., Tays, W.J. & Segalowitz, S.J.(2003). ERP indices of source memory deficits after mild head injury. *Acta Neurobiologiae Experimentalis, 63(3),* 285.
102. Pailing, P.E. & Segalowitz, S.J. (2002). Motivation and personality influences on the error-related negativity (Ne/ERN). *Psychophysiology, 39,* S63.
103. Mathewson, K., Dywan, J. & Segalowitz, S.J. (2002). The effect of task complexity and aging on the ERN. *Psychophysiology, 39,* S56.
104. Davies, P.L. & Segalowitz, S.J. (2002). Error-related negativity (ERN/Ne) in children and adolescents. *Psychophysiology, 39,* S30.
105. Davies, P.L. Gavin, W.J. & Segalowitz, S.J. (2002). Development of the contingent negative variation (CNV) in children and adolescents. *Psychophysiology, 39,* S30.
106. James, T., Dywan, J. & Segalowitz, S.J. (2002). ERPs to emotional words in a study on source monitoring and aging. *Journal of the International Neuropsychological Society, 8(2),* 273.
107. Coons, M., Murphy, T.I., & Segalowitz, S.J. (2002) The effect of sleepiness on attentional control: An ERP study. *Journal of the International Neuropsychological Society, 8(2),* 273.
108. Segalowitz, S.J. & Desjardins, J. (2001). Gamma band EEG and the P300. *Psychophysiology, 38,* S88.
109. Segalowitz, S.J. & Davies, P.L. (2001). Separating vigilance and motor preparation in the CNV. *Psychophysiology, 38,* S87.
110. Mathewson, K., Dywan, J., Segalowitz, S.J., Arsenault, A., Veenhof, W. & Parakh, R. (2001). Heart rate variability, event-related potentials and attentional control in older and younger adults. *Psychophysiology, 38,* S65.
111. Pailing, P., Segalowitz, S.J. & Dywan, J. (2000). The Relationship between Inhibition and Impulsivity: A Replication and Extension of Visser's Work. *Brain and Cognition, 43,* 12.
112. Baker, K., Segalowitz, S.J., & Ferlisi (2000). The Tower of London: Different scoring methods lead to different developmental hypotheses. *Brain and Cognition, 43,* 6.
113. McNeely, H.E., Dywan, J., & Segalowitz, S.J. (2000). ERPs in the context of familiarity, stimulus categorization and emotion: When familiarity meets its match. *Psychophysiology, 37,* S70.
114. Stemmer, B., Segalowitz, S.J., Witzke, W., Lacher, S., & Schoenle, P.W. (2000). Do patients with damage to the anterior cingulate and adjacent regions produce an error-related negativity (ERN)? *Psychophysiology, 37,* S95.
115. Dywan, J.D., Segalowitz, S.J. & Arsenault, A. (2000). Aging and the effect of attention allocation on ERP amplitude during source monitoring. *Psychophysiology, 37,* S37.
116. Segalowitz, S.J., Wintink, A.J., & Cudmore, L.J. (2000). P300 anterior-posterior slope: Effects of task complexity and habituation. *Psychophysiology, 37,* S89.
117. Murphy, T.I., & Segalowitz S.J. (2000). Eliminating the P3 rebound in a novel novelty paradigm. *Psychophysiology, 37,* S73.
118. Veenhof, W., Dywan, J., & Segalowitz, S.J. (2000). Effects of recollection and perceptual fluency on the ERP late positivity. *Psychophysiology, 37,* S101.
119. Pailing, P.E., Segalowitz, S.J., & Davies, P.L.(2000). Speed of responding and the likelihood of error-like activity in correct trial ERPs. *Psychophysiology, 37,* S76.
120. Davies, P.L., & Segalowitz, S.J.(2000). Motivational effect on CNV. *Psychophysiology, 37,* S34.
121. Segalowitz, S.J., Davies, P.L., Pailing, P.E., & Stemmer, B. (2000). Error-related responses: Error detection or beyond? *Psychophysiology, 37,* S10.
122. McNeely, H. E., Dywan, J., & Segalowitz, S. J. (1999). False recognition, emotion, and the ERP. *Psycholophysiology, 36,* S79.
123. Pailing, P. E., Davies, P. L., Segalowitz, S. J., & Dywan, J. (1999). Error-related negativity (ERN) and impulsive responding. *Psycholophysiology, 36,* S88.

124. Davies, P. L., Pailing, P. E., Segalowitz, S. J., & Dywan, J. (1999). Comparison of two prefrontally generated ERPs: Contingent negative variation (CNV) and error-related negativity (ERN). *Psycholophysiology, 36,* S45.
125. Cudmore, L.J., Segalowitz, S.J., & Dywan, J. (1999). Dorsal frontal-parietal EEG coherence differentiates divided from focussed attention. *Journal of Cognitive Neuroscience (Suppl), 11,* 68.
126. Ross, P. & Segalowitz, S.J. (1999). A P300 test of the frontal dorsal versus ventral hypothesis in n-back working memory. *Journal of Cognitive Neuroscience (Suppl), 11,* 34.
127. Segalowitz, N.S., Poulsen, C., & Segalowitz, S.J. RT coefficient of variation is differentially sensitive to executive control involvement in an attention switching task. *Brain and Cognition, 40,* 255, 1999.
128. Davies, P.L. Segalowitz, S.J., Chevalier, H., Bernstein, D.L., & Lawson, S. (1998). How the presence of novel stimuli affects ERPs to targets. *Society for Neuroscience Abstracts, 24,* 2119.
129. McNeely, H.E., Dywan, J., & Segalowitz, S.J. (1998). ERPs, emotion, and the illusion of familiarity. *Psychophysiology, 35,* S57.
130. Veenhof, W., Dywan, J., & Segalowitz, S.J. (1998). ERP and Vagal tone indices of source memory and inhibitory control in aging. *Psychophysiology, 35,* S84.
131. Hopkins, M.J., Dywan, J., & Segalowitz, S.J. (1998). Electrodermal activity to facial expression in TBI: Support for somatic marker theory. *Journal of the Int. Neuropsychological Society, 4,* 67.
132. Segalowitz, S.J., Chevalier, H., Rose-Krasnor, L., & Nadon, R. (1998). ERP correlates of neuroticism, extraversion and shyness. *Journal of the Int. Neuropsychological Society, 4,* 6.
133. Chevalier, H., Segalowitz, S., Dywan, J., Rose-Krasnor, L., & Nadon, R. (1997). ERP reactivity to socially-relevant stimuli: A test of Gray's model. *Psychophysiology.*
134. Veenhof, W., Hopkins, M., Chevalier, H., Pailing, P., Ogilvie, R.D., & Segalowitz, S.J. (1997). Vagal tone: Changes across sleep stage and time of night. *Sleep Research.*
135. Segalowitz, S.J. & Theal, G. (1996). Stimulus discriminability and dual task affect the N2 and P3 separately: An auditory oddball additive factors ERP study. *Psychophysiology, 33,* S76.
136. Chambers, E.A., Ostaniewicz, A.J., Segalowitz, S.J., Ogilvie, R.D., & Mericer, S. (1996). Information processing during slow wave sleep. *Psychophysiology, 33,* S28.
137. Ostaniewicz, A., Kacsmar, E., Ogilvie, R.D., & Segalowitz, S.J. (1996). Distribution of electrodermal activity in slow wave sleep. *Sleep Research, 25,* 49.
138. Velikonja, D. & Segalowitz, S.J. (1996). Effects of caffeine on ERP and EEG indices of attention. *Journal of the International Neuropsychological Society, 2,* 37.
139. Bernstein, D.L., Lawson, S. & Segalowitz, S.J. (1996). Subtle cognitive deficits in high functioning university students with mild head injury. *Journal of the Int. Neuropsychological Society, 2,* 18.
140. Segalowitz, S.J., Rose-Krasnor, L., Rae, H. (1995). ERP support for a limbic reactivity model of temperament inhibition. *Psychophysiology, 32,* S68.
141. Dywan, J., Segalowitz, S.J., Hendry, K. (1995). The late positivity P300 is not an automatic response to item repetition. *Psychophysiology, 32,* S29.
142. Segalowitz, S.J., Gasbarre, L., Busse, S. (1995). Acute ethanol-induced alterations of ERP components at a low dose. *Psychophysiology, 32,* S67.
143. Segalowitz, S.J., Van Roon, P., Dywan, J. (1995). Support for an index view of the repetition late positivity effect. *Psychophysiology, 32,* S68.
144. Segalowitz, S.J. & Armilio, M. (1995). There are many sufficient but no necessary factors modulating P300 amplitude: Support for a salience model. *Psychophysiology, 32,* S67.
145. Segalowitz, S.J., Bernstein, D.M., Lawson, S. (1995). Lower amplitude P300 in mild head injury in the absence of objective behavioural sequelae. *Psychophysiology, 32,* S67.
146. Velikonja, D. & Segalowitz, S.J. (1995). Sustained and selective attention as reflected in auditory ERP components. *Psychophysiology, 32,* S81.

147. Segalowitz, S.J., Dywan, J., & Unsal, A. (1995). P300 amplitude and attentional control in a TBI population. *Brain and Cognition, 28,* 108.
148. Segalowitz, S.J., Unsal, A., & Dywan, J. (1995). Cleverness and wisdom in 12-year-olds: Electrophysiological evidence for late maturation of the frontal lobe. *Brain and Cognition, 28,* 87.
149. Segalowitz, S.J. & Barnes, K.L. (1995). Two-year retest reliability of endogenous components of the auditory oddball ERP. *Brain and Cognition, 28,* 97.
150. Storrie-Baker, J., Segalowitz, S.J., Black, S.E., Crowne, D.P., McLean, J.A., & Sullivan, N. (1995). EEG support for the arousal hypothesis in hemispatial neglect among 42 unilateral stroke patients. *Journal of the International Neuropsychological Society, 1,* 159.
151. Dywan, J., Segalowitz, S.J., Murphy, W., Murphy, T., & Yonelinas, A. (1995). Source monitoring: ERP evidence for changes in memory experience with age. *Journal of the International Neuropsychological Society, 1, 183.*
152. Segalowitz, S.J., Marsman, I., Unsal, A., & Van Roon, P. (1994). Context, meaning, and subjective probability factors in P300 amplitude: Trying to sort them out. *Psychophysiology, 31,* S89.
153. Murphy, T., Alloway, C.E.D., Lamarche, C.H., Ogilvie, R.D., Bernstein, D.M., Marsman, I., & Segalowitz, S.J. (1994). The relationship between the AAT and objective and subjective measures of sleepiness during 28 hours of sleep deprivation. *Psychophysiology, 31,* S70.
154. Murphy, T., Bernstein, D.M., Marsman, I.A., Segalowitz, S.J., Alloway, C.E.D., Lamarche, C.H., & Ogilvie, R.D. (1994). EEG and ERP indices of arousal during 28 hours of sleep deprivation. *Psychophysiology, 31,* S70.
155. Velikonja, D. & Segalowitz, S.J. (1994). The effect of stimulant medications on the auditory ERP: A case study. *Psychophysiology, 31,* S102.
156. Murphy, W., Segalowitz, S.J., Dywan, J., Ogilvie, R., Murphy, T., & Lawson, S. (1994). Mild head injury, sleep dysfunction and stimulant intake. *Sleep Research,* p 86.
157. Segalowitz, S.J., Unsal, A. & Dywan, J. (1993). CNV evidence for the distinctiveness of frontal and posterior neural processes in a traumatic brain injured population. Brain and Language, 44, 447.
158. Segalowitz, S.J. & Stewart, J. (1993). Evidence for separated semantic systems for verbal and picture information. *Brain and Language, 44,* 449.
159. Segalowitz, N.S. & Segalowitz, S.J. (1993). Automatization of language skill: Clues from the coefficient of variation. *Brain and Language, 44,* 449.
160. Dywan, J., Segalowitz, S.J., Henderson, D. & Jacoby, L.L. (1993). Source monitoring as distinct from recall and recognition memory in traumatic brain injury. *Brain and Language, 44,* 448.
161. Dywan, J. & Segalowitz, S.J. (1993). Electrophysiological correlates of family-reported behaviour after traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology, 15,* 106.
162. Segalowitz, S.J., Lawson, S., & Berge, B. (1993). Unreported head injury in the general population: Subtle residual effects. *Journal of Clinical and Experimental Neuropsychology, 15,* 104.
163. Velikonja, D. & Segalowitz, S.J. (1993). The effects of caffeine on electrophysiological indicators of cortical arousal. *Journal of Clinical and Experimental Neuropsychology, 15,* 109-110.
164. Storrie-Baker, H.J., Segalowitz, S.J., Black, S.E., McLean, J.A.G., & Sullivan, N. (1993). Improvement of hemispatial neglect with cold-water calorics: An electrophysiological investigation. *Journal of Clinical and Experimental Neuropsychology, 15,* 110.
165. Unsal, A., Segalowitz, S.J. & Dywan, J. (1992). Latency jitter as a variable in the attentuation of P300 amplitude in head injured. *Journal of Clinical and Experimental Neuropsychology, 14,* 74.
166. Dywan, J., Segalowitz, S.J., & Williamson, L. (1992). Memory for source in older adults: Electrophysiological and psychometric correlates. *Journal of Clinical and Experimental Neuropsychology, 14,* 87.
167. Segalowitz, S.J., Unsal, A. & Dywan, J. (1992). ERP and behavioural reaction time variability in head injury. *Journal of Clinical and Experimental Neuropsychology, 14,* 73.
168. Berge, B. & Segalowitz, S.J. (1992). The power of the Geschwind-Behan hypothesis? *Journal of Clinical and Experimental Neuropsychology, 14,* 117-118.

169. Segalowitz, S.J., Ogilvie, R.D., Janicki, M., Simons, I. & Buetow, C. (1991) ERP Evidence for the Paradox of REM Sleep: Attention and Distraction While Awake and While Asleep. *Sleep Research, 20,* 159.
170. Segalowitz, S.J. & Ogilvie, R.D. (1991). ERP evidence of information processing at the onset and during sleep. *Journal of Clinical and Experimental Hypnosis, 39,* 270.
171. Segalowitz, S.J., Dywan, J. & Ismailos, L. (1991). Electrocortical evidence that hypnotically-induced hallucinations are experienced. *Journal of Clinical and Experimental Hypnosis 39,* 271.
172. Segalowitz, S.J., Ogilvie, R.D., Janicki, M., Simons, I. & Buetow, C. (1991). ERP Evidence for the Paradox of REM Sleep: Attention and Distraction While Awake and While Asleep. *Sleep Research, 20,* 159.
173. Dywan, J., Segalowitz, S.J. & Unsal, A. (1990). Neuropsychological correlates of health risk in the elderly. *Brain and Cognition, 39,* 600.
174. Segalowitz, S.J., Dywan, J. & Unsal, A. (1990). P300 correlates of memory span decline. *Brain and Cognition, 39,* 601.
175. Segalowitz, S.J. (1990). On the Nonspecial Nature of Neuropsychology. *Journal of Clinical and Experimental Neuropsychology, 12,* 108.
176. Simons, I.A., Ogilvie, R.D., Segalowitz, S.J., & Janicki, M. (1990). EEG power spectrum changes during behaviorally indicated arousals from stage 2 sleep. *Sleep Research, 19,* 131.
177. Segalowitz, S.J. (1989). Frontal lobe functions as a model for child development. *Canadian Psychology, 30,* 498.
178. Segalowitz, S.J. & Wagner, W. James (1989). Frontal lobe EEG correlates of memory and thinking in adolescence. *Canadian Psychology, 30,* 498.
179. Segalowitz, S.J., Wagner, W.J., Menna, R. & Watmough, D. (1989). Electrophysiological trait correlates of memory span in 15-year-olds. *Journal of Clinical and Experimental Neuropsychology, 11, 31.*
180. Segalowitz, S.J. & Schultz, K. (1989). Detecting inter- and intrahemispheric specialization of function: are 4 electrodes enough? *Journal of Clinical and Experimental Neuropsychology, 11,* 72.
181. Weber, M.A. & Segalowitz, S.J. (1989). The attentional capacity test (ACT) for children. *Journal of Clinical and Experimental Neuropsychology, 11, 28.*
182. Dywan, J., Segalowitz, S.J. & Otis, L. (1988). Recall interference and the prototype shift in recognition. *Canadian Psychology, 29* (2a), 221.
183. Schultz, K. & Segalowitz, S.J. (1988). Solution strategy, performance, and EEG activity. *Canadian Psychology, 29* (2a), 703.
184. Segalowitz, S.J., Menna, R. & MacGregor, L. (1987). Left and right hemisphere participation in reading: evidence from ERPs. *Journal of Clinical and Experimental Neuropsychology, 9,* 274.
185. Segalowitz, S.J. & MacGregor, L. (1987). ERP correlates of reading phonologically regular and nonregular English words. *Journal of Clinical and Experimental Neuropsychology, 9,* 49.
186. Orr, C. & Segalowitz, S.J. (1986). Psychometric and demographic variables in brain lateralization. *Canadian Psychology, 27* (2a), 444.
187. Ogilvie, R. & Segalowitz, S.J. (1974). The effect of 20% sleep reduction upon mood, learning and performance measures. *Sleep Research, 3.*

CONFERENCE PRESENTATIONS (refereed)

1. Henderson, S.E., Callegari, J., Desjardins, J.A., Segalowitz, S.J., Campbell, K.L. Age Differences in the Neural Underpinnings of Voluntary vs Involuntary Memory Retrieval. Cognitive Neuroscience Society, San Francisco, Mar 23-26, 2019.

2. Viczko, Jeremy, Segalowitz, Sidney J., Smart, Colette. On the nature of wakefulness: examining the relationship between self-report and electrophysiological markers of arousal in long-term Vajrayana Buddhist meditators. Presented at SPR, Quebec City, Oct 3-7, 2018.
3. Smart, C. & Segalowitz, S.J. Learning to put the brakes on: attention control differences in long-term practitioners of somatic meditation. Presented at SPR, Quebec City, Oct 3-7, 2018.
4. Coy, A., Tekok-Kilic, A., Libben, G., & Segalowitz, S.J. When is a threat less of a threat? ERP support for differentiating threat levels in the IAPS pictures. Presented at SPR, Quebec City, Oct 3-7, 2018.
5. Chattha, O., Libben, G., & Segalowitz, S.J. An ERP investigation of present/past tense verb production and morphological regularity. Presented at SPR, Quebec City, Oct 3-7, 2018.
6. Segalowitz, S.J., Samar, V.J., Desjardins, J.A., & Weissflog, M. Childhood socioeconomic status affects adult medial frontal negativity (MFN) demonstrated by independent component analysis (ICA). Presented at SPR, Quebec City, Oct 3-7, 2018.
7. Weissflog, M., Segalowitz, S.J., & Dywan, J. Factor 1 and Factor 2 Psychopathic Trait Severity Dissociated in Early Visual ERPs. Presented at SPR, Oct 10-15, 2017, Vienna, Austria.
8. Balakumar, S., Murphy, T. & Segalowitz, S.J. The Effect of Sleep Deprivation on Inter-Trial Coherence of the P100, ERN and CRN. Presented at SPR, Oct 10-15, 2017, Vienna, Austria.
9. Lackner, C., Santesso, D., Dywan, J., O'Leary, D., Wade, T. & Segalowitz, S.J. Adverse Childhood Experiences are Associated with the Magnitude of The ERN Difference. Presented at SPR, Oct 10-15, 2017, Vienna, Austria.
10. Segalowitz, S.J., Callegari, J., Chattha, O. & Smith, B. Is the Early Visual ERP Sensitive to Low-Level Visual Stimulus Properties? A Test of Luminance vs. Cognitive Factors. Presented at SPR, Oct 10-15, 2017, Vienna, Austria.
11. Sibalis, A., Phillips, M., Segalowitz, S.J., Schmidt, L.A. & Milligan, K. An ERP Study of Attentional Control: ADHD Subtype Differences in the P300 Component. Presented at CPA, June 9-12, 2017, Toronto.
12. Sibalis, A., Edwards, E., McKeough, T., Schmidt, L. A., Segalowitz, S. J., & Milligan, K. (April 2017). Examining the effects of mindfulness training on visual attention for youth with ADHD. Presented at the Biennial Meeting of the Society for Research in Child Development, Austin, TX.
13. Edwards, M. K, Sibalis, A., Phillips, M., Schmidt, L .A. , Segalowitz, S. J, & Milligan, K. (April 2017). Inattention underlies response inhibition abnormalities in ADHD. Presented at the Biennial Meeting of the Society for Research in Child Development, Austin, TX.
14. Mehak, A., Edwards, M. K., McKeough, T., Schmidt, L. A., Segalowitz, S. J. & Milligan, K. (April 2017). Mindfulness training leads to alterations in neural measures of selective attention in youth with ADHD. Presented at the Biennial Meeting of the Society for Research in Child Development, Austin, TX.
15. Matsuhashi, T., Segalowitz, S.J., Nagano, Y. & Masaki, H. Error-related negativity predicts improvement of a sequence motor learning.SPR, Sept 21-25, 2016, Minneapolis, MN.
16. Maurer, D., Segalowitz, S.J., Gao, X., Collignon, O., Chen, Y-C., Lewis, T. The Neural Underpinnings of Visual Critical Periods: New Evidence from Adults treated for Bilateral Congenital Cataracts. International Conference on Infant Studies, New Orleans, May 26-28, 2016.
17. Jetha, Michelle K., Willner, Cynthia J., Segalowitz, S.J. & Gatzke-Kopp, Lisa M. Medial Prefrontal Activity during Response Monitoring from Kindergarten to 2nd Grade: The Use of the N2 as a Predictor of Academic Success and Classroom Behavior. APS, Chicago, May 26-29, 2016.
18. Tang, A., Santesso, D.L., Segalowitz, S.J., Schulkin, J., & Schmidt, L.A. Electrocortical and Neuroendocrine Correlates of Shyness in Adults. Society of Biological Psychiatry, Atlanta, GA., May 12-14, 2016.
19. Callegari, J., Chattha, O., & Segalowitz, S.J. How early is the visual ERP sensitive to stimulus content? SONA, Waterloo, ON, May 6, 2016.
20. Smith, B., & Segalowitz, S.J. Shedding some light on luminance and the extrastriate cortex:

an ERP study. SONA, Waterloo, ON, May 6, 2016.

21. Gogo, Cody E., van Noordt, Stefon J. , Desjardins, James A., Segalowitz, Sidney J. & Tekok-Kilic, Ayda. Cognitive control is in the eye of the beholder: Spectral EEG analysis of a cued pro-saccade/anti-saccade task. SPR, Seattle, Sept 30-Oct 4, 2015.
22. Tang, A., Santesso, D.L., Segalowitz, S.J., & Schmidt, L.A. Neurocognitive correlates of shyness and sociability in children. Society of Biological Psychiatry, Toronto, May 14-16, 2015. Also accepted at the annual McMaster Psychiatry Conference (April 29, 2015), Hamilton, ON.
23. Milligan, K., Lackner, C.L., McKeough, T., Schmidt, L.A., & Segalowitz, S.J. Impact of Integra Mindfulness Martial Arts on ERP indices of attentional control. Jean Piaget Society, Toronto, June 4-6, 2015.
24. Borges, C., Milligan, K., McKeugh, T., Mathewson, K.J., Segalowitz, S.J., & Schmidt, L.A. Respiratory Sinus Arrhythmia (RSA), executive functioning, and a mindfulness intervention in adolescent males with self-regulation disorders. Jean Piaget Society, Toronto, June 4-6, 2015.
25. Jetha, M.K., Gatzke-Kopp, L., & Segalowitz, S.J. The stability of visual ERP components in young children: Retest reliability over 14-16 months. Jean Piaget Society, Toronto, June 4-6, 2015.
26. Lackner, C.L., Santesso, D., Gorodetsky, E., Ernst, M., Dywan, J., Wade, T., & Segalowitz, S.J. Allelic variants of monoamine-related genes moderate the association between self-regulation and markers of frontal lobe function. Jean Piaget Society, Toronto, June 4-6, 2015.
27. Borges, C., Milligan, K., Spiroiu, F., Badali, P., Mathewson, K., Segalowitz, S. & Schmidt, L. (April, 2014). Change in youth with self-regulation disorders. Poster presentation at the 26th annual McMaster Department of Psychiatry and Behavioural Neurosciences Research Day, Hamilton, ON.
28. Gavin, William J., Taylor, Brittany K., Segalowitz, Sidney J. & Davies, Patricia L. A trial-by-trial distribution-based, outlier-rejection approach to creating averaged ERPs for contingent negative variation paradigms. SPR, Sept 10-14 2014, Atlanta, GA.
29. Willner, Cynthia J., Jetha, Michelle K., Segalowitz, Sidney J. & Gatzke-Kopp, Lisa M. Emotional face processing biases and children's social withdrawal and externalizing behaviors in school. SPR, Sept 10-14 2014, Atlanta, GA.
30. Sternin, Avital, Segalowitz, Sidney J., Lewis, Terri L., Dywan, Jane & Maurer, Daphne. Electrophysiological evidence of altered visual processing in adults with blocked pattern vision during infancy. SPR, Sept 10-14 2014, Atlanta, GA.
31. Davis, Charles P., Libben, Gary & Segalowitz, Sidney J. Compounding matters: the P1 as an index of semantic access to compound words. SPR, Sept 10-14 2014, Atlanta, GA.
32. Davis, C. P., & Libben, G. (2014). Morphological transcendence: Morphemic boundary ambiguity produces conflict at the N4. Presented at the 9th International Meeting on the Mental Lexicon, Sept 2014, Niagara-on-the-Lake, ON, Canada.
33. Dzyundzyak, Angela, Santesso, Diane L. & Segalowitz, Sidney J. Problem gambling and the FRN. SPR, Sept 10-14 2014, Atlanta, GA.
34. Capuana, Lesley J., Dywan, Jane, Gibson, Raechelle M. & Segalowitz, Sidney J. Cardiac autonomic regulation and cognitive control in older and younger adults. SPR, Sept 10-14 2014, Atlanta, GA.
35. Lackner, C.L., Milligan, K., Wilkins, L., Spiroiu, F., Badali, P., Schmidt, L.A. & Segalowitz, S.J. Mindfulness martial arts training maintains intertrial coherence indices of selective attention in adolescents with ADHD and/or learning disabilities over repeated task administration. SPR, Sept 10-14 2014, Atlanta, GA.
36. Milligan, K., Wilkins, L., Sibalis, A., Spiroiu, F., Badali, P., Schmidt, L., & Segalowitz, S.J. (September, 2014). Mindfulness treatment for boys with ADHD improves ERP indices of attention. SPR, Sept 10-14 2014, Atlanta, GA.
37. Borges, C., Milligan, K., Spiroiu, F., Badali, P., Mathewson, K.J., Segalowitz, S.J., & Schmidt, L.A. Change in respiratory sinus arrhythmia (RSA) in response to a mindfulness training intervention in adolescent males with self-regulation disorders. Development 2014, Ottawa, May 8-9, 2014.

38. Lackner, C. L., Milligan, K., Wilkins, L., Schmidt, L., & Segalowitz, S. J. Mindfulness martial arts training improves ERP indices of selective attention in adolescents with ADHD and/or learning disabilities. Development 2014, Ottawa, May 8-9, 2014.
39. Milligan, K., Wilkins, L., Sibalis, A., Spiroiu, F., Badali, P., Schmidt, L., & Segalowitz, S.J. (May, 2014). Improving Working Memory in Adolescents with ADHD+LD through an Activity-Enhanced Mindfulness Treatment. Poster Presentation at Development 2014: A Canadian Conference on Developmental Psychology, Ottawa, ON.
40. Doidge, J., Wilkins, L., Milligan, K., Badali, P., Schmidt, L., & Segalowitz, S. (July, 2014). Mindfulness treatment decreases ERP indices of affect intensity following negative feedback in adolescents with ADHD. Poster Presentation at Canadian Society for Brain, Behaviour, and Cognitive Science, Toronto, ON.
41. Samar, V.J., Desjardins, J.A., & Segalowitz, S.J. Adverse Childhood Conditions May Impair Adults' Cortical Executive Attention Mechanisms: ERP Evidence. APS, San Francisco, May 22-25, 2014.
42. Campopiano, A. & Segalowitz, S.J. Understanding the Regularization Parameter in sLoreta: A Simulation Study. SPR, Florence, Italy, Oct 2-6, 2013.
43. Dzyundzyak, A., Santesso, D.L., & Segalowitz. Influences of Expectation and Sense of Control on the Feedback-Related Negativity. SPR, Florence, Italy, Oct 2-6, 2013.
44. Samar, V.J., Segalowitz, S.J., Desjardins, J.A., & Skyler, M. Adverse Childhood Conditions May Impair Deaf Adults' Cortical Attention Mechanisms: ERP Evidence. APS, Washington, D.C., May 23-26, 2013
45. Mulligan, B. P., Smart, C. M., MacDonald, S. W. S., & Segalowitz, S. J. Utility of neural and behavioral markers of intra-individual variability in the discrimination of healthy older adults from those with subjective cognitive impairment. International Neuropsychological Society, Waikoloa Village, HI, Feb 2013.
46. Smart, C. M., Segalowitz, S. J., Mulligan, B.P., & MacDonald, S. W. S. (2013). Mindfulness Training Increases Error Processing in Older Adults With and Without Subjective Cognitive Impairment. International Neuropsychological Society, Waikoloa Village, HI, Feb 2013.
47. Smart, C. & Segalowitz, S.J. Reacting or Responding? The Impact of Mindfulness Training on the Feedback Error-Related Negativity (*f*ERN) in Older Adults With and Without Subjective Cognitive Impairment. Rotman Research Institute Conference: Brain Plasticity & Neurorehabilitation, Toronto, Mar 3-6, 2013.
48. Segalowitz, S.J., Marshall, W.J., & Lackner, C.L. Phase Shifting Granger Causality: A measure of directed coherence (symposium talk). SPR, New Orleans, LA. Sept 19-23, 2012.
49. Jetha, M.K., Gatzke-Kopp, L.M., & Segalowitz, S.J. The prefrontal cortex is a moving target in early childhood: Implications for ongoing neural maturation for ERP research in longitudinal studies (symposium talk). SPR, New Orleans, LA. Sept 19-23, 2012.
50. Zheng, X. & Segalowitz, S.J. Putting a face in its place: in- and out-group membership alters the N170 response. SPR, New Orleans, LA. Sept 19-23, 2012.
51. Weissflog, M.W., Munro, G.E., Wirz, L.M., Segalowitz, S.J., & Dywan, J. Callous affect and the early visual processing of fearful faces. SPR, New Orleans, LA. Sept 19-23, 2012.
52. van Noordt, S.J.R., Desjardins, J.A. , & Segalowitz, S.J. It's time for a change: Examining anterior cingulate cortex activation to cues signaling switches in response context. SPR, New Orleans, LA. Sept 19-23, 2012.
53. Marshall, W.J., Lackner, C.L., Marriott, P., Santesso, D.L., & Segalowitz, S.J. Using phase shifting and granger causality to measure effective connectivity in EEG recordings. SPR, New Orleans, LA. Sept 19-23, 2012.
54. Jetha, M.K., Gatzke-Kopp, L.M, & Segalowitz, S.J. The stability of visual ERP components in young children. SPR, New Orleans, LA. Sept 19-23, 2012.
55. Maurer, D., Mondloch, C.J., Robbins, R., Dywan, J., & Segalowitz, S.J.. The influence of early experience on the later development of face expertise: lessons from cataract-reversal patients. ICIS, June 7-9, 2012.

56. Van Noordt, S.J.R., Desjardins, J.A., & Segalowitz, S.J. Automated pre-processing of continuous EEG/ERP data using high performance cluster computing. SHARCNet Research Day, Guelph, May 23, 2012.
57. Desjardins, J.A., & Segalowitz, S.J. Visual information processing in the brain: Examining early electrophysiological responses using independent components analysis and robust estimation. SHARCNet Research Day, Guelph, May 23, 2012.
58. Lackner, Christine L., Marshall, William, Santesso, Diane L., & Segalowitz, Sidney J. Phase reset variables are differentially associated with anxiety and aggression in a typically developing adolescent sample. SPR, Boston, MA. Sept 14-18, 2011.
59. Zheng, Xin, & Segalowitz, Sidney J. The N170 face inversion effect is both face-specific and domain-general: separate amplitude and latency effects. SPR, Boston, MA. Sept 14-18, 2011.
60. Desjardins, James A. & Segalowitz, Sidney J. Time course and robustness of the N170 face effect at the scalp and in independent components: separating the N170 and P100 face effects. SPR, Boston, MA. Sept 14-18, 2011.
61. van Noordt, Stefon J.R. & Segalowitz, Sidney J. Error-related brain potentials are associated with transient increases in spectral power and phase alignment of on-going EEG oscillations. SPR, Boston, MA. Sept 14-18, 2011.
62. Dzyundzyak, Angela, MacLean, Mary H., & Segalowitz, Sidney J. Influence of reward information on anticipatory processes: CNV and alpha event-related desynchrony study. SPR, Boston, MA. Sept 14-18, 2011.
63. Capuana, Lesley J., Gibson, Raechelle M., Tays, William J., Segalowitz, Sidney J., & Dywan, Jane. Cortical and cardiac associations with performance monitoring and accuracy of response. SPR, Boston, MA. Sept 14-18, 2011.
64. Weissflog, Meghan J., Dywan, Jane, & Segalowitz, Sidney J. Manipulation of spatial attention while viewing emotional faces delays electrophysiological indices of early visual processing. SPR, Boston, MA. Sept 14-18, 2011.
65. Santesso, Diane L., Segalowitz, Sidney J., Dywan, Jane, Wade, Terrance L., & Pizzagalli, Diego A. Enhanced acc responses to negative feedback are related to depressive symptoms in adults and adolescents. SPR, Boston, MA. Sept 14-18, 2011.
66. Segalowitz, Sidney J., Santesso, Diane L., & Lackner, Christine L. Individual differences in the role of the medial frontal cortex in adolescent self-regulation. SPR, Boston, MA. Sept 14-18, 2011.
67. Santesso, D. L., Dywan, J., Wade, T. J., & Segalowitz, S. J. (2010). Enhanced feedback-related ACC activity in relation to negative emotionality during adolescence. SPR, Portland, OR. Sept 29-Oct 3, 2010.
68. Lackner, C. L., Santesso, D. L., Dywan, J., Wade, T. J., & Segalowitz, S. J. (2010). Medial prefrontal NoGo activation during an emotion Go/NoGo Task is related to worrying in adolescence. SPR, Portland, OR. Sept 29-Oct 3, 2010.
69. Weissflog, M. J., van Noordt, S. J. R., Choma, B. L., Dywan, J., & Segalowitz, S. J. (2010). Machiavellianism, sociopolitical ideology, and the ERN. SPR, Portland, OR. Sept 29-Oct 3, 2010.
70. Tays, W. J., Witherspoon, R. L., Capuana, L. J., Segalowitz, S. J., & Dywan, J. (2010). Resolving interference one component at a time: Dissociation between N2 and N450 in a modified Stroop paradigm. SPR, Portland, OR. Sept 29-Oct 3, 2010.
71. Capuana, L. J., Elmers, J. L., Tays, W. J., Segalowitz, S. J., & Dywan, J. (2010). Autonomic correlations of response control in the context of memory-based interference and reward contingencies. SPR, Portland, OR. Sept 29-Oct 3, 2010.
72. Jetha, M.K., Segalowitz, S.J., Gatzke-Kopp, Lisa & Ly, D. (2010). The Nogo-N2 effect predicts externalizing behavior in 5-6 year old children at risk for reduced inhibitory control. SPR, Portland, OR. Sept 29-Oct 3, 2010.
73. Dzyundzyak, A., & Segalowitz, S.J. (2010). Anticipating wins and losses: CNVs appear to be similar but reflect different traits. SPR, Portland, OR. Sept 29-Oct 3, 2010.

74. Desjardins, J., Lackner, C.L., & Segalowitz, S.J. (2010). Perfecting the P50 gating paradigm: The benefits of using ICA and bootstrapping techniques. SPR, Portland, OR. Sept 29-Oct 3, 2010.
75. Meghan J. Weissflog, Sidney J. Segalowitz, Gillian E. S. Munro, Jane Dywan. Disentangling psychopathic status from general incarceration status in event-related potential responses to emotional faces. Presented at Cognitive Neuroscience Society, Montreal, Apr 16-20, 2010.
76. Christine L. Lackner, Diane L. Santesso, Jane Dywan, Terrance J. Wade, Sidney J. Segalowitz. The N100 response to unattended stimuli relates to adolescent executive function within a normally developing population. Presented at Cognitive Neuroscience Society, Montreal, Apr 16-20, 2010.
77. Angela Dzyundzyak, Diane Santesso, Sidney Segalowitz. The task matters: sensitivity of the FRN to feedback valence in gambling versus nongambling paradigms. Presented at Cognitive Neuroscience Society, Montreal, Apr 16-20, 2010.
78. Michelle Jetha, Xin Zheng, Louis A. Schmidt, Sidney J. Segalowitz. Shyness and the first 100 milliseconds of emotional face processing. Presented at Cognitive Neuroscience Society, Montreal, Apr 16-20, 2010.
79. Diane Santesso, Angela Dzyundzyak, Sidney Segalowitz. Acc activity and punishment sensitivity: comparing adolescents and adults during a monetary feedback task. Presented at Cognitive Neuroscience Society, Montreal, Apr 16-20, 2010.
80. Lesley Capuana, Jane Dywan, William Tays, Segalowitz Sidney. Relationship of Nogo N2/P3 and ERN/Pe across working memory load to autonomic cardiac regulation in younger and older adults. Presented at Cognitive Neuroscience Society, Montreal, Apr 16-20, 2010.
81. Xin Zheng, Catherine J. Mondloch, Sidney J. Segalowitz. ERP correlates of facial distinctiveness: P2 sensitivity to identity strength. Presented at Cognitive Neuroscience Society, Montreal, Apr 16-20, 2010.
82. James Desjardins & Sidney J. Segalowitz. Deconstructing the P1 and N170 Face-Effect Using Independent Component Analysis. SPR, Berlin, Oct 21-24, 2009.
83. Xin Zheng, Mark D. Vida, Catherine J. Mondloch, & Sidney J. Segalowitz. The N170 ERP Relates to Both Featural and Configural Information Important for Face Processing. SPR, Berlin, Oct 21-24, 2009.
84. Diane L. Santesso, Angela Dzyundzyak, & Sidney J. Segalowitz. The Relation of Punishment Sensitivity to ACC Activation in an ERP Gambling Paradigm is Greater in Younger Adolescents. SPR, Berlin, Oct 21-24, 2009.
85. Sidney J. Segalowitz & Diane L. Santesso. ERN, FRN, and Stressors: ACC Activation Patterns as Related to the Comfort of Losing. SPR, Berlin, Oct 21-24, 2009.
86. Diane L. Santesso, Irene E. Drmic, Michelle K. Jetha, Karen J. Mathewson, Susan E. Bryson, Joel O. Goldberg, Geoffrey B. Hall, Sidney J. Segalowitz, & Louis A. Schmidt. An ERP Source Localization Study of Performance Monitoring in Autism Spectrum Disorder. SPR, Berlin, Oct 21-24, 2009.
87. Karen J. Mathewson, Irene E. Drmic, Michelle K. Jetha, Diane L. Santesso, Susan E. Bryson, Joel O. Goldberg, Geoffrey B. Hall, Sidney J. Segalowitz, & Louis A. Schmidt. Cardiac Responses to Affective Auditory and Visual Stimuli in Adults with Autism Spectrum Disorder (ASD). SPR, Berlin, Oct 21-24, 2009.
88. James Desjardins & Sidney J. Segalowitz. EEG Dynamics Underlying the P1 and N170 Face Effect. SPR, Berlin, Oct 21-24, 2009.
89. Lesley J. Capuana, Jane Dywan, William J. Tays, & Sidney J. Segalowitz. Cardiac Autonomic Function and Response Control Deficits in Older Adults. SPR, Berlin, Oct 21-24, 2009.
90. Xin Zheng, Mark D. Vida, Catherine J. Mondloch, & Sidney J. Segalowitz. N170 is Sensitive to Several Factors Important for Differentiating Individual Faces. SPR, Berlin, Oct 21-24, 2009.
91. Meghan J. Weissflog, Sidney J. Segalowitz, Gillian E. S. Munro, & Jane Dywan. ERP Correlates of Emotional Face Processing in Psychopathy. SPR, Berlin, Oct 21-24, 2009.

92. Angela Dzyundzyak, Diane L. Santesso, & Sidney J. Segalowitz. Processing Reward Magnitude and Valence: Dissociations and Individual Differences in the FRB and P300. SPR, Berlin, Oct 21-24, 2009.
93. William J. Tays, Jane Dywan, & Sidney J. Segalowitz. Identifying the Functional Role of the Interference-Elicited Medial Frontal Negativity". SPR, Berlin, Oct 21-24, 2009.
94. Michelle K. Jetha, Sidney J. Segalowitz, & Lisa Gatzke-Kopp. Frontal EEG Asymmetry in Highly Aggressive 56 Year Old Girls. SPR, Berlin, Oct 21-24, 2009.
95. Dywan, J., Mathewson, K.J., Capuana , L.J., Tays, W.J., & Segalowitz, S.J. Cortical and autonomic indices of age-related change in attentional control. Physiology of Human Development, Moscow, Russia, June 22-24, 2009.
96. Zheng, X. & Segalowitz, S.J. ERP evidence of early semantic access with a randomized semantic priming paradigm. SPR, Austin TX, Oct 1-5, 2008.
97. Mathewson, K.J., Dywan J., Tays, W.J. & Segalowitz, S.J. Aging decline in cardiac vagal regulation: Implications for complex cognition? SPR, Austin TX, Oct 1-5, 2008.
98. Munro, G.E.S., Dywan, J., Lim, W., & Segalowitz, S.J. Subclinical levels of psychopathy associated with an affect-specific processing deficit. SPR, Austin TX, Oct 1-5, 2008.
99. Masaki, H., Murphy, T.I., Desjardins, J., & Segalowitz, S.J. A test of the response-conflict hypothesis in the production of error-related negativity. SPR, Austin TX, Oct 1-5, 2008.
100. Zheng, Xin & Segalowitz, S.J. The first 200 ms of reading: A high-density ERP study of visual word recognition. Annual CSBBCS meeting, London, ON, June 19-21, 2008.
101. Davies, P.L., Gavin, W.J., & Segalowitz, S.J. An ERP Study of Error-Monitoring in Adolescence: Correlating Executive Functions to Within-Subject Variability in Brain Response. Society for Research in Adolescence, Chicago, March 6-9, 2008.
102. Segalowitz, S.J. The development and personality correlates of medial frontal cortex activation across adolescence. Society for Research in Adolescence, Chicago, March 6-9, 2008.
103. Segalowitz, S.J. Differences in Medial Prefrontal Cortex Activity with respect to Development and Personality across Adolescence: ERP studies of the Error-Related Negativity. 4th Cuban Congress of Neurophysiology. Varadero, Mar 11-14, 2008.
104. Capuana, L., Tays, W.J., Mathewson, K., Segalowitz, S.J., & Dywan, J. Respiratory Sinus Arrhythmia (RSA) and the N450 in Younger and Older Adults. SPR, Savannah, October 17-21, 2007.
105. Mathewson,, K.J. Dywan, J., Tays, W.J., Snyder, P.J. & Segalowitz, S.J. Heart Rate Variability and Maze-Learning Performance in Older and Younger Adults. SPR, Savannah, October 17-21, 2007.
106. Munro, G.E.S., Dywan, J., & Segalowitz, S.J. Subclinical Psychopathy (SRP-III) and ERP Responses to a Visual Oddball Task. SPR, Savannah, October 17-21, 2007.
107. Tays, W.J., Dywan, J. Capuana, L., & Segalowitz, S.J. General Proactive Interference and the N450 Response. SPR, Savannah, October 17-21, 2007.
108. Zheng, X, & Segalowitz, SJ. A High-Density ERP Study on Word Frequency and Neighborhood: Lexical Status Effects in the P100. SPR, Savannah, October 17-21, 2007.
109. Gavin, W.J., Segalowitz, S.J., & Davies, P.L. ERP Measures of Efficiency During Error Processing in Children. SPR, Savannah, October 17-21, 2007.
110. Segalowitz, S.J. & Dipoce, M. Eliciting Early VEP Components: A Comparison of Paradigms. SPR, Savannah, October 17-21, 2007.
111. Foster, C.N. & Segalowitz, S.J. The Psychology of Being Careful: Sensitivity to Punishment and Obsessive-Compulsiveness. CPA, Ottawa, June 7-9, 2007.
112. Martel, G., Stemmer, B. & Segalowitz, S.J.. Étude électroencéphalographique du traitement syntaxique de phrases françaises : le cas de la Early Left Anterior Negativity (ELAN). ACFAS, Trois Rivieres, QC, May 7-11, 2007.
113. Baker, T.E., Brocki, K., Kerns, K.A., Segalowitz, S.J., & Holroyd, C.B. Neural mechanisms of hot and cold executive functions in typical and atypical development: An electrophysiological investigation. Jean Piaget Society, Amsterdam, May 31-Jun 2, 2007.

114. Zheng, X., Segalowitz, S.J. Even lowest level semantic challenge alters cortical activation in lexical decision: A high-density ERP study of lexical access. TENNET, Montreal, June 21-24, 2007.
115. Zheng, X., Segalowitz, S.J. Early components of word reading: A high-density ERP study of lexical access. Cognitive Neuroscience Society, New York, May 5-8, 2007.
116. Tays, W.J., Segalowitz, S.J., Mathewson, K.J., and Dywan, J. Topographical Variability of ERP Response in Older Adults is Inversely Related to Interference in a Working Memory Task. Cognitive Neuroscience Society, New York, May 5-8, 2007.
117. Segalowitz, S.J., Marshall, W., Mathewson, K.J., Tays, W.J., Dywan, J. Cross-Cortical Communication in Healthy Human Aging: A Mutual Information Analysis of EEG. Cognitive Neuroscience Society, New York, May 5-8, 2007.
118. Gillian E. Munro, Jane Dywan, Sidney J. Segalowitz, Grant T. Harris, Shari McKee, and Ayse Unsal. Frontal N2, Response Inhibition and Psychopathy. Society for Psychophysiological Research, Oct 25-29, 2006, Vancouver.
119. Timothy I. Murphy, Michael J. Coons, and Sidney J. Segalowitz. You May Respond when Sleepy but your Frontal Lobe may not: The Effect of Sleep Deprivation and Incentive on the Contingent Negative Variation. Society for Psychophysiological Research, Oct 25-29, 2006, Vancouver.
120. Diane L. Santesso and Sidney J. Segalowitz. Poor Error Monitoring Response is Related to Lack of Empathy. Society for Psychophysiological Research, Oct 25-29, 2006, Vancouver.
121. Sidney J. Segalowitz and Diane L. Santesso. A Lack of Inhibitory Components in the Nogo N2 and the ERN. Society for Psychophysiological Research, Oct 25-29, 2006, Vancouver.
122. Guillaume Martel, Brigitte Stemmer and Sidney J. Segalowitz. ERP Responses to French Phrase Structure Violations. Society for Psychophysiological Research, Oct 25-29, 2006, Vancouver.
123. Dyke, D.I., Segalowitz, S.J., Dywan, J., & Santesso, D.L. The Prefrontal Cortex and Late Adolescence: A Test of Specificity in Executive Functions. Canadian Psychological Association, Calgary, AB, June 8-10, 2006.
124. Beaton, E.A., Hall, G.B.C., Ashbaugh, A.R., Santesso, D.L., Segalowitz, S.J., Antony, M.M., Noseworthy, M.D., Swinson, R.P., Schulkin, J.,& Schmidt, L.A. Individual Differences in Frontal Brain Activation and Salivary Cortisol in Temperamental Shyness. Society for Behavioral Neuroendocrinology 2006 Annual Meeting Pittsburgh, PA, June 17-20, 2006
125. Sanichara, S., Segalowitz, S.J., Davies, P.L., Gavin, W.J., & Dywan, J. (2005). EEG gamma responses in the auditory modality: investigating stimulus, topographical and developmental effects. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
126. Stemmer, B., Segalowitz, S.J., Dywan, J., Panisset, M. (2005). Dopaminergic medication and the ERN in Parkinson's Disease. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
127. Munro, G.E., Dywan, J., Harris, G.T., Mckee, S., Unsal, A., Segalowitz, S.J. (2005). Source modeling of the error-related negativity in criminal psychopaths. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
128. Murphy, T.I., Pine, M., Segalowitz, S.J. (2005). P300 latency is dangerously lengthened for dual-task when sleepy. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
129. Martel, G., Stemmer, B., Segalowitz, S.J. (2005). Processing French visual phrase structure violations: an ERP study on the ELAN. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
130. Tays, W.J., Dywan, J., Mathewson, K.J., Segalowitz, S.J. (2005). Age-related change in ERPs associated with context-based vs response-based interference. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
131. Santesso, D.L., Segalowitz, S.J., Dyke, S.I. (2005). "Sensation seeking and reward sensitivity are related to poor performance monitoring (ERN) and decision-making (IGT). Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.

132. Davies, P.L., Segalowitz, S.J., Gavin, W.J. (2005). Relationship of error-related negativity to cognitive skills from 7 to 18 years. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
133. Masaki, H., Murphy, T.I., Desjardins, J., Segalowitz, S.J. (2005). ERN characteristics on partial versus complete errors. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
134. Segalowitz, S.J., Santesso, D., Dywan, J. (2005). The ERN and the emotional modulation to events. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
135. Mathewson, K.J., Dywan, J., Tays, W. J., Segalowitz, S.J., & Snyder, P.J. (2005). ERPs to error-related feedback during a spatial memory task in older and younger adults. Society for Psychophysiological Research, Lisbon, Sept 21-24, 2005.
136. Stemmer, B., Segalowitz, S.J., Dywan, J., & Panisset , M. The Error-related Negativity in mild to moderate Parkinson's Disease. ICON 9, Havana, Cuba, Sept4 - 9, 2005.
137. Stemmer, B., Segalowitz, S.J., Dywan, J., & Panisset , M. Performance monitoring in medicated and non-medicated patients with Parkinson disease. Psychology and the Brain: Workshop on Psychophysiological Methodology, Bochum, Germany, May 26-29, 2005.
138. Segalowitz, S.J., Mondloch, C., Freire, A., Maurer, D, & Dywan, J. The N170 Response to Standard versus Scrambled Mooney Faces: The Eyes Don't Have It! Cognitive Neuroscience Society, NY, Apr 9-12, 2005.
139. Mozolic, B.E., Davies, P.L., Segalowitz, S.J., & Gavin, W.J. Contingent negative variation and attention in children. Society for Psychophysiological Research, Santa Fe, Oct 20-24 2004.
140. Folino, A., Desjardins, J., & Segalowitz, S.J. The attentional model of induced EEG gamma: A manipulation comparison with P300. Society for Psychophysiological Research, Santa Fe, Oct 20-24 2004.
141. Santesso, D.L., Segalowitz, S.J. & Dywan, J. Stability and reliability of the error-related negativity (ERN). Society for Psychophysiological Research, Santa Fe, Oct 20-24 2004.
142. Munro, G.E., Dywan, J., Harris, G.T., McKee, S., Unsal, A., & Segalowitz, S.J. Emotional specificity of ERN and error monitoring deficits associated with psychopathy. Society for Psychophysiological Research, Santa Fe, Oct 20-24 2004.
143. Schmidt, L.A., Vaillancourt, T., Santesso, D.L., Segalowitz, S.J., Ashbaugh, A.R., Antony, M.M., McCabe, R.E. and Beaton, E.A. Adrenocortical activity in the origins and maintenance of temperamental shyness: A developmental perspective. Canadian Psychological Association, St. John's, June 2004.
144. Santamaria, B., Dywan, J., & Segalowitz, S.J. (2004). Early structural encoding and face processing deficits after CHI. International Neuropsychological Society, Baltimore, Feb 4-7, 2004.
145. Anum, A., Segalowitz, S.J.& Dywan, J. Information Processing Consistency in Event-Related Potentials (ERP): Effects of Aging and Attention Demands. Society for Psychophysiological Research, Chicago, Oct 29-Nov 2 2003.
146. Masaki, H., Desjardins, J.A., Murphy, T.I., & Segalowitz, S.J. A Test of Functional Origins of the Error-Related Negativity. Society for Psychophysiological Research, Chicago, Oct 29-Nov 2 2003.
147. Mathewson, K., Dywan, J. Segalowitz, S.J.. Error-monitoring, Aging and Heart Rate Variability. Society for Psychophysiological Research, Chicago, Oct 29-Nov 2 2003.
148. Murphy, T.I., Richard, M., Masaki, H., & Segalowitz, S.J.. Whoops, DARN, who cares: The Effect of Sleepiness on the Error-Related Negativity. Society for Psychophysiological Research, Chicago, Oct 29-Nov 2 2003.
149. Tays, W.J., Folino, A., Dywan, J. & Segalowitz, S.J. EEG Gamma Relates to Clarity of Thinking and Source Monitoring ERPs after Mild Head Injury. Society for Psychophysiological Research, Chicago, Oct 29-Nov 2 2003.

150. Santesso, D., Segalowitz, S.J., & Schmidt, L.A. Diminished Error-Related Negativity in 10-Year-Old Children with Poor Social Behavior. Society for Psychophysiological Research, Chicago, Oct 29-Nov 2 2003.
151. Pailing, P.E., & Segalowitz, S.J. The Role of Uncertainty in Error Monitoring: An ERP Investigation. Society for Psychophysiological Research, Chicago, Oct 29-Nov 2 2003.
152. Segalowitz, S.J., Folino, A., Dywan, J. (2003). Reductions in gamma band EEG and cognitive performance associated with post-concussive symptoms. 6th annual meeting of the Polish Neuroscience Society, Warsaw, July 16-19, 2003.
153. Dywan, J., Tays, W.J. & Segalowitz, S.J.(2003). ERP indices of source memory deficits after mild head injury. 6th annual meeting of the Polish Neuroscience Society, Warsaw, July 16-19, 2003.
154. Schmidt, L.A., Santesso, D.L. & Segalowitz, S.J. (2003). Psychophysiological correlates of atypical social behavior in children. TENNET June 19-21, 2003, Montreal.
155. Davies, P.L., Gavin W. & Segalowitz, S.J. (2002). ERPs and Neuropsychological Tasks Show Prefrontal Maturation in Adolescents. Society for Neuroscience, Nov 2-7, 2002, Orlando FL. (Selected for press release)
156. Pailing, P.E. & Segalowitz, S.J. (2002). Motivation and personality influences on the error-related negativity (Ne/ERN). Society for Psychophysiological Research, Washington D.C., Oct 2-6, 2002.
157. Mathewson, K., Dywan, J. & Segalowitz, S.J. (2002). The effect of task complexity and aging on the ERN. Society for Psychophysiological Research, Washington D.C., Oct 2-6, 2002.
158. Davies, P.L. & Segalowitz, S.J. (2002). Error-related negativity (ERN/Ne) in children and adolescents. Society for Psychophysiological Research, Washington D.C., Oct 2-6, 2002.
159. Davies, P.L. Gavin, W.J. & Segalowitz, S.J. (2002). Development of the contingent negative variation (CNV) in children and adolescents. Society for Psychophysiological Research, Washington D.C., Oct 2-6, 2002.
160. James, T. M., Dywan, J. & Segalowitz, S.J.(2002). False Recognition for Emotional Words in Younger and Older Adults: An ERP Study. ICON8, Porquerolles, France, Sept 9-16, 2002.
161. Segalowitz, S.J. & Pailing, P.E. (2002). Error Negativity as State and Trait: Motivation, Personality and ERPs to Errors. ICON8, Porquerolles, France, Sept 9-16, 2002.
162. Schmidt, L.A., Segalowitz, S.J., Santesso, D.L., Trainor, L.L., & Galay, L.A. Do infants' brain electrical activity (EEG) lok like their mothers' during the processing of emotion? 13th Biennial International Conference on Infant Studies, April 2002, Toronto.
163. James, T., Dywan, J. & Segalowitz, S.J. (2002). ERPs to emotional words in a study on source monitoring and aging. International Neuropsychological Society, Toronto, Feb 13-17, 2002.
164. Coons, M., Murphy, T.I., & Segalowitz, S.J. (2002) The effect of sleepiness on attentional control: An ERP study. International Neuropsychological Society, Toronto, Feb 13-17, 2002.
165. Segalowitz, S.J. & Desjardins, J. (2001). Gamma band EEG and the P300. Society for Psychophysiological Research Conference, Montreal, Oct. 10-14, 2001.
166. Segalowitz, S.J. & Davies, P.L. (2001). Separating vigilance and motor preparation in the CNV. Society for Psychophysiological Research Conference, Montreal, Oct. 10-14, 2001.
167. Mathewson, K., Dywan, J., Segalowitz, S., Arsenault, A., Veenhof, W. & Parakh, R. Heart rate variability, event-related potentials, and attentional control in older and younger adults. Society for Psychophysiological Research Conference, Montreal, Oct. 10-14, 2001.
168. Keenan, T., White, S., & Segalowitz, S.J. (2001). Speed of processing, working memory, and the child's theory of mind: Evidence for a mediational model. Society for Research in Child Development, April 19-22, 2001, Minneapolis.
169. Stemmer, B., Segalowitz, S.J., Witzke, W., Lacher, S., & Schoenle, P.W. (2001). Error detection, the anterior cingulate region, and the error negativity ERP. 19th European Workshop on Cognitive Neuropsychology, Jan 21-26, 2001, Bressanone, Italy.

170. McNeely, H.E., Dywan, J., & Segalowitz, S.J. (2000). ERPs in the context of familiarity, stimulus categorization and emotion: When familiarity meets its match. Society for Psychophysiological Research, October 18-22, 2000, San Diego.
171. Stemmer, B., Segalowitz, S.J., Witzke, W., Lacher, S., & Schoenle, P.W. (2000). Do patients with damage to the anterior cingulate and adjacent regions produce an error-related negativity (ERN)? Society for Psychophysiological Research, October 18-22, 2000, San Diego.
172. Dywan, J.D., Segalowitz, S.J. & Arsenault, A. (2000). Aging and the effect of attention allocation on ERP amplitude during source monitoring. Society for Psychophysiological Research, October 18-22, 2000, San Diego.
173. Segalowitz, S.J., Wintink, A.J., & Cudmore, L.J. (2000). P300 anterior-posterior slope: Effects of task complexity and habituation. Society for Psychophysiological Research, October 18-22, 2000, San Diego.
174. Murphy, T.I., & Segalowitz S.J. (2000). Eliminating the P3 rebound in a novel novelty paradigm. Society for Psychophysiological Research, October 18-22, 2000, San Diego.
175. Veenhof, W., Dywan, J., & Segalowitz, S.J. (2000). Effects of recollection and perceptual fluency on the ERP late positivity. Society for Psychophysiological Research, October 18-22, 2000, San Diego.
176. Pailing, P.E., Segalowitz, S.J., & Davies, P.L.(2000). Speed of responding and the likelihood of error-like activity in correct trial ERPs. Society for Psychophysiological Research, October 18-22, 2000, San Diego.
177. Davies, P.L., & Segalowitz, S.J.(2000). Motivational effect on CNV. Society for Psychophysiological Research, October 18-22, 2000, San Diego.
178. Segalowitz, S.J., Davies, P.L., Pailing, P.E., & Stemmer, B. (2000). Error-related responses: Error detection or beyond? In M. Falkenstein (Chair), Action monitoring, evaluation and control. Symposium presented at the Society for Psychophysiological Research, October 18-22, 2000, San Diego.
179. Baker, K., Segalowitz, S.J., & Ferlisi, M-C. (2000). The relation between performance on the Wisconsin Card Sorting Test and working memory, inhibition and complex attention in children and adults. Rotman Research Institute Conference on "The Frontal Lobes", March 20-24, 2000, Toronto.
180. McNeely, H.E., Dywan, J., & Segalowitz, S.J. (2000). ERP evidence for age differences in susceptibility to emotional distraction in a source monitoring task. Rotman Research Institute Conference on "The Frontal Lobes", March 20-24, 2000, Toronto.
181. McNeely, H. E., Dywan, J., & Segalowitz, S. J. (1999). False recognition, emotion, and the ERP. Society for Psychophysiological Research, Granada, Oct 6-10, 1999.
182. Pailing, P. E., Davies, P. L., Segalowitz, S. J., & Dywan, J. (1999). Error-related negativity (ERN) and impulsive responding. Society for Psychophysiological Research, Granada, Oct 6-10, 1999.
183. Davies, P. L., Pailing, P. E., Segalowitz, S. J., & Dywan, J. (1999). Comparison of two prefrontally generated ERPs: Contingent negative variation (CNV) and error-related negativity (ERN). Society for Psychophysiological Research, Granada, October 6-10, 1999.
184. Chevalier, H., Metz-Lutz, M-N., & Segalowitz, S.J. (1999). Impulsivity and control of inhibition in benign focal childhood epilepsy. TENNET, Montreal, June 17-19.
185. Ross, P. & Segalowitz, S.J. (1999). An EEG coherence test of the frontal dorsal-versus-ventral hypothesis in n-back working memory. TENNET, Montreal, June 17-19.
186. Cudmore, L.J., & Segalowitz, S.J. (1999). Signal-to-Noise Ratio Sensitivity in ERPs to Stimulus and Task Complexity: Different Effects for Early and Late Components. TENNET, Montreal June 17-19.
187. Pailing, P., Segalowitz, S.J. & Dywan, J.(1999). The Relationship between Inhibition and Impulsivity: A Replication and Extension of Visser's Work. TENNET, Montreal June 17-19.

188. Baker, K., Segalowitz, S.J., & Ferlisi (1999). The Tower of London: Different scoring methods lead to different developmental hypotheses. TENNET, Montreal June 17-19.
189. Cudmore, L.J., Segalowitz, S.J., & Dywan, J. (1999). Dorsal frontal-parietal eeg coherence differentiates divided from focused attention. Cognitive Neuroscience, Washington D.C., April 11-13 1999.
190. Ross, P. & Segalowitz, S.J. (1999). A p300 test of the frontal dorsal versus ventral hypothesis in n-back working memory. Cognitive Neuroscience, Washington D.C., April 11-13, 1999.
191. Cudmore, L.J., Segalowitz, S.J., & Dywan, J. (1999). EEG Coherence Shows Altered Frontal-Parietal Communication in TBI During a Dual-Task. Rotman Conference on TBI, Toronto, March 24-25, 1999.
192. Davies, P.L. Segalowitz, S.J., Chevalier, H., Bernstein, D.L., & Lawson, S. (1998). How the presence of novel stimuli affects ERPs to targets. Society for Neuroscience, Los Angeles, Nov 1998.
193. McNeely, H.E., Dywan, J., & Segalowitz, S.J. (1998). ERPs, emotion, and the illusion of familiarity. Society for Psychophysiological Research, Denver, Sept 1998.
194. Veenhof, W., Dywan, J., & Segalowitz, S.J. (1998). ERP and Vagal tone indices of source memory and inhibitory control in aging. Society for Psychophysiological Research, Denver, Sept 1998.
195. Veenhof, W., Murphy, T., Hopkins, M., Chevalier, H., Pailing, P., Ogilvie, R.D., & Sgelaowitz, S.J. (1998). Vagal tone during EEG-defined sleep transitions. Sleep Research Society, June 1998, New Orleans.
196. Veenhof, W., Dywan, J., Segalowitz, S.J., & James, T. (1998). Physiological reactivity to repetition recency influences source memory decisions in older adults. Cognitive Aging Conference, April 1998, Atlanta.
197. Hopkins, M.J., Dywan, J., & Segalowitz, S.J. (1998). Electrodermal activity to facial expression in TBI: Support for somatic marker theory. International Neuropsychological Society, Feb 1998, Honolulu.
198. Segalowitz, N.S., Poulsen, C., & Segalowitz, S.J. (1998). RT coefficient of variation is differentially sensitive to executive control involvement in an attention switching task. TENNET, June 1998, Montreal.
199. Hopkins, M.J., Dywan, J., & Segalowitz, S.J. (1998). Electrodermal activity to facial expression in TBI: Support for somatic marker theory. International Neuropsychological Society, Feb 1998, Honolulu.
200. Segalowitz, S.J., Chevalier, H., Rose-Krasnor, L., & Nadon, R. (1998). ERP correlates of neuroticism, extraversion and shyness. International Neuropsychological Society, Feb 1998, Honolulu.
201. Chevalier, H., Segalowitz, S., Dywan, J., Rose-Krasnor, L., & Nadon, R. (1997). ERP reactivity to socially-relevant stimuli: A test of Gray's model. Society for Psychophysiological Research, Oct 1997, Cape Cod, MA.
202. Veenhof, W., Hopkins, M., Chevalier, H., Pailing, P., Ogilvie, R.D., & Segalowitz, S.J. (1997). Vagal tone: Changes across sleep stage and time of night. Associated Professional Sleep Societies, June 1997, San Francisco.
203. Segalowitz, S.J. & Theal, G. (1996). Stimulus discriminability and dual task affect the N2 and P3 separately: An auditory oddball additive factors ERP study. Society for Psychophysiological Research, October 16-20, 1996, Vancouver.
204. Chambers, E.A., Ostaniewicz, A.J., Segalowitz, S.J., Ogilvie, R.D., & Mericer, S. (1996). Information processing during slow wave sleep. Society for Psychophysiological Research, October 16-20, 1996, Vancouver.
205. Ostaniewicz, A., Kacsmar, E., Ogilvie, R.D., & Segalowitz, S.J. (1996). Distribution of electrodermal activity in slow wave sleep. Associated Professional Sleep Societies, June 1996, Washington, D.C.

206. Segalowitz, S.J., Segalowitz, N.S., & Wood, A.G. (1996). Assessing the development of automaticity in second language word recognition. International Congress of Psychology, August 16-21, 1996, Montreal, Canada.
207. Velikonja, D. & Segalowitz, S.J. (1996). Effects of caffeine on ERP and EEG indices of attention. International Neuropsychological Society, February 14-17, 1966, Chicago, IL.
208. Bernstein, D.L., Lawson, S. & Segalowitz, S.J. (1996). Subtle cognitive deficits in high functioning university students with mild head injury. International Neuropsychological Society, February 14-17, 1966, Chicago, IL.
209. Segalowitz, S.J., Rose-Krasnor, L., Rae, H. (1995). ERP support for a limbic reactivity model of temperament inhibition. Society for Psychophysiological Research, October 11-15, 1995, Toronto.
210. Dywan, J., Segalowitz, S.J., Hendry, K. (1995). The late positivity P300 is not an automatic response to item repetition. Society for Psychophysiological Research, October 11-15, 1995, Toronto.
211. Segalowitz, S.J., Gasbarre, L., Busse, S. (1995). Acute ethanol-induced alterations of ERP components at a low dose. Society for Psychophysiological Research, October 11-15, 1995, Toronto.
212. Segalowitz, S.J., Van Roon, P., Dywan, J. (1995). Support for an index view of the repetition late positivity effect. Society for Psychophysiological Research, October 11-15, 1995, Toronto.
213. Segalowitz, S.J. & Armilio, M. (1995). There are many sufficient but no necessary factors modulating P300 amplitude: Support for a salience model. Society for Psychophysiological Research, October 11-15, 1995, Toronto.
214. Segalowitz, S.J., Bernstein, D.M., Lawson, S. (1995). Lower amplitude P300 in mild head injury in the absence of objective behavioural sequelae. Society for Psychophysiological Research, October 11-15, 1995, Toronto.
215. Velikonja, D. & Segalowitz, S.J. (1995). Sustained and selective attention as reflected in auditory ERP components. Society for Psychophysiological Research, October 11-15, 1995, Toronto.
216. Segalowitz, N., Watson, V., Segalowitz, S.J. (1995). New RT variability analysis identifies automatization of word recognition in n=1 design. American Psychological Society, July 1995, New York, NY.
217. Dywan, J., Segalowitz, S.J., DiMatteo, L., & Murphy, W. (1995). Late slow potential indices of face recognition in prosopagnosia. TENNET, May 10-12, 1995, Montreal.
218. Storrie-Baker, J., Segalowitz, S.J., Black, S.E., Crowne, D.P., McLean, J.A., & Sullivan, N. (1995). EEG support for the arousal hypothesis in hemispatial neglect among 42 unilateral stroke patients. International Neuropsychological Society, February 8-11, 1995, Seattle, WA.
219. Dywan, J., Segalowitz, S.J., Murphy, W., Murphy, T., & Yonelinas, A. (1995). Source monitoring: ERP evidence for changes in memory experience with age. International Neuropsychological Society, February 8-11, 1995, Seattle, WA.
220. Segalowitz, S.J., Marsman, I., Unsal, A., & Van Roon, P. Context, meaning, and subjective probability factors in P300 amplitude: Trying to sort them out. Society for Psychophysiological Research, October 6-9, 1994, Atlanta, GA.
221. Murphy, T., Alloway, C.E.D., Lamarche, C.H., Ogilvie, R.D., Bernstein, D.M., Marsman, I., & Segalowitz, S.J. The relationship between the AAT and objective and subjective measures of sleepiness during 28 hours of sleep deprivation. Society for Psychophysiological Research, October 6-9, 1994, Atlanta, GA.
222. Murphy, T., Bernstein, D.M., Marsman, I.A., Segalowitz, S.J., Alloway, C.E.D., Lamarche, C.H., & Ogilvie, R.D. EEG and ERP indices of arousal during 28 hours of sleep deprivation. Society for Psychophysiological Research, October 6-9, 1994, Atlanta, GA.
223. Velikonja, D. & Segalowitz, S.J. The effect of stimulant medications on the auditory ERP: A case study. Society for Psychophysiological Research, October 6-9, 1994, Atlanta, GA.

224. Murphy, W., Segalowitz, S.J., Dywan, J., Ogilvie, R., Murphy, T., & Lawson, S. Mild head injury, sleep dysfunction and stimulant intake. Association of Professional Sleep Societies, June 4-9, 1994, Boston, MA.
225. Storrie-Baker, H.J., Segalowitz, S.J., Black, S.E., Crowne, D.P., Maclean, J.A.G., & Sullivan, N. An electrophysiological test of the arousal-hemispatial neglect hypothesis. Society for Neuroscience, 1993, Washington, D.C.
226. Segalowitz, S.J., Dywan, J., & Unsal, A. P300 amplitude and attentional control in a TBI population. TENNET, May 1993, Montreal.
227. Dywan, J. & Segalowitz, S.J. Electrophysiological correlates of family-reported behaviour after traumatic brain injury. INS, Galveston TX, February 1993.
228. Segalowitz, S.J., Lawson, S., & Berge, B. Unreported head injury in the general population: Subtle residual effects. INS, Galveston TX, February, 1993.
229. Velikonja, D. & Segalowitz, S.J. The effects of caffeine on electrophysiological indicators of cortical arousal. INS, Galveston TX, February 1993.
230. Storrie-Baker, H.J., Segalowitz, S.J., Black, S.E., McLean, J.A.G., & Sullivan, N. Improvement of hemispatial neglect with cold-water calorics: An electrophysiological investigation. INS, Galveston TX, Feb 1993.
231. Velikonja, D. & Segalowitz, S.J. The effects of caffeine on cortical arousal. Society for Neuroscience, October 1992.
232. Segalowitz, N.S. & Segalowitz, S.J. Effects of practice on performance: Distinguishing speedup from automatization. XXV International Congress of Psychology, Brussels, July 1992.
233. Segalowitz, S.J. The Developmental Neurobiology of Max de Crinis: Neuropsychology catches up 60 years later. TENNET, May 1992, Montreal.
234. Segalowitz, S.J., Unsal, A., & Dywan, J. Cleverness and wisdom in 12-year-olds: Electrophysiological evidence for late maturation of the frontal lobe. TENNET, May 1992, Montreal.
235. Segalowitz, S.J. & Barnes, K.L. Two-year retest reliability of endogenous components of the auditory oddball ERP. TENNET, May 1992, Montreal.
236. Unsal, A., Segalowitz, S.J. & Dywan, J. Latency jitter as a variable in the attentuation of P300 amplitude in head injured. International Neuropsychological Society, February 1992, San Diego.
237. Dywan, J., Segalowitz, S.J., & Williamson, L. Memory for source in older adults: Electrophysiological and psychometric correlates. International Neuropsychological Society, February 1992, San Diego.
238. Segalowitz, S.J., Unsal, A. & Dywan, J. ERP and behavioural reaction time variability in head injury. International Neuropsychological Society, February 1992, San Diego.
239. Berge, B. & Segalowitz, S.J. The power of the Geschwind-Behan hypothesis? International Neuropsychological Society, February 1992, San Diego.
240. Segalowitz, S.J. & Ogilvie, R.D. ERP evidence of information processing at the onset and during sleep. Society for Clinical and Experimental Hypnosis, October, 1991, New Orleans.
241. Segalowitz, S.J., Dywan, J. & Ismailos, L. Electrocortical evidence that hypnotically-induced hallucinations are experienced. Society for Clinical and Experimental Hypnosis, October, 1991, New Orleans.
242. Segalowitz, S.J., Ogilvie, R.D., Janicki, M., Simons, I. & Buetow, C. ERP Evidence for the Paradox of REM Sleep: Attention and Distraction While Awake and While Asleep. Sleep Research Society, June, 1991, Toronto.
243. Segalowitz, S.J., Unsal, A. & Dywan, J. CNV evidence for the distinctiveness of frontal and posterior neural processes in a traumatic brain injured population. TENNET, May 1991, Montreal.
244. Segalowitz, S.J. & Stewart, J. Evidence for separated semantic systems for verbal and picture information. TENNET, May 1991, Montreal.

245. Segalowitz, N.S. & Segalowitz, S.J. Automatization of language skill: Clues from the coefficient of variation. TENNET, May 1991, Montreal.
246. Dywan, J., Segalowitz, S.J., Henderson, D. & Jacoby, L.L. Source monitoring as distinct from recall and recognition memory in traumatic brain injury. TENNET, May 1991, Montreal.
247. Segalowitz, S.J. & Brown, D. Mild head injuries as a source of developmental disabilities. Presented at Society for Research in Child Development, April 18-20, 1991, Seattle, WA.
248. Dywan, J., Segalowitz, S.J. & Unsal, A. Neuropsychological correlates of health risk in the elderly. TENNET, Montreal, May 10-12, 1990.
249. Segalowitz, S.J., Dywan, J. & Unsal, A. P300 correlates of memory span decline. TENNET, Montreal, May 10-12, 1990.
250. Segalowitz, S.J., Ogilvie, R.D & Simons, I.A. An ERP State Measure of Arousal Based on Behavioral Criteria. European Sleep Research Society, Strasbourg, France, May 20-25, 1990.
251. Segalowitz, S.J. On the Nonspecial Nature of Neuropsychology. In the symposium "Group studies or the single case design? Methodological problems in cognitive neuropsychology", International Neuropsychological Society, Orlando, Florida, February 1990.
252. Organizer of symposium for CPA Section 23 on Clinical Neuropsychology "The Role of Frontal Lobe Maturation in Child Development." Canadian Psychological Society, June 1989, Halifax, N.S.
253. Segalowitz, S.J. Frontal lobe functions as a model for child development. Canadian Psychological Society, June 1989, Halifax, N.S.
254. Segalowitz, S.J. & Wagner, W. J. Frontal lobe EEG correlates of memory and thinking in adolescence. Canadian Psychological Society, June 1989, Halifax, N.S.
255. Segalowitz, S.J., Wagner, W.J., Menna, R. & Watmough, D. Electrophysiological trait correlates of memory span in 15-year-olds. International Neuropsychological Society, Feb 1989, Vancouver, B.C.
256. Segalowitz, S.J. & Schultz, K. Detecting inter- and intrahemispheric specialization of function: are 4 electrodes enough? International Neuropsychological Society, February 1989, Vancouver, B.C.
257. Weber, M.A. & Segalowitz, S.J. The attentional capacity test (ACT) for children. International Neuropsychological Society, February 1989, Vancouver, B.C.
258. Dywan, J., Segalowitz, S.J. & Otis, L. Recall interference and the prototype shift in recognition. Canadian Psychological Association, June 1988, Montreal.
259. Schultz, K. & Segalowitz, S.J. Solution strategy, performance, and EEG activity. Canadian Psychological Association, June 1988, Montreal.
260. Segalowitz, S.J., Menna, R. & MacGregor. Left and right hemisphere participation in reading: evidence from ERPs. International Neuropsychological Society, July, 1987, Barcelona, Spain.
261. Segalowitz, J.S. & Chapman, J.S. Laterality development in prematurely born children. Society for Research in Child Development, April 1987, Baltimore, Maryland.
262. Archer, L., Campbell, D., Segalowitz, S.J. & Cunningham, C. Handedness in toddlers and its relation to language development. Society for Research in Child Development, April 1987, Baltimore, MD.
263. Segalowitz, S.J. & MacGregor, L. ERP correlates of reading phonologically regular and nonregular English words. International Neuropsychological Society, February 1987, Washington D.C.
264. Orr, C. & Segalowitz, S.J. Psychometric and demographic variables in brain lateralization. Canadian Psychological Association, June 1986, Toronto.
265. Segalowitz, S.J. Hemispheric EEG asymmetries for emotional faces. International Neuropsychological Society, February 1985, San Diego, CA.
266. Segalowitz, S.J. & Plantery, P. The left ear hears music louder and the right ear hears speech louder. International Neuropsychological Association, February 1984, Houston.
267. Segalowitz, S.J. Left visual field dominance in free-field perception of ambiguous faces. Canadian Psychological Association, June 1984, Ottawa.

268. Segalowitz, S.J. Organizer of a symposium on "Genetic Determinism and Developmental Psychology", Biennial Waterloo Conference on Child Development, May 1984, including paper "The concept of epigenesis and the psychology/biology interface."
269. Horne, B. & Segalowitz, S.J. Metaphorical language use and users. Canadian Psychological Association, June 1983, Winnipeg.
270. Segalowitz, S.J. & Cohen, H. Right hemisphere sensitivity to speech. Canadian Psychological Association, June 1982.
271. Segalowitz, S.J. Some metatheoretical problems in psychology: reversals of logic, fudge factors and Godel's theorem. University of Waterloo Conference on Child Development. May 1982.
272. Organizer of a symposium "Inferring brain organization in individuals from experimental procedures." International Neuropsychological Society, February 1982.
273. Segalowitz, S.J. Evaluation of some paradigms for statistical treatment of case studies. International Neuropsychological Society, February 1982.
274. Segalowitz, S.J. & Orr, C. How to measure individual differences in brain lateralization: demonstration of a paradigm. International Neuropsychological Society, February 1981.
275. Segalowitz, S.J. & McNaughton, H. Lateral eye movements and cerebral activation: effect of question types. International Neuropsychological Society, February 1980.
276. Segalowitz, S.J. Does bilateral word reading measure brain lateralization, differential information in the words, or attentional scanning? APA, September 1979.
277. Segalowitz, S.J. & Chapman, J.S. Cerebral asymmetry for speech in neonates: a behavioural measure. American Psychological Association, August 1978.
278. Organizer of symposium "Mental representation of agent-patient relations," Canadian Psychological Association, June 1978.
279. Segalowitz, S.J. The agent priority in events in motion and still pictures. Canadian Psychological Association, June 1978.
280. Bebout, L.J., Segalowitz, S.J. & White, G. The development of children's comprehension of cause-effect sentences. Canadian Psychological Association, June 1978.
281. Petrie, B. & Segalowitz, S.J. The use of fetal heart rate as a predictor of sex. Canadian Psychological Association, June, 1977.
282. Stewart, C. & Segalowitz, S.J. Sex differences in hemispheric specialization. Canadian Psychological Association, June 1977.
283. Segalowitz, S.J. & Benjafield, J. The Golden Section: some horses refuse to die. Canadian Psychological Association, June, 1976.
284. Segalowitz, S.J. & Brown, C. Does verbal man perceive events differently from preverbal man? McMaster University Annual Conference on Child Development, May, 1976.

INVITED TALKS

University Colloquia:

1. Queen's University (Psychology) 15/11/2019 "Free Will, Agency, and Strategies for Build Developmental Neural Models"
   Brock University (Psychology) 9/3/2017 "When does meaning happen in the brain? And What does 'meaning' mean?"
2. McMaster University (Language & Linguistics) 23/11/2016, "When Do We Know the Meaning of a Word (or a Picture), and What Does this Meaning Mean?
3. Leiden University (Psychology Department) 17/10/2016, "Redefining the role of the Medial Prefrontal Cortex from Advances in ERP Methods"
4. McMaster University (Psychology, Neuroscience & Behaviour) 24/04/2015, "The current revolution in EEG/ERPs Getting past the scalp, the Time-Frequency confound and the GLM, and getting into the brain on its terms!"
5. York University (Psychology, Developmental Labs), 14/3/2014, "An Inside Look at Brain Responses to Reading: Mapping word fluency onto neural (EEG) networks, their consistency and connectivity using ICA and bootstrapping".
6. McMaster University (Psychology, Neuroscience and Behaviour) 17/11/11, "Self-regulation and the medial prefrontal cortex: on the automaticity of controlled processing".
7. University of Haifa (Edmond J. Safra Brain Research Center for the Study of Learning Disabilities) 26/05/10, "Medial Frontal Cortex and Self-Regulation: Individual Differences and Development".
8. Université Paris Descartes (Institut de Psychologie) 17/05/10, "Tracing the Individual Face and the Individual Perceiver with the P100 and N170 of the Event-Related Potential".
9. Pennsylvania State University (Child Study Centre/Psychology Dept) 3/12/09, "The Development of and Individual Differences in Medial Frontal Cortex and Self-Regulation"
10. University of Padova (Psychology Dept) 27/05/08, "Self-regulation and the Medial Prefrontal Cortex: from Normal Development to Psychopathy"
11. University of Tübingen (Institute for Medical Psychology) 19/05/08, "Self-regulation and the Medial Prefrontal Cortex: from Normal Development to Psychopathy"
12. University at Buffalo (Psychology Dept) 29/04/08 "The anterior cingulate cortex: Its high variability and the implications for self-regulation"
13. OISE (U of Toronto, Human Development and Applied Psychology) 22/2/08 "The caring and coordinated cortex: A developmental and individual differences view of performance monitoring ERPs"
14. Brock University (Psychology, LDRC) 2/3/07 "The brain's response to making errors: Why some people seem to care more than others"
15. Brock University (Child and Youth Studies), 25/1/07 "The role of neuroscience in historical and contemporary theories of human development"
16. McMaster University (Psychology, Neuroscience & Behaviour), 23/11/06 "Individual differences in the error-related negativity (ERN): A window on self-regulation?"
17. Brock University (Psychology), 10/2/05 "The rapid rise of Phrenology in the 19 C and the struggle to save the soul"
18. Université de Montréal (GRENEC), 21/11/03 "The Error-Related Negativity (ERN) and Performance Monitoring the neural interface between cognition and emotion?"
19. Brock University (Psychology), 3/3/03 "Oops ERPS"
20. Brock University (Physics), 13/2/03, "Finding electrical source generators in the human brain from scalp EEG"
21. Brock University (Psychology), 9/2/00
22. State University of New York at Buffalo (Center for Cognitive Science), "Pushing around the P300 event-related potential: Attentional control and allocation", 2/12/98
23. University of Toronto (Psychology - Scarborough Campus), 12/11/98
24. University of Otago (Psychology Dept), 22/6/98
25. University of Canterbury (Psychology Dept), 25/5/98
26. University of Waterloo (Behavioural Neuroscience Division (Psychology)), 15/12/97
27. York University (Cognitive Science (Psychology) group), 4/12/97
28. Rochester Technical Institute of the Deaf (RIT, Rochester), CRTL, 2/6/97
29. University of Ottawa (Psychophysiology Group), 7/5/97

30. Brock University (Biology Dept), 13/2/97
31. Rotman Research Institute (at Baycrest Centre), University of Toronto, 27/1/97
32. Brock University (Psychology Dept), 5/12/96
33. INSERM (Salpetriere Hospital) Neuropsycholgie clinique de l'enfant & CNRS Cognition et dévellopement (Paris V), 20/6/96
34. U of Tuebingen (Dept of Medical Psychology), 14/6/96
35. Kliniken Schmieder, Allensbach (U Konstanz), Germany (12/6/96)
36. MRC Applied Psychology Unit, Cambridge, U.K. (8/5/96)
37. MRC Applied Psychology Unit, Cambridge U.K. (18/4/96)
38. Cuban Neuroscience Center, Havana (22/12/95)
39. National Autonomous University of Mexico, Faculty of Psychology (16/8/95)
40. McMaster University, Dept of Psychology (Psychobiology) (2/12/94)
41. CNRS Unité de Psychophysiologie Cognitive (Univ de Paris 6), Hôpital de la Salpétrière (3/6/94)
42. Brock University, Dept of Psychology (25/3/94)
43. University of Waterloo, Dept of Psychology (Biopsych) (15/3/93)
44. Brock University, Dept of Biology (4/2/93)
45. Brock University, Dept of Psychology (11/11/92)
46. University of North Carolina at Chapel Hill, Developmental Psychology (2/4/1992)
47. University of Victoria, Department of Psychology (10/2/1992)
48. Bowman Gray Medical School, Department of Neuropsychology (19/1/1992)
49. University of North Carolina at Greensboro, Department of Psychology (17/1/1992)
50. University of Ottawa, Faculty of Education (14/11/1991)
51. OISE, Dept of Applied Cognitive Science (1990)
52. York University, Department of Psychology, Cognitive Science Program (1989)
53. Brock University, Department of Biology (1988)
54. University of Winnipeg, Dept. of Psychology (1988)
55. Concordia University, Dept. of Psychology (1988)
56. University of Waterloo, Dept. of Psychology (Division of Biopsychology) (1987)
57. University of Victoria, Dept. of Psychology (1987)
58. University of Winnipeg, Dept of Psychology (1987)
59. Université du Québec à Montréal, Groupe en neurosciences (1986)
60. University of Wisconsin, Dept of Psychology (1986)
61. Southern Illinois University, Dept of Psychology,
62. The Center for Psycho-and Neurolinguistic Studies (1986)
63. Université de Québec à Montréal, Groupe en neurosciences (1985)
64. Brock University, Humanities group (1982)
65. Clarke Institute of Psychiatry (1982)
66. University of Waterloo, Dept of Psychology (1980)
67. Brock University, Department of Psychology (1979)
68. University of Alberta, Dept of Linguistics (1977)

Others (*=invited):

1. *Segalowitz, S.J. "The Meaning of "Meaning" as a Cortical Process" Keynote Address, TABU Dag 2018, Groningen, Netherlands, June 14-15 2018.
2. *Segalowitz, S.J. "Self-Control of Self-Control: How do We Get to be in Charge?" Keynote Address, Science Atlantic (Psychology), Cape Breton University, Sydney, NS, May 25, 2017.
3. *Segalowitz, S.J. & Desjardins, J. "EEG/ERP: Advanced analyses and the role of high performance computing". Ontario Brain Institute workshop on "EEG/MEG/ERP: Identifying Priorities and Opportunities in Methodologies and Standardization". Toronto, Apr 23, 2014.
4. *Segalowitz, S.J., van Noordt, S., & Desjardins, J. "Why Cognitive Electrophysiology Needs High Performance Computing". Second Brock-Kobe Bilateral Workshop On Scientific Computation, Brock University, Aug 20-21, 2013.

5. *Desjardins, J. & Segalowitz, S.J. Integrating Electrophysiology into High Performance Computing. Second Brock-Kobe Bilateral Workshop on Scientific Computation, Brock University, Aug 20-21, 2013.
6. *Jetha, M.K. & Segalowitz, S.J. "Brain Developmental from Pre-Adolescence to Young Adulthood: Implications for Policy and Service Delivery", keynote address to the SPARKS Research Conference (webcast), Ontario Ministry of Children and Youth Services, Nov 23 2011.
7. *Segalowitz, S.J. "The Development of Cognitive and Emotional Self-Regulation in Children and Adolescents", keynote address: Science Learning and Educational Neuroscience, National Kaohsiung University, Taiwan, May 10-12, 2011.
8. *Segalowitz, S.J. "Adolescent Brain Development", keynote address: Science Learning and Educational Neuroscience, National Kaohsiung University, Taiwan, May 10-12, 2011.
9. *Dywan, J. & Segalowitz, S.J. ""Scientific Publication and the Peer Review Process" Panel Discussion, National Kaohsiung University, Taiwan, May 10-12, 2011.
10. Symposium Organizer: Behavioral and emotional self-regulation in children: Relations with the Nogo N2. SPR, Portland, OR, Sept 29 – Oct 3, 2010.
11. Symposium Organizer: The N170s Special Relation with Face Perception: How, Why and Where? SPR, Berlin, Oct 21-24, 2009.
12. *Segalowitz, S.J. "The development of individual differences in medial frontal cortex and self-regulation". Keynote address: Physiology of Human Development, Moscow, Russia, June 22-24, 2009.
13. *Southern Ontario Neuroscience Association (SONA) plenary address: "Risk-taking and the anterior cingulate cortex: How the brain regulates our unwise behaviour (or doesn't !)". May 8 2009
14. *Segalowitz, S.J. "The Meaning of the MFN: Learning from Individual Differences". Presented at Humboldt University workshop "Conflict as signals", Binz, Germany Sept 21-23, 2007.
15. Dywan, J., Mathewson, K.J., Choma, B.L., Rosenfeld, B. & Segalowitz, S.J. Cardiac Vagal Tone Predicts both Negative Affect and Error-Related ERPs in Older and Younger Adults. Presented at "Errors, Conflicts, and Rewards: The role of medial frontal cortex in cognitive control and performance monitoring", Amsterdam June 8-10, 2006.
16. *Segalowitz, S.J. "Using individual differences to explore medial frontal cortex functions". Invited presentation to "Errors, Conflicts, and Rewards: The role of medial frontal cortex in cognitive control and performance monitoring", Amsterdam June 8-10, 2006.
17. Anthony Folino, James Desjardins & Sid Segalowitz "Induced cortical EEG gamma and the attentional visual P300". Southern Ontario Neuroscience Association (SONA), May 4, 2004.
18. Karen Mathewson, Jane Dywan & Sid Segalowitz "Error-monitoring ERPs, aging, and heart-rate variability". Southern Ontario Neuroscience Association (SONA), May 4, 2004.
19. Bill Tays, Anthony Folino, Jane Dywan & Sid Segalowitz "EEG gamma relates to clarity of thinking and source monitoring ERPS after mild head injury". Southern Ontario Neuroscience Association (SONA), May 4, 2004.
20. *Segalowitz, S.J., "The development of the error negativity in children and adolescents", Symposium on Errors, Conflicts, and the Brain, Dortmund, Germany, July 3-6, 2003.
21. *Dywan, J., Mathewson, K., & Segalowitz, S.J. "Error-related neural response to source-memory error in older and younger adults" , Symposium on Errors, Conflicts, and the Brain, Dortmund, Germany, July 3-6, 2003.
22. *Masaki, H. & Segalowitz, S.J. "Error negativity: A test of the response-conflict versus error detection hypotheses", Symposium on Errors, Conflicts, and the Brain, Dortmund, Germany, July 3-6, 2003.
23. *"Individual differences in Oops! ERPs: Effects of personality and motivation on error monitoring ERPs" EPOS conference on Performance Monitoring and Interference Control, Amsterdam, April 11-12, 2003
24. *"Electrophysiological Measures of Adaptive Information Processing from a Developmental Perspective" Conference on Development of Orbitofrontal Function, University of Toronto, Mar 21-23, 2002.
25. *Invited discussant for a symposium "Theoretical and Methodological Issues in EEG Research with Infants and Young Children", Society for Psychophysiological Research, Montreal, Oct 10-14, 2001.
26. *"Brain structures associated with error detection and response conflict" Symposium organized for TENNET, Montreal, June 21-23, 2001, and gave the introductory talk.
27. "From Cell to Psyche: Early development of the brain and person in the embryo" Brock University Panel Discussion on "Human Cloning: Facts and Issues". Brock University, Dec 16, 2001.

28. *"Neural Networks and Neuroscience: What are connectionist simulations good for?" Reassessing the Cognitive Revolution, York University, Glendon College, October 22-24, 1993.
29. *"Attentional allocation and capacity in waking arousal" Sleep Onset Mechanisms conference, Niagara-on-the-Lake, June 11-14, 1993.
30. *"The neuropsychology of being 'on' in performance." Interdisciplinary conference on Advanced Musical Performance: An Artist-Scientist Perspective. Concordia University, October 6-9, 1992.
31. *"The brain controlling itself: Attentional control and the development of thinking." Conference on Television and the Preparation of the Mind for Learning (U.S. Dept of Health and Human Services, Administration for Children and Families), Washington, D.C., Oct 2, 1992.
32. "Psychological and institutional barriers to pay equity". As part of the symposium "Men and women in the university", Brock University, November 27, 1989.
33. Undergraduate Thesis Conference (Man., Sask., Alberta, N. Dakota), Keynote address "Recall is bad for your memory". Winnipeg, May 14, 1988.
34. *Southern Ontario Neuropsychology Group (SONG), November 27, 1987, Waterloo. "Reading and ERPs".
35. *Niagara Linguistics Society, November 8, 1984, Buffalo. "The brain's approach to meaning."
36. *NATO Advanced Research Workshop, "Measuring individual variation in lateralization." October 1984, Maratea, Italy.
37. *Semiotic Society of Toronto Symposium on the Semiotics of the Human Face, University of Toronto, June 1984.
38. *Symposium on Research in Language and Cognition in Bilingual Education, May 1984, Buffalo.
39. *Semiotic Society of Toronto Symposium on Gesture and Communication, University of Toronto, June 1982.
40. Concordia University, Seminar on Speech and Language Studies, "Electrophysiological techniques in speech perception." June 1982, Montreal.
41. *Linguistic Society of America Summer Institute, "Individual differences in brain lateralization: going beyond sex and handedness." Invited paper in symposium "Bilingualism and Neurolinguistics." Albuquerque, July 1980.

WORKSHOPS (since 1985)

"An Introduction to Cognitive Electrophysiology EEG/ERP Methods - Past, Present and Future", given at STEP 2019, University of Alberta, Centre for Computational Linguistics, May 15-17 2019.

"Workshop on EEG/ERP Analysis", May 6-10, 2019, Brock University

"Workshop on ERP History, Methods, and Advanced Techniques", April 23-27, 2018, Brock University

"The Coming Revolution in ERP Research", June 13 2018, Center for Language and Cognition, U of Groningen

"Workshop on ERP History, Methods, and Advanced Techniques", April 24-28, 2017, Brock University

"Middle Years Research Think Tank: Using Evidence to Support Healthy Middle Years Development", Nov 25, 2016, Ontario MCYS, Toronto

"Workshop on ERP History, Methods, and Advanced Techniques", April 25-29, 2016, Brock University

"Workshop on ERP History, Methods, and Advanced Techniques", May 25-29, 2015, Brock University

"Workshop on ERP History, Methods, and Advanced Techniques", May 19-23, 2014, Brock University

"SSHRC Day", participant-leader on grantsmanship, May 13, 2013, Brock University

"ERP technology and use", University of Victoria, Psychology Dept., July 30 – Aug 2, 2012.

"Consciousness and the Brain", PLATO group at St. Catharines Public Library, Jan 8, 2004.

"Emotion and the Brain", PLATO group at St. Catharines Public Library, Jan 18, 2003.

"The Brain", PLATO group at St. Catharines Public Library, Nov, 2001.

"Brain Growth and its Implications for Learning" workshop presented to Northern Centre for Instructional Leadership, simultaneously in North Bay, Sudbury, Timmins, and Sault Ste. Marie., June 1, 1999.

"The Growing Brain in the Developing Child" all-day Workshop delivered to University of Wisconsin-Green Bay Outreach Program, Green Bay, WI, March 13, 1998.

"Mild Head Injury: Accepting the Hypothesis of 'No Effect'", part of invited mini-workshop on Neuropsychological Assessment of Traumatic Brain Injury at the Ontario Psychological Association, Feb 20, 1998.

Discussant at the McMaster University MRC Research Group Workshop on brain plasticity, Hamilton, May 28-30, 1997.

Delegate to the National Conference on Psychology as a Science, Ottawa, May 8-11, 1997.

Workshop on "Computers and Cognitive Development", University of California, Berkeley, organized by the Center for Ecoliteracy, Nov 15-17, 1996.

Pacific Coast Brain Injury Conference, "Brain maturation during childhood and the implications of mild head injury for psychological development," October 17,1996.
National Autonomous University of Mexico, Faculty of Psychology, a one-day course on Cognitive Electrophysiology, August 13, 1995.
Niagara Rehab Speech Pathology Department, on electrophysiology of attention and arousal, June 17, 1993.
Pebble Beach Residents' Association, on "Head injury and community concerns", March 20, 1991
Welland County Separate School Board special education department, on "Building a Brain for Good Learning", November 29, 1990.
Lincoln County Board of Education presentation on "Dyslexia and brain development", October 23, 1990.
Head Injury Association Community Re-entry program (Niagara) on "The neuropsychology of closed head injury", Aug. 2, 1990.
Ontario Association for Children with Learning Disabilities annual convention, "Neuropsychological models of reading disability", April 27, 1990.
Lincoln County Public School Board, Special Services group, December 6, 1989, "Left brain/right brain/front brain/back brain: Neurodevelopmental correlates of reading disability."
FutureTech presentation on neuropsychology (Lincoln County Pub. Sch Bd), April 14, 1989.
Birds Hill School, Winnipeg, Man.: Workshop on developmental neuropsych. May 11, 1988.
Hamilton Hebrew Academy (with Dr. H. Bernstein) PTA "Child burnout: When is much too much?" May 4, 1988.
St. Catharines Unitarian Church lecture series, October 1987.
Lincoln County Public School Board, Special Services workshop, November 1985.
Hamilton-Wentworth Separate School Board interest group, June 1985.
Pemican Special Services group (Lincoln County PSB), St. Catharines, June 1985.
Ontario Secondary School Teachers Federation meeting, April 1985, Toronto. "The child and the double brain: Language and the growth of intelligence."
Presentations annually to groups of schoolchildren in enrichment classes on topics in "Brain and Behaviour", including a 2-day presentation for enrichment classes (St. Catharines S.S.B.) November 21-22, 1990 and a 3-day presentation for "Girls and Science" program, May 1990.

Public media:
St. Catharines Standard interview on memory and aging (reprinted in Toronto Star, K-W Record, La Presse, and several other Ontario newspapers), February 1988.
CBC Fresh Air, February 1989 on the neuropsychology of Aging.
CHSC (St. Catharines) Radio interview (aired on November 6, 1990) on dyslexia and brain development.
Redbook Magazine, March 1992, interview on head injury in children.
CBC Sunday Morning, June 21, 1992. Program 1 of the brain series "Cranial Pursuits".
Toronto Star, February 25, 1993, page C1.
CFRB (Toronto) interview on caffeine and electrical brain response (Feb 27, 1993).
Hamilton radio (Oldies 1150) interview on caffeine and electrical brain response (March 1, 1993).
CJAD (Montreal) interview (March 2, 1993).
Niagara Fall Review interview (March 4, 1993).
CKTB (St. Catharines) interview (March 12, 1993).
WebMD Canada Medical News, May 4, 2001
Interview with Charles Choi of UPI concerning Science paper by R. Ridderinkhof (Nov 5, 2002)
COGECO and St. Catharines Standard interviews on the founding of the Jack and Nora Walker Canadian Centre for Lifespan Development Research
Interviewed by Michael Saunders for *Inquisitive Minds* radio CFBU-FM (October 28, 2013)
St. Catharines Standard article on "Brock Research Hunts for Autism Clues" on our EEG collaboration. Aug 22, 2017, p 1.

AWARDS and HONOURS:
First Annual Research Award, Canadian Brain Injury Coalition, May 16, 1997
Brock University Award for Distinguished Research, 1997
Fellow, American Psychological Society (Association for Psychological Science), elected June 2002
Graduate (MA/PhD) Mentorship Award, April 2013

Release time awards (Brock U)
Release Time Research Award, Brock University, 1992-93.

Release Time Research Award, Brock University, 1994-95.
Release Time Research Award, Brock University, 1996-97.
Release Time Research Award, Brock University, 1998-99.

TEACHING EXPERIENCE

Undergraduate courses:
History of Psychology
Research Methods in Psychology
Maturation and Development
Human Neuropsychology
Cognitive neuropsychology
Neurolinguistics
Honours Seminar: Contemporary issues in psychology
Child Psychology
Advanced Issues in Developmental Psychology
Language Development
Introductory Psychology (special 5-week summer course)

Graduate courses:
Human Neuropsychology (at UNCG 1992)
Cognitive Electrophysiology
Statistics (univariate).
Child Psychology and Developmental Neuroscience.

External examiner
for Ph.D.

City University of New York (Department of Psychology) 1986
Queen's University (Department of Psychology) 1986
McMaster University (Department of Psychiatry) 1987
University of Waterloo (Department of Kinesiology) 1987
University of Waterloo (Department of Psychology) 1988
University of Toronto (Dept of Applied Cognitive Science - OISE) 1989
University of Toronto (Dept of Applied Cognitive Science - OISE) 1989
Queen's University (Department of Psychology) 1990
York University (Department of Psychology) 1993
University of Ottawa (Department of Psychology) 2001
Université de Montréal (Neuroscience) 2007
University of Tasmania (Psychology) 2010
Western University (Psychology) 2011
University of Toronto (Dept of Human Development and Applied Psychology– OISE) 2012
Waterloo (Psychology) 2015

for Masters

Brock University (Faculty of Education) 1987
Brock University (Faculty of Education) 1990
McGill University (Dept of Communication Sciences and Disorders) 1994

Reviewing of external PhD Proposal:

Dissertation research proposal – U of Haifa, Dept of Psychology, Sept 2013

REVIEWING EXPERIENCE

Journals

Brain and Cognition, Oct 2002 - 2014: Editor-in-Chief
Brain and Cognition, 1998 -2002: Associate Editor

Editorial Board Membership:

Laterality, 1995 - present

Developmental Neuropsychology, 1993 - present.
Canadian Journal of Experimental Psychology, 1988 - 2004
Brain and Language, 1984 - 2000.
Semiotic Review of Books, Neuropsychology Section Editor, 1989 - 1998
Child Development, 1980 - 1983.

Guest Consulting Editor (in addition to above):
Behavior Research Methods, Instruments, & Computers
Behavioral and Brain Sciences (BBS Associate)
Biological Psychology
Brain and Cognition
Brain Research
Canadian Journal of Education
Child Neuropsychology
Cognitive, Affective and Behavioral Neuroscience
Cognitive Development
Cognitive Neuropsychology
Culture and Psychology
Developmental Psychology
Developmental Science
Frontiers
Genes, Brain, and Behavior
International Journal of Behavioral Development
International Journal of Clinical and Experimental Hypnosis
Journal of Child Psychology and Psychiatry
Journal of Psychophysiology
Mental Lexicon
Music Perception
NeuroImage
Neuropsychologia
Neuropsychology (APA)
Perceptual and Motor Skills
Psychological Science
Psychological Bulletin
Psychological Review
Psychophysiology
Public Opinion Quarterly
Science

Granting agencies:
Ontario Mental Health Foundation, member of Grants Committee (1986-1991)
Natural Sciences and Engineering Research Council of Canada
NSERC Steachie Awards
Social Science and Humanities Research Council of Canada
Medical Research Council of Canada
National March of Dimes (U.S.A.)
Sunnybrook Medical Centre (University of Toronto)
Michael Smith Foundation
Hospital for Sick Children Foundation
National Science Foundation (U.S.A.)
National Academy of Sciences/National Research Council
Killam Fellowship Foundation (Canada Council)
International Science Foundation
US-Israel Binational Science Foundation
Fonds pour la Formation de Chercheurs et l'Aide (FCAR, Québec)
NIH (USA)
Wellcome Trust (UK)
MRC (UK) of their Cognition and Brain Sciences Unit, Cambridge

Bellagio Committee (Rockefeller Foundation)
Canadian Institutes of Health Research
City University of New York (CUNY Collaborative Incentive research grant Program)
German Research Foundation

Evaluation of colleagues for promotions at other institutions (not job applications)
U of Toronto (Psychology)
York U (Psychology)
McMaster U (Psychiatry)
U California, Riverside (Psychology)
U Boston (Psychology)
Southern Illinois U (Psychology, Medicine)
SUNY Buffalo (Medicine)
U California, Riverside (Psychology)
Rice University (Psychology)
University of Connecticut (Psychology)
American Psychological Society (as Fellow)
Colorado State University (Psychology)
University of California, Riverside (Psychology)
University of Amsterdam (Psychology)
Yale University (Child Study Center, Yale School of Medicine), 2007
CUNY (Psychology), 2007
Steacie Award, 2007
Freiberg (Psychology), 2007
University of Victoria (Psychology), 2007
New School for Social Research (Psychology), 2007
Brown University (Dept of Clinical Neurosciences), 2007
Simon Fraser University (Psychology), 2008
University of Haifa (Psychology), 2009
State University of New York at Stonybrook (Psychology), 2009
Dartmouth College (Education), 2010
University of Haifa (Dept of Communication Sciences and Disorders), 2012
Tel Aviv-Yaffo Academic College (Behavioral Sciences), 2012
CUNY (John Jay College of Criminal Justice, Psychology), 2013
Yale University (Child Study Center), 2018

CONFERENCE ORGANIZATION

Reward and Regulation in Adolescence: contexts for positive growth, June 23 -24, 2011, Brock University
Scientific committee for ICON9, Havana, Sept 2005.
Founding Chair and Member of the Programme Committee and co-organizer of BABBLE: An Annual Conference Reporting Research in the Neuropsychology of Language. Niagara Falls, 1978, 1979, 1980, 1981, 1982, 1983, 1984, 1985, 1986, 1987, 1988, 1989. Continuing as TENNET (Theoretical and Experimental Neuropsychology / Neuropsychologie Expérimentale et Théorique), Montreal 1990, 1991, 1992, 1993, 1994, 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004.
Member of the Program Committee for the March 2004 meeting of EPIC 14, Leipzig.
Member of the Program Committee for the 2002 meeting of the INS meeting, Toronto, ON (Journal of International Neuropsychological Society, 8(1), 2002).
Co-organizer (with D. Molfese, Southern Illinois University) of "A Developmental Agenda for Neuropsychology" held at Brock University, July 13-15, 1995.
Program Co-chair (with J. Dywan) of the International Neuropsychological Society meeting, February 8-11, 1995, in Seattle, WA (Journal of the International Neuropsychological Society, 1(2), 1995).
Co-organizer (with L. Rose-Krasnor) of "The Role of Frontal Lobe Maturation in Cognitive and Social Development" held at Brock University, May 12, 1989.
Member of the Program Committee for the 1989 meeting of the INS meeting, Vancouver, B.C. (Journal of Clinical and Experimental Neuropsychology, 11(1), 1989).

Co-organizer (with D. Molfese, Southern Illinois University) of "Developmental Implications of Brain Lateralization" held at Brock University, May 16-18, 1985.
Co-organizer (with L. Cooper, Cornell University) of the LOVE Conference on Perception and Cognition, February 1983.
Co-organizer (with G. Glavin, Brock University) of the 1978 Psychology Undergraduate Thesis Conference (Ontario), held at Brock University, April 1978.
Co-organizer (with N. Johnston, Brock U., and F. Gruber, Niagara CDC) of "Language Development and Neurological Theory" held at Brock University, May 1975.

GRANTS RECEIVED

Canada Council Doctoral Fellowships, 1971-1974
Canada Council Conference Grant, 1975 $ 3,474
Canada Council: "The language of causality and its acquisition", 1977-1979 $ 9,985
National Research Council: "A process approach to cerebral asymmetries", 1976-79 $ 19,800
Ontario University Program in Instructional Development: "Improving writing skills in university students", 1977-1979 $ 2,250
NSERC: "Measures of individual differences in cerebral asymmetries", 1980-1983 $ 25,500
SSHRC: "Hemisphericity: a clue to personality/cognitive style?" Leave Fellowship, 1980-1981 $ 2,500
Health and Welfare Canada, with J.S. Chapman: "Incidence and degree of laterality preference and cerebral dominance for speech as related to prematurely born 5 year olds", 1981-1984 $ 81,000
Natural Sciences and Engineering Research Council: "Concept formation: brain correlates using ERPs" 1983-1986 (extended to 1988) $ 32,400
Natural Sciences and Engineering Research Council: Equipment grant for a PDP-11/23+, with R. Ogilvie & J.O. Mitterer, 1983-84 $ 12,750
Instructional Development Grant (Brock University) 1984-1985 $ 1,500
NSERC: Conference grant for "Developmental Implications of Brain Lateralization, 1985 $ 6,118
National Institute of Disability and Rehabilitation Research (USA): "Behavioural and electrophysiological correlates of traumatic head injury" as part of a proposal for a Research and Training Center on Community Integration of Persons with Traumatic Brain Injury, with J. Dywan. 1988-1993 $229,500
NSERC: "Attentional resources and Attentional Control in Neuropsychological Performance" (1993-1997) $80,000
Brock University Conference/Speakers Fund Support: for conference "A Developmental Agenda for Neuropsychology", July 13-15, 1995, Brock University $ 4,225
Brock University Advancement Fund: "Cognitive Dysfunction and Disability in Fibromyalgia", with Jane Dywan: 1995-1998 $ 9,995
NSERC: "The cognitive neuropsychology of attention: ERP and EEG investigations": 1997-98 $15,000
NIH: Consultant on grant. PI: Patricia L. Davies "Cognitive Event-Related Potentials and Brain Maturation", # 1K01HD001201-01A1: Location: Fort Collins, Colorado. 1998-2003 US $418,153
NSERC: "Event-related potentials and the neuropsychology of attention and working memory": #122222-98: 1998-2002 $57,200
Ontario Neurotrauma Foundation: "The Psychophysiological Bases of Persistent Post-Concussive Complaint", with Jane Dywan and Sherrie Bieman-Copland: 1998-2001 $177,000
ORDCF BRAIN Project (Ontario-wide consortium 2001-06). Behavioral Research and Imaging Network (BRAIN). PI: A.R. McIntosh. $16,200,410 Amount for our lab: $83,000
CFI: Canadian Foundation for Innovation (PI: R Racine, McMaster university, 2002, Co-Investigators: Elliott, D., Maurer, D., Murphy, K., Offord, D., Rosenbaum, P., Schmidt, L.A., Segalowitz, S., Szatmari, P., & Trainor, L.J. Project number 5678): Optimal human development: Understanding experiential influences on brain/behaviour maturation. Total = $5,635,800. Portion for our electrophysiology labs: ~ $700,000
Ontario Ministry of Culture and Tourism: "Determining the practical value of computer based assessments in the evaluation of concussion among adolescents", Program: recreation development fund. May 2002-Aug 2003. B. Willer & S.J. Segalowitz $50,000
NIMH: Consultant on grant co-PIs: D. Peppler, J. Granic "Treating antisocial youth: Brain and behavioural changes" 1 R21 MH067357-01 Child and Adolescent Interdisciplinary Research Network: Location: Toronto. Nov 2002- Nov2005 US$405,000 US$9000
NSERC: "Event-related potentials associated with the anterior cingulate cortex" 2003-2007 #122222-03 $88,000
Pfizer, Inc, "Electrophysiological responses on the hidden spatial maze learning test" (pilot study) 2003 $32,500
CIHR: "The influence of visual deprivation on the development of human visual pathways: Neuroimaging of patients treated for congenital cataract during infancy" Maurer, D.,

Dywan, J., Segalowitz, S.J., Grady, C.L., O'Craven, K. 2004 - 2007. CIHR #36430 $312,954

CIHR: "Error-related EEG potentials as an index of change in dopaminergic systems", Stemmer, B., Segalowitz, S.J. & Dywan, J. 2004-2005 $44,814

CFI: Canadian Foundation for Innovation (P.I.: S.J. Segalowitz, with T. Willoughby & J. Dywan) "Lifespan Development Research Centre", 2004. CFI and OIT portions = $2.6M each total = $6,518,855

NSERC: "ERP Measures of Anterior Cingulate Cortex Activation" 2008-2013 #122222-2008 $134,680

OPGRC: Neurophysiological Reflections of Reward and Regulatory Responses in Gambling Tasks with Young Adults 2008-2009 $35,000

CIHR: A multidisciplinary examination of cognitive and socioemotional self-regulation in adolescence: psychosocial, neurocognitive and autonomic determinants. Segalowitz, S.J., Dywan, J., Wade, T., McCormick, C., O'Leary, D. 2008-2009 #200804MOP-190259-CHl-16209 $100,000

CFI: 2009/8 - 2013/3 Leading Edge Fund (PI: Laurel Trainor, Co-investigators : Balasubramaniam, R., Becker, S., Brown, S., Bruce, I., Roberts, L., Schmidt, L., Segalowitz, Si.J., Shore, D., Sonnadara, R.): "Auditory interaction and communication in complex environments: Neural, developmental and applied aspects". $5,866,030

CFI: Neurovisceral models of mental health and personality. Project # 24561 $91,020 Segalowitz, S.J. & Dywan, J. 2010-2015

SSHRC (RDI): "Personality and the automatic processing of facial emotion"; 2010-2012 Segalowitz, S.J., Mondloch, C., Ashton, M. (collaborator), Hodson, G. (collaborator) $34,000

Ontario Ministry of Child and Youth Services: "Research Synthesis on Adolescent Brain Development and Implications for Behaviour" 2010-2011 Segalowitz, S.J. & Jetha, M.K. $71,160

Canadian Foundation on Fetal Alcohol Research: "Mindfulness Training and Its Impact on Cognitive & Emotional Functioning in FASD" Smart, C., Kerns, K. & Segalowitz, S.J. 2012-2014 $65,000

OPGRC: The role of prefrontal regulatory control in response and choice impulsivity in gamblers: A behavioural and electrophysiological study (#3482). 2013 – 2014. Santesso, D., Harrigan, K. & Segalowitz, S.J. $42,000

Brock University Transdisciplinary Space Program: Community-based research and training. Jan 2013 – Dec 2018. Segalowitz, S.J. & Willoughby, T. $1,000,000

NSERC: "ERPs and the Dynamics of Adaptive Attentional Control in the Prefrontal Cortex", 2013-2018 #122222-2013 $200,000

Ontario Brain Institute (OBI): Childhood Cerebral Palsy Integrated Discovery Network "CP-NET": 2013-2018. PI: D. Fehlings. CP-NET Executive: Fehlings D (Lead), deVeber G, Fehlings M, Menon R, Rosenbaum P, Scherer S. CP-NET Research Team: Ansari D, Biddiss E, Campbell C, Carter M, Chau T, Chen R, Cheyne D, Ferro M, Frid P, Gorter JW, Graham N, Hall G, Henkelman M, Kawamura A, Kingsnorth S, McCormick A, Mesterman R, Miller S, Morshead C, Palisano R, Paterson A, Pelland L, Raybaud C, Samdup D, Scott S, Segalowitz S, Shroff M, Strothers S, Taylor M, van der Kooy D, Wintle R, Wright V. $7,500,000

SSHRC: "New directions in the psychology of deservingness" Hafer, C. & Segalowitz, S.J. 2014-2019 SSHRC# 435-2014-0551 $230,310

Milligan, K., Schmidt, L.A., & Segalowitz, S.J. Enhancing Executive Functions and Emotion Regulation in Youth with Learning Disabilities through Activity-Enhanced Mindfulness Training. Harry Rosen Stress Research, 2014-2015 $3000

Milligan, K., Schmidt, L.A., & Segalowitz, S.J. Using mindfulness to address cognitive processing and emotion regulation challenges in youth with learning disabilities. Scottish Rite Charitable Foundation of Canada, 2014-2017 $104,811

Libben, G., Buchanan, L.L., Kuperman, V., Kehayia, E., Jarema, G., Järvikivi, J., & Segalowitz, S.J. Words in the World. SSHRC, 2016-2022 (#895-2016-1008) $2,499,832

Willoughby et al. Brock Healthy Youth Project. CIHR 2016-2021 (#201163) $1,433,440

MEMBERSHIPS IN PROFESSIONAL ORGANIZATIONS

Canadian Psychological Association 1974 - 2004
American Psychological Association 1974 - 2002
International Neuropsychological Society 1978 - 2006
Society for Research in Child Development 1972 - 1997
Society for Psychophysiological Research 1990 - present
Canadian Society for Brain, Behaviour and Cognitive Science 1991 - 2000
Association for Psychological Science 2001-present

RESEARCH ADMINISTRATIVE EXPERIENCE

Member of PI Committee of the Research and Training Center (USA) on Community Integration of Persons with Traumatic Brain Injury (SUNYAB, Medical School) 1988 - 1993
Director, *Lifespan Development Research Institute*, Brock University, 2007- present
Member, planning committee for the Neuroscience Initiative of the Cuba-Mexico-Canada Research Agreement of the Council for Early Child Development (Canada) 2003-2010.
McMaster Institute for Music and the Mind (MIMM), Research Management Committee member 2006-present

ADMINISTRATIVE EXPERIENCE

Psychology Department colloquium organizer 1978-1980, 1981-1982, 1986-1987, 1997-1999, 2001-02, 2010-2012
Faculty Board executive 1975-1977
Secretary of Faculty Board 1976-1977
Brock University Academic Planning Committee 1976-1977
Brock University Faculty Association (BUFA) executive, Councillor 1978-79
Merit reform committee chair of BUFA 1978-1979
Director, Child Studies Programme, July 1983 - June 1987
Fine Arts Committee of Brock University 1983-1986
Advisory Committee on the Appointment/Reappointment of a Dean of Social Sciences, 1984-85, 1990-91
Senate Subcommittee on the future of the TESL programme 1985
Member of the Advisory Board of the Niagara Head Injury Association 1987 - 1990
Member of Brock U. Research Board Committee July 1988 - 1989.
Curriculum Committee, Dept. of Psychology 1988-95.
Councillor, Brock University Faculty Association (BUFA) Executive 1989-1990
Director, Institute of Applied Human Development, 1990 - 1992
Brain Injury Community Re-entry program (Niagara), Member of Board of Directors 1990-97.
Chair, Departmental Committee on Restructuring of Duties of Chair, 1990-91.
Brock Committee on Gender-related Salary Differences 1989 - 1991.
Faculty of Social Sciences Program Committee 1992-93.
Ontario Council on Graduate Studies (OCGS) 1992-1995.
Status of Women Committee of the Brock University Faculty Association 1992-1993.
Psychology Dept Graduate Program Committee and Graduate Admissions Committee 1992-1995.
Chair, Space Committee, Dept of Psychology 7/1993 – 6/2009.
Brock University Senate: 1998-2001.
Brock University Senate Nominations Committee, Chair: 1998-99
Brock University Senate Research Committee, member: 1998-99
BUFA observer on the University Senate Research Award Committee, 1998-99
Chair, Psychology Department, 2000-2003.
Member, University Committee for selection of V.P. Administration & Finance, 2001-02
Member, Board of Trustees, 2004-2007.
Member, Users' committee, Lifespan Development Research Centre, 2004-
Member, Presidential Search Committee, 2005.
Member, CRC search committee in Aging (NSERC), 2005
Member, Provost/Academic VP Search Committee, 2008-2009.
Director, Jack and Nora Walker Canadian Centre for Lifespan Development Research, 2007-present
Member of the Reviewers Panel for the MATH department evaluation (March 2011)
ACE Advisory Committee (2011 - 15)
Mental Health Innovations Fund committee (2012)
Member, Provost/Academic VP Re-appointment/Search Committee, 2013.
Member, Brock NSERC awards adjudication committee 2012
Member, Brock SSHRC doctoral awards adjudication committee 2013
Senate faculty member, 2014-2017
Senate, Chair of Committee on Informational Technology & Infrastructure (IT&I), 2014-15
Senate, Member of Committee on Informational Technology & Infrastructure (IT&I), 2015-16, 2016-17
Senate, Member of PP&BAC, 2014-2015
Senate, Member of Policy Planning subcommittee of PP&BAC, 2014-2015

NSERC USRA selection committee, March 2018
OGS PhD University Selection committee Jan 2018

Administrative reports:
Report to Faculty Association of a study to identify possible salary anomalies attributable to gender, 1991.
Report to Faculty Association on Merit Reform, 1979.

Thesis Supervision

Service on thesis committees:
Current: 0
Life Total: 32 Ph.D., 50 Masters (supervisor on 15 Ph.D., 18 M.A.)
83 Honours theses supervised

Mentoring:
Postdoc supervisor for Michelle Jetha (Aug 2008 – 2012)
Postdoc supervisor for Diane Santesso (July 2008-2010)
Postdoc supervisor for Abbie Coy (June 15 2017-)
Postdoc supervisor for Meghan Weissflog (June 2017-)
Postdoc supervisor for Hiroaki Masaki (Japan Society for Advancement of Science), 2002.
N.I.H. mentor in electrophysiology for Dr. Patricia Davies K-01 recipient, 1998-2003.
Summer fellowship students: Avital Sternin (NSERC USRA, 2013), Alan Campopiano (NSERC USRA, 2012), David Ly (2010); William Marshall (NSERC USRA 2005, 2006), Anthony Folino (NSERC USRA 2003), Kirsti Van Dorsser (NSERC USRA, 2003).
5 NEUR coop supervisions

Thesis Supervision

Masters:
Supervisor:
1. Diane Henderson (M.Ed., Brock, 1993)
2. Ian Marsman (M.A. Brock, 1995)
3. Patricia Pailing (M.A. Brock, 1998)
4. Hélène Chevalier (M.A. Brock, 1997)
5. Mary-Claire Ferlisi (M.A. Brock, 1999)
6. Karen Baker (M.A. Waterloo, 1999)
7. Sonia Sanichara (MA, Brock, 1999-2006)
8. Diane Santesso (MA, Brock, 2000-2003)
9. Danielle Dyke (M.A., Brock, 2002-2005)
10. Xin Zheng (M.A., Brock, 2006-2008)
11. Angela Dzyundzyak, M.A., Brock, 2007-2009)
12. James Desjardins (MA, Brock, 2008-2011)
13. Meghan Weissflog (MA, Brock, 2008-2010)
14. Stefon Van Noordt (MA, Brock, 2009-2011)
15. Alan Campopiano (MA, Brock, 2013-2015)

Supervisor for students registered elsewhere:
16. Rosanne Menna (M.A., OISE, 1992)
17. Carol Orr (M.A., York, 1986)
18. Barbara Horne (M.A.Sc., Waterloo, 1988)

On committee as nonsupervisor:
1. Debby Watmough (M.Ed, Brock, 1989)
2. Wendy Murphy (M.A., Brock, 1995)
3. Tim Murphy (M.A., Brock, 1995)
4. Christi Alloway (M.A., Brock, 1995)
5. Laurie Cesnick (M.Ed., Brock, 1995)
6. Wilma Veenhof (M.A., Brock, 1997)
7. Melanie Hopkins (M.A., Brock, 1997)
8. Lorissa Goertzen (M.A., Brock, 1999)
9. Ben Williams (M.A., Brock, 1999)
10. Craig Stewart (M.A., Brock, 2000)
11. Tammy James (M.A., Waterloo, 2001)
12. Esko Vaisenan (M.A., Brock, 1997-2000)
13. Belinda SantaMaria (M.A., Brock, 1999-2003)
14. Karen Mathewson (M.A., Brock, 2000-02)
15. Gillian Munro (M.A., Waterloo, 2002-2004)
16. Bill Tays (M.A., Brock, 2002-2005)
17. Brian Smith (MA, Brock, 2005-2008)
18. Rona Kertesz (MA, Brock, 2005-2008)
19. Natalie Elms (MA, Brock, 2005-2007)
20. Lesley Capuana (MA, Brock, 2006-2008)
21. Mary Maclean (MA, Brock, 2007-2009)
22. Julie St-Cyr-Baker (MA, Brock 2007-2009)
23. Kirk Stokes (M.A., Brock, 2008-2010)
24. Ryan Renn (MA, Brock, 2010-2012)
25. Kevin MacDonald (MA, Brock, 2013-2014)
26. Nathalie Gauthier (MA, Brock, 2013-2014)
27. Sean Robb (MA, Brock, 2012-2015)
28. Josh Augustino (MA, Brock CPCF, 2012-2014)
29. Nicole Barry (MA, Brock, 2013-2016)
30. Kari Lustig (MA, Brock 2014-2016 Sept)
31. Joel Robitaiile (MA, Brock 2014-2016 Sept)
32. Brent Pitchford (MA, Brock, 2016-2018)
33. Carolyn Hare (MA, Brock, CHYS, 2018-)
34. Blake LaRiviere (MA, Brock, 2019-)
35. Sarah Henderson (MA, Brock, 2017-)

Ph.D.
Supervisor:
1. Ayse Unsal (Ph.D., Waterloo, 1988-1991)
2. Jane Storrie-Baker (Ph.D., Waterloo, 1991-1994)
3. Diane Velikonja (Ph.D., Waterloo, 1997)
4. Linda Cudmore (Ph.D., Waterloo, 1999)
5. Patty Ross (Ph.D., Waterloo, 1999)
6. Tim Murphy (Ph.D., Waterloo, 1996-2007)
7. Patricia Pailing (Ph.D., Waterloo, 1998-2004)
8. Cynthia Chan (Ph.D., Waterloo, 1999-2003)
9. Adote Anum (Ph.D., Brock, 2001-2006)
10. Diane Santesso (Ph.D., Brock, 2002-2006)
11. Xin Zheng (Ph.D., Brock, 2008-2012)
12. Chrissy Lackner (Ph.D., Brock, 2009-2015)
13. Angela Dzyundzyak (Ph.D., Brock, 2009-2014)
14. Meghan Weissflog (PhD, Brock, 2010-2017)
15. Stefon Van Noordt (PhD, Brock, 2011-2016)

On committee:
1. Linda Archer (Ph.D., McMaster, 1985)
2. Cheryl Gibson (Ph.D., Waterloo, 1986)
3. Heather McNeely (Ph.D., Waterloo, 1999)
4. Wilma Veenhof (Ph.D., Waterloo, 1997-2001 withdrawn)
5. Karen Mathewson (PhD, Brock, 2002-2008)
6. Suguna Loganathan (PhD, EDUC, 2002-2008)
7. Bill Tays (Ph.D., Brock, 2004 - 2011)
8. Gillian Munro (Ph.D., Waterloo, 2004-2008)
9. Cornelia Lamm (PhD., OISE 2003-2007)
10. Amber Pakulak (Ph.D., OISE, 2005-2006)
11. Lesley Capuana (Ph.D., Brock, 2008-2014)
12. Julie St-Cyr-Baker (PhD, Brock 2009-2014)
13. Kirk Stokes (PhD, Brock 2010-2016/05/04)
14. Bryce Mulligan (PhD, Victoria 2012-2017/08/14)
15. Nathalie Gauthier (PhD, Brock, 2014-)
16. Joel Robitaille (PhD, PSYC, 2016-)
17. Erika Walter (PhD, Humanities, 2016-)

Post-Doctoral Supervisor:
Patricia Davies (2000-2005): NIH KO1
Hiroaki Masaki (2002): Japan Soc Promotion Sci
Diane Santesso (2008-10): Ontario PDF Program
Michelle Jetha (2008-10): Penn. Dept of Health
Abbie Coy (2017-2019): SSHRC Partnership grant
Meghan Weissflog (2017-19): SSHRC Discovery

Honours (graduating year): (some missing in 1980s)
1. Calvin Brown (1976)
2. Catherine Stewart (1977)
3. Greg White (1978)
4. Bruce Petrie (1979)
5. Lino Lagrotteria (1980, BIOL)
6. Sharon Armstrong (1980, BIOL)
7. Harry McNaughton (1978)
8. Kim Ness (1982)
9. Carol Orr (1982)
10. Karen Engall (1985)

11. Leslie Macgregor (1986)
12. Lynn Otis (1987)
13. Rosanne Menna (1987)
14. Linda Ismailos (1988)
15. David Schultz (1988, COSC)
16. John Radley (1989, COSC)
17. Michelle Sliz (1990)
18. Debbie Brown (1990)
19. JoAnn Stewart (1990)
20. Sharon Smith (1990)
21. Kerry Barnes (1991)
22. Sheila Lawson (1991)
23. Anthony Wood (1992)
24. Brenda Berge (1992)
25. Tricia Kaczmarck (CHST, 1992)
26. Tim Murphy (1993)
27. Kelly Bowman (1993)
28. Heather Rae (1994)
29. Steve Busse (1995)
30. Patricia Van Roon (1995)
31. Lisa Gasbarre (1995)
32. Glenn Theal (1996)
33. Shelley Van Helvert (1997)
34. Kim Bell (1997, COSC)
35. Nancy San Cartier (1998)
36. Korri Lane (1998)
37. Gabriella Nagy (1998)
38. Barbara Schoonings (APLl, 1998)
39. Pauline Huizinga (1999)
40. Heather Askes (2000)
41. Jennifer Hallam (NEUR, 2000)
42. James Desjardins (2001)
43. Michael Coons (2001)
44. Susan Andrews (NEUR, 2001)
45. Stephanie Osip (NEUR 2002, 2nd reader)
46. Kirsti Van Dorsser (2003)
47. Mary Richard (2004)
48. Anthony Folino (2004)
49. Joyce Penner (2005)
50. Tyler Scott (NEUR, 2005)
51. Xin Zheng (PSYC, 2006)
52. Dimitra Chantziantoniou (PSYC, 2006)
53. Christina Foster (PSYC, 2006)
54. Adam Aubin (NEUR, 2006, 2nd reader)
55. Matthew Dipoce (NEUR, 2007)
56. Angela Dzioundziak (NEUR, 2007, 2nd reader)
57. Ryan Young (PSYC, 2007)
58. Matt Goldhawk (BIOL, 2008)
59. Liu Liu (PSYC, 2008)
60. Ryan Renn (NEUR, 2009, 2nd reader)
61. Matt Cecchin (NEUR 2010, 2nd reader)
62. Laura Demoe (PSYC, 2010)
63. Kasey Dunn (DRAM, 2010, co-supervisor)
64. Caitlin Gabriel (PHYS, 2010, co-supervisor)
65. Anthony Romyn (PSYC, 2011)
66. Lindsay Oakes (NEUR, 2011)
67. Marlee Green (PSYC, 2011)
68. Lisa Marie Wirz (PSYC-Maastrich, 2011)
69. Julie Billing (NEUR, 2013)
70. Cassandra Jones (NEUR, 2013)
71. Avital Sternin (NEUR, 2013)
72. Frieda Franken (PSYC-Maastrich, 2013)
73. Philip Zawada (PSYC, 2014)
74. Jazmine Que (NEUR, 2014)
75. John Krzeczkowski (NEUR, 2014, 2nd reader)
76. Osama Chattha (NEUR, 2015)
77. Jessica Callegari (NEUR, 2015)
78. Blayne Smith (PSYC, 2015)
79. Emily Davis (PSYC, 2016, co-)
80. Sahithya Balakumar (2016, NEUR, co-)
81. Sam Laffin (PSYC, 2016)
82. Valerie Montaldo (PSYC, 2018)
83. Sara Stephenson (NEUR, 2018)

NEUR Coop supervision

1. David Li (2010)
2. Helen Dykstra (2010)
3. Charles Davis (2010-2011)
4. Valerie Montaldo (PSYC, 2016)
5. Sahithya Balakumar (NEUR, 2016)

Thesis Titles

MA Supervision

1. Diane Henderson (M.Ed., Brock, 1993). "Effectiveness of computer training on attentional skills"
2. Ian Marsman (M.A., Brock, 1995). "Negative and positive priming in poor and good readers: an ERP study"
3. Patricia Pailing (M.A. Brock, 1998): "Predictors of academic achievement and social competence in adolescence: Facilitation, inhibition and general cognitive processing"
4. Hélène Chevalier (M.A. Brock, 1997): "Gray's motivational systems, inhibitory control and attention allocation: Behavioural and electrophysiological correlates of behavioural inhibition and activation"
5. Karen Baker (M.A. Waterloo, 1999) "Construct validity of the Wisconsin Card Sorting Task and the Tower of London from 7 years to young adults"
6. Mary-Claire Ferlisi (M.A. Brock, 1999) "Speed of perceptual processing, spatial ability and executive functions underlying fluid intelligence in childhood and adolescence"
7. Diane Santesso (M.A. Brock, 2003) "Developmental and individual differences in novelty and error detection in 10-year-old children and young adults"
8. Danielle Dyke (M.A. Brock, 2005) "Individual Differences in Risk-taking and Associated Characteristics: A Test of Specificity in Executive Functions"
9. Sonia Sanichara (M.A. Brock, 2006) "Charting Developmental EEG Gamma Changes In the Auditory Modality"
10. Xin Zheng (M.A. Brock, 2008) "What happens in the first 200 ms of word reading: ERP studies on visual word recognition with top-down and bottom –up approaches"
11. Angela Dzioundziak (M.A. Brock, 2009) "Risk-taking and Personality:Event-Related Potentials Pilot Study"
12. Meghan Weissflog (M.A., Brock, 2010) "Behavioural and Neural Correlates of Emotion Recognition as a Function of Psychopathic Personality Traits"
13. James Desjardins (M.A., Brock, 2011) "Electrophysiological constituents of the P100 and N170 ERP complex: Deconstructing the critical timing and robustness of face processing using independent component analysis and robust estimation"
14. Stefon Van Noordt (M.A., Brock, 2011) "Hot Cognition and Activation of the Medial Prefrontal Cortex: Self-regulating and Contexts Involving Motivational Pressures"
15. Allan Campopiano (2013 - 2015) "Blocking Top-Down Awareness of Kanizsa Figures: An ERP Investigation into Bottom-Up Processing of Illusory Contours"

Ph.D. Supervisor:

1. Ayse Unsal (Ph.D., Waterloo, 1991) "An investigation of sources of ERP variance in head injured and controls"
2. Jane Storrie-Baker (Ph.D., Waterloo, 1994) "An electrophysiological test of the arousal-hemispatial neglect hypothesis"
3. Diane Velikonja (Ph.D., Waterloo, 1997): "An electrophysiological study of selective and sustained attentional processing and arousal in the human cerebral cortex"
4. Linda Cudmore (Ph.D., Waterloo, 1999) "Behavioral and electrophysiological investigation of attention and executive functions with and without minor head injury"
5. Patti Ross (Ph.D., Waterloo, 1999) "Electrophysiology of working memory: Task modality and load effects"
6. Cynthia Chan (Ph.D., Waterloo, 2003): "Electrophysiology of reading: Distinguishing phonological and orthographic processes"
7. Patricia Pailing (Ph.D., Waterloo, 2004): "ERP investigations of error monitoring: performance, motivation, and personality effects on the error-related negativity"
8. Tim Murphy (Ph.D., Waterloo, 2007): "Subtle effects of sleepiness on electrocortical indices of attentional resources and performance monitoring".
9. Diane Santesso (Ph.D., Brock, 2006): "Electrophysiological correlates of performance monitoring in middle and late adolescence"
10. Adote Anum (Ph.D. Brock, 2006): "Predicting Performance on Fluid Intelligence from Speed of Processing, Working Memory, and Controlled Attention"
11. Xin Zheng (Ph.D., Brock, 2012): " Electrophysiological investigations of the timing of face processing"
12. Chrissy Lackner (Ph.D., Brock, 2015): "Genetic and Electrophysiological Correlates of Self-Regulation in Adolescence"
13. Angela Dzioundziak (Ph.D., Brock, 2014): "Top-down and Bottom-up influences on ACC activation: Evaluation of a proposed model of the feedback-related negativity"
14. Stefon van Noordt (Ph.D., Brock, 2016): "A domain-general perspective on medial frontal brain activity during performance monitoring"
15. Meghan Weissflog (Ph.D., Brock, 2017): "Affective Traits of Psychopathy and the Role of Early Visual Attention: An Electrophysiological Study"

This is Exhibit "B" to the affidavit of Sidney Segalowitz, sworn before me this 9th day of January, 2020

A Commissioner for taking Affidavits etc.

Spenser Wesley Alexander Chalmers, a Commissioner etc. Province of Ontario for Clarke Child and Family Law. Expires September 4, 2021.

When does the adolescent brain reach adult maturity?[1]

Sidney J. Segalowitz, Ph.D.
Brock University
St. Catharines, ON L2S 3A1
January 4, 2020

A brief historical summary of the trajectory of this research question.

Ignoring the brain in early developmental psychology. Academic developmental psychology started as an empirical discipline in earnest about 120 years ago. The vast majority of studies for the first 70 years were behavioural, whether with humans or with animals, describing factors associated with learning. In North America, the primary approach during the first half of the 20th century was that of Behaviourism, in which psychological development was seen to be primarily a function of experience and various types of conditioning. This was first inspired by Pavlov and then expanded by a number of American psychology researchers – especially Edward Thorndike, John B. Watson and B.F. Skinner. At the time, there were few technologies to explore the neural bases of the models being touted. In 1949, Donald Hebb outlined ideas on how brain circuits would have to be organized in order to account for thinking processes that were central to the cognitive psychology of the day.[32] His emphasis on the growth of neural networks (which he called cell assemblies) captured the general model of brain circuitry. The developmental question was, How do networks 'know' how to get connected? Roger Sperry's work in the 1950s outlined some important advances, demonstrating inherent organizing principles.[67] However, developmental psychologists continued with the notion that whatever could be learned could be unlearned, at least in theory, as suggested by Behaviourists.

[1] I would like to thank Sara Stephenson, BSc, and Dawn Ryan, MA, for their help in reviewing the literature on such short notice, and Jane Dywan, PhD, Professor of Psychology, for discussions and suggestions in the writing of this Report.

Brain development enters the scene. A breakthrough occurred in the early 1960s, when David Hubel and Torsten Wiesel outlined the initial organization of the visual system and, most importantly for us, how early experiences could alter that organization, even into a dysfunctional system.[34,35,36,37] What they showed was that the developing neurocircuits altered themselves to efficiently code the input provided, thus demonstrating a mutual influence between structure and function. Similarly, Conel published a series of atlases based on detailed studies showing growth of cortical neurons in the human brain from birth to 6 years.[11] Thus, it was abundantly clear by the end of the 1960s that the cortex develops rapidly after birth in mammals and that experience can alter the trajectory of that growth, perhaps permanently. Another important piece of the puzzle was a summary of how the white matter of the brain, critical for communication between neurons, rapidly grows during childhood but also continues to grow throughout the entire lifespan, albeit more slowly as we age.[91] Thus, the notion that all brain development is more or less finished by the end of early childhood was shown to be wrong. Neuroscience technologies improved rapidly and, by the 1990s, brain imaging and bench neuroscience provided yet more evidence of continual changes throughout child development. For example, language skills in the child grow in parallel with the growth of white matter connecting the language regions in the brain[58] and neurons mature earlier in sensory regions and later in regions of the cortex associated with more abstract thinking.[38,86]

The first three years and beyond. Meanwhile, behavioural and ethological data supported the new concept of "critical periods", whereby healthy psychological development usually requires that normal developmental experiences (such as the presence of a consistent and warm caregiver after birth) occur within specific developmental timelines (e.g., work of Konrad Lorenz and Harry Harlow with animals; John Bowlby, René Spitz and Wayne Dennis with orphaned children after WWII). Without these time-sensitive experiences, individuals developed along abnormal tracks that were increasingly hard to correct. However, this emphasis on the earliest period of rapid growth led to an almost total research emphasis on the first 3 years after birth. This focus on only the earliest stages of development was subsequently criticized in an influential paper outlining how the critical aspects of brain development do not stop at 3 years, and that later development is also crucial.[6]

Simultaneously during the 1990s, it was discovered that a class of cognitive processes collectively referred to as 'executive functions' continue to develop right through later childhood and adolescence at least, and that these are associated with specific regions of the frontal lobe. Some neurological studies had shown that the neurons in the forward sections of the frontal lobe, referred to as the prefrontal cortex (PFC), are not tied to specific sensory modalities but are rather involved in the integration of sensory experiences, multimodal in nature, with internal drives, as well as memories of past experience and future intentions. It is this integration that permits such higher order executive functions, such as planning, attention control, problem solving, and emotional self-regulation. Moreover, the PFC is the last part of the brain to mature. Such findings have led to much of the developmental research being done today with respect to the question of when mature levels of self-regulation become fully "adult".

With the advent of magnetic resonance imaging (MRI) of the brain, researchers could examine neural structures, and with functional MRI (fMRI), they could examine neuronal activation. Initially, researchers did not anticipate how late in development it might be before these maturational changes reached adult levels. The initial landmark studies of Jay Giedd, Nitin Gogtay and their associates[25,27] demonstrated that there are continued structural changes right up until the maximum age of participants in their study (20 years), especially in the multi-modal (i.e., highly integrative) regions such as the PFC. Similarly, primate studies demonstrated that dopamine-related neurons, upon which the PFC is highly dependent, continue to change in density until late adolescence at least, expanding beyond adult levels and then pruning back (as is normal).[47] Data from humans also demonstrated this rise-and-decline in dopamine sensitivity during adolescence.[83,84,85] Behavioural work meanwhile continued past the age of 20, showing that risk-taking and decision-making associated with "hot" cognition (decisions made in the context of high emotional arousal) continue to be an issue into young adulthood. In the context of adolescence, this can have forensic implications.[68,69,70,71,72,74]

Thus, the field has gone from not considering brain growth as necessary to understanding the development of behaviour in humans to an appreciation that the various neural processes involved in brain maturation underlie behavioural, cognitive and psychological development through adolescence. Most recently we have now come to realize that normative changes do not stop there, and that the very late adolescence period (or "emerging adulthood") needs to be

examined. In this report, adolescence will refer to the period from pubertal onset to 18 years of age, and emerging adulthood from 18 to 25 years.

Bottom line

There is a growing consensus that, *for many important functions, the average age* at which brain development in healthy individuals asymptotes is about 25 years. However, there will a sizable group whose trajectory is behind this schedule as well as some ahead of it. This can be for a number of reasons. Below is a more detailed discussion of the research that has led us to this average figure of 25 years for some developmental processes and the various factors that can interfere with this normative trajectory. This conclusion has come from work both with human and animal brains. The general principles of brain maturation are similar across mammals, with obvious species differences that are taken into account. Such species differences are especially the case for regions associated with abstract thought, such as the PFC, which expanded especially in primate evolution, and then again considerably more in homo sapiens evolution. Thus, animal research is often appropriate for studying human brain growth and function with respect to general principles and with nonhuman primates for basic cognitive and emotional processes; clinical extrapolation can sometimes be made but must be done carefully.[7]

Data related to issues of general brain maturation

There are many aspects relating to brain growth and maturation, three of which are listed below. Current research has focused primarily on the first (part 'a' below).

a. Research has shown that brain maturation occurs in several basic neural processes:
    i. Development patterns of the grey matter (comprising the neuronal cell bodies in both the cortex and in subcortical structures),
    ii. The growth of white matter (commonly known as 'myelin' that coats the axons that carry signals from a neuron to others), and
    iii. The alteration of connectivity structures and patterns (the networks apparent from patterns of white matter, and the activity of those networks evident in brain imaging data).

b. Brain activity is based on chemical factors – the availability of neurotransmitters and receptors for those neurotransmitters, with developmentalists focusing especially on dopamine, norepinephrine and serotonin. However, these present very complex patterns, interacting with genetics. Therefore, at present, all we can map out are very general patterns.

c. Developmental patterns that are closely linked to specific genomic factors are now known to be subject to epigenetics (the influence of experience and biology on the activation of specific genes). Thus genetic correlates can themselves be influenced by important biological variables such as activity of the stress system and hormonal changes.

Below is a series of examples to illustrate general findings. A comprehensive review is not possible given the volume of publications (over 7500 research reports in the last 5 years alone in PubMed using the search item 'adolescent brain development', although only a segment of these address the current question).

Anatomical growth:

Grey matter development: Grey matter in the cortex follows a pattern of growth (increasing thickness) and reduction (thinning) as a result of a process referred to as "pruning". There are actually several periods of growth and pruning, the latter seen as a mark of increased sophistication of function. The enhancement of well-used connections occurring simultaneously with the reduction in less-used connections associated with pruning is thought of as a process of specialization.

Early studies examined brains only for the first 2 decades after birth, and reported that cortical pruning continues to reshape the organization of the cortex at least through to 20 years of age.[25,27] More recently, this timing has been extended past emerging adulthood (to 25 or 30 years of age).[1,77,78]

More specifically with respect to the PFC and executive functions, researchers used a task requiring the integration of multiple relations among objects. Adolescents (14-18 y) and adults (22-30 y) were found to be significantly different with respect to the amount of grey matter volume involved and also different in the degree to which these regions were activated during

the task.[18] Similarly, while performing memory and attention tasks, those in emerging adulthood showed greater activation of more tightly focused regions of the PFC than did young adolescents.[9]

With newer methods for analyzing cortical structures and functional integrations, other patterns indicating yet later maturation periods are surfacing. For example, results of a recent study document changes from birth to 88 years in a very large sample of normally developing participants. Reported were dramatic changes in cortical structures until 30 years of age. These changes continued in the same direction but at a slower pace afterwards.[22]

Also of interest are subcortical regions. These were traditionally thought to mature very early in childhood in that they are essential for the basic neural processing of sensory signals, affective valence and the planning and execution of movement. However, this appears to be too simple a generalization. In addition to the usual cortical grey matter decreases and white matter increases into emerging adulthood and beyond, many *subcortical regions* actually asymptote in size only by ages 18-20, and some continue to change up to 25 to 30 years. These include the cerebellum grey matter, putamen, pallidum, accumbens.[56] Similarly, microstructural development of many subcortical regions proceeds until after age 25.[48]

White matter (myelin): White matter is critical to the efficient transfer of signals around the brain and to the muscles and these and white matter cells multiply rapidly after birth. Unless it is attacked by white matter diseases, myelin continues to grow throughout the lifespan but at slower and slower rates. Many studies have documented significant growth of white matter well into the 4th decade or later after birth.[27,49] The increase in white matter has been shown to correlate with the consistency of responses, indicating their importance in the efficiency of neural function.[18,66,76]

Neural network connectivity: It goes without saying that it is the activity of neural networks in the brain that account for mental functioning, not simply the existence of grey and white matter. The technologies for mapping out networks and detecting their level of activation are relatively new, and are improving rapidly to allow us to detect the level of microstructure function as well as gross functioning. For example, Dennis and colleagues have shown, based on a large sample ranging in

age from 12 to 30 years, that connectivity continues to be refined through the 20's.[16] Similarly, findings reported in a large study of structure-function coupling demonstrates changes to mid 20s at least.[4] Porter and colleagues have shown the dynamic nature of these changes in a study examining participants from 9 to 44 years of age. They found that the increases in connectivity of dorsal striatum (important for cognitive processes) stabilize after the mid-twenties. However, there are decreases in ventral striatum networks (central to emotional processes) that persist into mid-adulthood, indicating changes in motivation networks that occur well past 25 years.[57] Similarly, an NIMH group document the stabilization of cortical function components around 25 years of age.[46] The anterior cingulate is a cortical structure that is central to attention control, self-monitoring and executive functions. Its networking is documented to show gradual development into early 20's at least.[39] Another critical connective path is the one between the amygdala, a structure central to emotional behaviour, especially for negative emotions, and the cortex. In an animal study of these networks, it was found that they continue to grow into young adulthood, accounting for continued growth of emotion self-regulation.[12] Thus, whereas some neuronal networks are mature by the end of adolescence (18 years), others continue to mature later (19-29 years), indicating that further age differentiation in needed in future studies.[2]

Data related to individual differences

Individual differences arise for many reasons, and therefore in the present context it is probably safest to set a date of adult-level maturity that would capture not only the average but rather the majority. This is because individuals who are latest to develop an adult level of maturity with respect to judgement, planning, or impulse control, are the ones who are at most risk. There are several sources of individual variation.

First, and most obvious, are the effects of frank compromises of the nervous system, whether resulting in psychiatric/psychological diagnoses such as ADHD,[17,26,30,44,53,59,64] OCD,[54,75] autism,[17,60,61] anxiety or depressive disorders, [3] and thought disorders,[26,45] or neurological disruption such as cerebral palsy, FASD and FAEs,[23,31,50] and genetic disorders such as Fragile X, Williams syndrome, Turner syndrome,[17] etc.

Also central are effects of adverse childhood experiences (ACEs) including childhood poverty and its correlates of pollution, poor nutrition, adverse drug exposure, poor educational opportunities, and other various home stressors. These ACEs are expected to interact with many factors, including temperament and sex, resulting in different levels of adaptability. They may interact as well with gender, but this is less documented. There are now studies that demonstrate that the ACEs of early childhood poverty affect outcome through emerging and full adulthood as a function of the physiological stress experienced during early stages of development.[19,20,29,33,40,92]

Whereas sex and gender differences have been reported in conjunction with various aspects of cognitive, emotional and social development, it is difficult to draw a general conclusion at this time about physiological correlates of these differences from the trajectories outlined in the studies referred to here other than that females appear to mature somewhat earlier than males. However, it is difficult at this time to tell whether this is sometimes masked by different end-points and whether this is true throughout the developmental period.[13,16,28,88] There are certainly bound to be such effects involving neural structures, but they are hard to articulate at this time.

Some specific functions central to psychological health, integration and growth during adolescence and emerging adulthood

What is meant by "adulthood" or "maturity"? If peak development is the target, then clearly there are differences depending on the aspect examined. Peak physical development occurs quite early, as we all know. What of emotional development? Cognitive development? Social development? The latter three functions are well documented as continuing to change into one's third decade and beyond.

The mental functions most associated with adult maturity involve emotional self-regulation and complex cognitive functions involving attention, memory and inhibitory control. These functions are associated with various regions of the prefrontal cortex, areas that are documented as being the last to mature, as already noted. Some of the social-cognitive functions subserved include theory of mind, understanding irony, and picking up subtle social cues. Not only do these

functions continue to improve into adulthood, how they are mediated by cortical regions significantly alters. For example, thinking about intentions is a primary social function, and adolescents (12 to 18 y) and adults (23 to 38 y) differ in their cortical activation. Blakemore and colleagues reported that whereas adolescents processed the intentions of others using the more cognitive medial PFC region, adults activated the more social region of the right superior temporal sulcus.[5] In fact, there are many such differences. For example, subtle emotions like embarrassment and guilt activate connectivity patterns differently in adolescents and adults.[8] Similarly, there is an increased neural response to rewards among adolescents (13-17 y) compared to emerging adults and adults (18-30 y), which has been linked to adolescents' vulnerability to poor decision-making and risk-taking behaviour.[24]

Empathy and issues of social acceptance are complex. See pp 33-36 in Jetha & Segalowitz (2012) for a brief outline.[38] These concepts overlap with theory of mind, and relate to aggression and moral reasoning, with PFC crucially involved among other regions.[14,15] The neural basis for dealing with such thoughts, however, changes dramatically from childhood to adulthood. For example, scenarios illustrating accidentally inflicted pain versus those illustrating intentionally inflicted pain elicited age-related differences in regions of brain activation, indicating a shift from visceral to evaluative responses between 10 to 30 years with some leveling off by 30 years.[15]

Similarly, *social acceptance versus rejection* has been studied in children, adolescents and adults, with the finding that adolescents (14-16 y) show more distress at being socially excluded, but also show brain activation patterns different from those of adults: a decrease in orbitofrontal cortex activity in teens versus an increase in that activation in adults (23-38 y). The orbitofrontal cortex has been shown to activate when the individual is trying to control their emotions, suggesting that adults are more likely to engage in this activity than adolescents.[62] More work is needed to know exactly when this change reaches the adult pattern. Interestingly, the degree to which activation increased in medial PFC during social exclusion (over inclusion) correlated significantly with susceptibility to peer influence in the adolescents, but not adults. Thus, the neural processing associated with social inclusion/exclusion experiences are processed in significantly different ways in these two developmental stages.[63]

Risk-taking is often considered a primary issue of concern. The differences in brain maturity and activation patterns during adolescence compared with adulthood are often embedded in discussions on risk-taking behaviours. It is not that adolescents and young adults cannot reason carefully about risks. The predominant thinking in the field is that they are less likely to reason carefully when in a social context, very often associated with higher emotional valence.[65,72,73] Capturing this is the Dual Process model, whereby the attraction force of an exciting or rewarding stimulus (or situation or plan) is greater than the cautionary or evaluative force elicited through executive functions. This is due to increased activation of the dopamine-sensitive ventral striatum (the "reward centre") during adolescence together with the more slowly maturing PFC (see Figure 1). There is an abundance of data documenting increased risk-taking during adolescence, especially in the presence of peers, with this being the key factor in a brief to the US Supreme Court by one of the leaders in the field, Lawrence Steinberg.[71,72,74]

To illustrate the repeated findings of this research group, 3 groups of individuals (14-16 y, 19-22 y, 24-29 y) play a video game while their brains are being scanned with fMRI. The game involves driving a vehicle in a videogame whereby points are gained for the further distance driven. However, there are traffic lights and cross traffic. Taking chances (shooting a red light) can gain points because of time saved but can also lose points if a crash occurs. In one condition the participant is aware that peers are watching their performance. In general, adolescents are much more likely to show activation of the ventral striatum (reward centre) when taking a risky chance than are young adults, and the adults show no such activation at all. But the influence of peers is most interesting and dramatic: it leads to increases in PFC activation most in adults, much less in young adults and very little with adolescents. Conversely, emotional regions – especially the ventral striatum (registering reward) and orbitofrontal cortex (registering emotional valence) – are much more active with peers present for adolescents, less so in young adults and actually less active in adults than when alone.[10] Thus, it is not surprising that risk preferences continue to decline after adolescence, into emerging adulthood and right into full adulthood.[69]

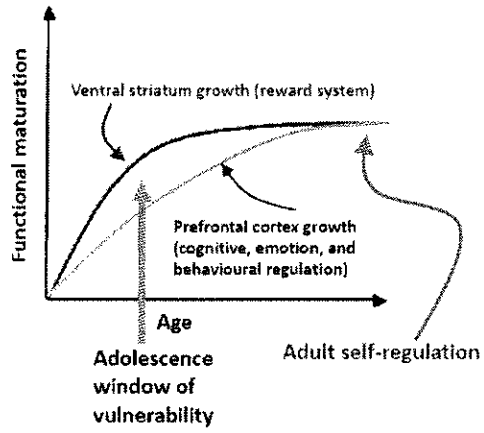

Figure 1. This schematic illustrates the Dual-Process Model, whereby the ventral striatum (the central aspect of the so-called reward centre) matures earlier than the prefrontal cortex (central to behaviour regulation) and therefore controls behaviour during the adolescent 'window of vulnerability'. Our question concerns the age at which the prefrontal cortex catches up and is able to regulate behaviour in an adult fashion.

It is important to note, however, that risk-taking is more complicated than just being the result of impulsive decision making or being with peers. Adults often take premeditated risks, such as with financial gambles, planned marital infidelities, and so on, but in the context of peer-influenced, high arousal risks, youth in the emerging adulthood stage may take even more risks than adolescents, especially with drugs and alcohol and sexual behaviours. The difference is that for adolescents, many of these behaviours are illegal, while the opportunities and legality are more available to young adults.[65] However, the same brain circuits are still in play with young adults, not always with a fully mature PFC.[90] Consistent with this perspective are self-report data from Steinberg's lab: While impulsivity and sensation-seeking behaviours do decrease gradually through adolescence, there is relatively little drop off up to age 22-25 years, with a major drop in the 26-30 years range.[68]

Another prime variable in this dynamic is the distinction between "hot" vs "cold" cognition mentioned above. During states of high arousal and emotionality, adolescents and young adults are more prone to poor judgment calls than are adults. Interestingly, during discussions in a "cold cognition" context, adolescents make many judgments very similar to those of adults.[10,21,72] Thus, the distinction between "saying" wise things and "doing" wise things should be kept in mind.

Implications

The role of major stressors in influencing brain development has been studied extensively over the last 20 years. Such stress has been shown to alter fundamental circuits in the stress system itself (the hypothalamic-pituitary-adrenal axis), reducing the ability to regulate one's stress response, resulting in a downward spiral (removing the stressors can allow rebuilding of those healthy circuits to some extent). These circuits involve the medial PFC, the hippocampus and the amygdala, and help form contemporary models of PTSD. Application of this to conditions of early abuse have been documented,[79,80,81,82,87,88,89] as well as overall effects of stressors on brain growth[41,42,43] and specifically on the brain growth in adolescence.[51,52,55]

In the current context, early life experiences are very important, especially when they put the developing child and youth at risk by compromising brain growth in regions related emotion self-regulation and cognitive information processing. This is especially the case when they affect the normal growth of the PFC and its network of connections. This happens in situations involving chronic stress, poor nutrition, aspects of air and water pollution, pre- and post-natal drug exposure, traumatic brain injury, and PTSD. Central to this, of course, is the issue of poverty.

Thus, the large range in developmental experiences result in individual differences in brain characteristics and these variations can increase with age, both in positive and negative directions. When negative factors, such as strong and chronic stress, are present during periods of rapid developmental change, this puts at risk the individual's mental health trajectory. Individual differences occur also because of different prenatal and perinatal contexts (such as drug experiences) and because of varying epigenetic processes. The latter result from factors that alter hormone levels that can influence the activation of specific genes central to brain function, leading to yet more developmental risks or at least variations. Thus, even with respect to genetic influences, environment counts.

REFERENCES

1. Amlien, I. K., Fjell, A. M., et al. (2016). Organizing Principles of Human Cortical Development--Thickness and Area from 4 to 30 Years: Insights from Comparative Primate Neuroanatomy. *Cerebral Cortex* 26, 257-267.
2. Asato, M. R., Terwilliger, R., Woo, J. & Luna, B. (2010). White matter development in adolescence: a DTI study. *Cereb Cortex* 20, 2122-31.
3. Auday, E. S. & Perez-Edgar, K. E. (2019). Limbic and prefrontal neural volume modulate social anxiety in children at temperamental risk. *Depression and anxiety* 36, 690-700.
4. Baum, G. L., Cui, Z., et al. (2019). Development of structure-function coupling in human brain networks during youth. *Proceedings of the National Academy of Sciences of the United States of America.*
5. Blakemore, S.-J., den Ouden, H., Choudhury, S. & Frith, C. (2007). Adolescent development of the neural circuitry for thinking about intentions. *Social, Cognitive, and Affective Neuroscience* 2, 130-139.
6. Bruer, J. (1997). Education and the brain: a bridge too far. *Educational Researcher* 26, 4-16.
7. Buffalo, E. A., Movshon, J. A. & Wurtz, R. H. (2019). From basic brain research to treating human brain disorders. *Proceedings of the National Academy of Sciences of the United States of America.*
8. Burnett, S., Sebastian, C., Cohen Kadosh, K. & Blakemore, S. J. (2011). The social brain in adolescence: Evidence from functional magnetic resonance imaging and behavioural studies. *Neurosci Biobehav Rev* 35, 1654-1664.
9. Casey, B. J., Giedd, J. N. & Thomas, K. M. (2000). Structural and functional brain development and its relation to cognitive development. *Biol Psychol* 54, 241-57.
10. Chein, J., Albert, D., O'Brien, L., Uckert, K. & Steinberg, L. (2011). Peers increase adolescent risk taking by enhancing activity in the brain's reward circuitry. *Dev Sci* 14, F1-F10.
11. Conel, J. L. (1939-67). *The postnatal development of the human cerebral cortex*, Harvard, Cambridge, MA.
12. Cunningham, M. G., Bhattacharyya, S. & Benes, F. M. (2002). Amygdalo-cortical sprouting continues into early adulthood: implications for the development of normal and abnormal function during adolescence. *The Journal of Comparative Neurology* 453, 116-30.
13. De Bellis, M. D., Keshavan, M. S., Beers, S. R., Hall, J., Frustaci, K., Masalehdan, A., Noll, J. & Boring, A. M. (2001). Sex Differences in Brain Maturation during Childhood and Adolescence. *Cerebral Cortex* 11, 552-557.
14. Decety, J. (2010). The neurodevelopment of empathy in humans. *Developmental neuroscience* 32, 257-67.
15. Decety, J. & Michalska, K. J. (2010). Neurodevelopmental changes in the circuits underlying empathy and sympathy from childhood to adulthood. *Developmental Science* 13, 886-899.
16. Dennis, E. L., Jahanshad, N., et al. (2013). Development of brain structural connectivity between ages 12 and 30: a 4-Tesla diffusion imaging study in 439 adolescents and adults. *Neuroimage* 64, 671-84.
17. Dennis, E. L. & Thompson, P. M. (2013). Mapping connectivity in the developing brain. *Int J Dev Neurosci* 31, 525-42.
18. Dumontheil, I., Houlton, R., Christoff, K. & Blakemore, S. J. (2010). Development of relational reasoning during adolescence. *Developmental Science* 13, F15-F24.
19. Evans, G. W. & Schamberg, M. A. (2009). Childhood poverty, chronic stress, and adult working memory. *Proc Natl Acad Sci U S A* 106, 6545-6549.
20. Farah, M. J., Shera, D. M., Savage, J. H., Betancourt, L., Giannetta, J. M., Brodsky, N. L., Malmud, E. K. & Hurt, H. (2006). Childhood poverty: specific associations with neurocognitive development. *Brain Res* 1110, 166-74.

21. Figner, B., Mackinlay, R. J., Wilkening, F. & Weber, E. U. (2009). Affective and deliberative processes in risky choice: age differences in risk taking in the Columbia Card Task. *J Exp Psychol Learn Mem Cogn* 35, 709-30.
22. Fjell, A. M., Chen, C.-H., Sederevicius, D., Sneve, M. H., Grydeland, H., Krogsrud, S. K., Amlien, I., Ferschmann, L., Ness, H. & Folvik, L. (in press). Continuity and Discontinuity in Human Cortical Development and Change From Embryonic Stages to Old Age. *Cereb Cortex*.
23. Franks, A. L., Berry, K. J. & DeFranco, D. B. (2019). Prenatal drug exposure and neurodevelopmental programming of glucocorticoid signalling. *Journal of neuroendocrinology*, e12786.
24. Geier, C. F., Terwilliger, R., Teslovich, T., Velanova, K. & Luna, B. (2010). Immaturities in reward processing and its influence on inhibitory control in adolescence. *Cerebral Cortex* 20, 1613-1629.
25. Giedd, J. N. (2004). Structural magnetic resonance imaging of the adolescent brain. *Ann N Y Acad Sci* 1021, 77-85.
26. Gogtay, N., Giedd, J. & Rapoport, J. L. (2002). Brain development in healthy, hyperactive, and psychotic children. *Arch Neurol* 59, 1244-8.
27. Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., Nugent, T. F., 3rd, Herman, D. H., Clasen, L. S., Toga, A. W., Rapoport, J. L. & Thompson, P. M. (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proc Natl Acad Sci U S A* 101, 8174-9.
28. Gogtay, N. & Thompson, P. M. (2010). Mapping gray matter development: implications for typical development and vulnerability to psychopathology. *Brain Cogn* 72, 6-15.
29. Gottlieb, G. & Blair, C. (2004). How early experience matters in intellectual development in the case of poverty. *Prev Sci* 5, 245-52.
30. Greven, C. U., Bralten, J., Mennes, M. & et al. (2015). Developmentally stable whole-brain volume reductions and developmentally sensitive caudate and putamen volume alterations in those with attention-deficit/hyperactivity disorder and their unaffected siblings. *JAMA Psychiatry* 72, 490-499.
31. Harvey, R. E., Berkowitz, L. E., Hamilton, D. A. & Clark, B. J. (2019). The effects of developmental alcohol exposure on the neurobiology of spatial processing. *Neuroscience and Biobehavioral Reviews* 107, 775-794.
32. Hebb, D. O. & Hebb, D. (1949). *The organization of behavior*, 65, Wiley New York.
33. Hotez, P. J. (2014). NEglected infections of poverty in the united states and their effects on the brain. *JAMA Psychiatry* 71, 1099-1100.
34. Hubel, D. H. (1981). Nobel Lecture: Evolution of ideas on the primary visual cortex, 1955-1978: a biased historical account.
35. Hubel, D. H. & Wiesel, T. N. (1959). Receptive fields of single neurones in the cat's striate cortex. *Journal of Physiology* 148, 574-591.
36. Hubel, D. H. & Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *Journal of Physiology (London)* 160, 106-154.
37. Hubel, D. H. & Wiesel, T. N. (1979). Brain mechanisms of vision. *Scientific American* 241, 150-162.
38. Jetha, M. K. & Segalowitz, S. J. (2012). *Adolescent Brain Development: Implications for Behavior*, Academic Press, San Diego, CA.
39. Kelly, A. M., Di Martino, A., Uddin, L. Q., Shehzad, Z., Gee, D. G., Reiss, P. T., Margulies, D. S., Castellanos, F. X. & Milham, M. P. (2009). Development of anterior cingulate functional connectivity from late childhood to early adulthood. *Cereb Cortex* 19, 640-57.
40. Kim, P., Evans, G. W., Angstadt, M., Ho, S. S., Sripada, C. S., Swain, J. E., Liberzon, I. & Phan, K. L. (2013). Effects of childhood poverty and chronic stress on emotion regulatory brain function in adulthood. *Proc Natl Acad Sci U S A* 110, 18442-7.
41. Kolb, B. & Gibb, R. (2011). Brain plasticity and behaviour in the developing brain. *J Can Acad Child Adolesc Psychiatry* 20, 265-76.
42. Kolb, B., Harker, A., Mychasiuk, R., de Melo, S. R. & Gibb, R. (2017). Stress and prefrontal cortical plasticity in the developing brain. *Cognitive Development* 42, 15-26.

43. Kolb, B., Mychasiuk, R. & Gibb, R. (2014). Brain development, experience, and behavior. *Pediatr Blood Cancer* 61, 1720-3.
44. Kong, X. Z., Boedhoe, P. S. W., et al. (2019). Mapping Cortical and Subcortical Asymmetry in Obsessive-Compulsive Disorder: Findings From the ENIGMA Consortium. *Biological Psychiatry.*
45. Koshiyama, D., Fukunaga, M., et al. (2019). White matter microstructural alterations across four major psychiatric disorders: mega-analysis study in 2937 individuals. *Molecular Psychiatry.*
46. Kundu, P., Benson, B. E., Rosen, D., Frangou, S., Leibenluft, E., Luh, W. M., Bandettini, P. A., Pine, D. S. & Ernst, M. (2018). The Integration of Functional Brain Activity from Adolescence to Adulthood. *The Journal of Neuroscience* 38, 3559-3570.
47. Lambe, E. K., Krimer, L. S. & Goldman-Rakic, P. S. (2000). Differential postnatal development of catecholamine and serotonin inputs to identified neurons in prefrontal cortex of rhesus monkey. *Journal of Neuroscience* 20, 8780-8787.
48. Lebel, C., Walker, L., Leemans, A., Phillips, L. & Beaulieu, C. (2008). Microstructural maturation of the human brain from childhood to adulthood. *Neuroimage* 40, 1044-55.
49. Li, T. Q. & Noseworthy, M. D. (2002). Mapping the development of white matter tracts with diffusion tensor imaging. *Developmental Science* 5, 293-300.
50. Long, X., Kar, P., Gibbard, B., Tortorelli, C. & Lebel, C. (2019). The brain's functional connectome in young children with prenatal alcohol exposure. *NeuroImage. Clinical* 24, 102082.
51. Lupien, S. J., Maheu, F., Tu, M., Fiocco, A. & Schramek, T. E. (2007). The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition. *Brain Cogn* 65, 209-37.
52. Lupien, S. J., McEwen, B. S., Gunnar, M. R. & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nat Rev Neurosci* 10, 434-45.
53. Mahone, E. M., Crocetti, D., Ranta, M. E., Gaddis, A., Cataldo, M., Slifer, K. J., Denckla, M. B. & Mostofsky, S. H. (2011). A Preliminary Neuroimaging Study of Preschool Children with ADHD. *The Clinical Neuropsychologist* 25, 1009-1028.
54. Maia, T. V., Cooney, R. E. & Peterson, B. S. (2008). The neural bases of obsessive-compulsive disorder in children and adults. *Dev Psychopathol* 20, 1251-83.
55. McEwen, B. S. (2012). Brain on stress: how the social environment gets under the skin. *Proc Natl Acad Sci U S A* 109 Suppl 2, 17180-5.
56. Ostby, Y., Tamnes, C. K., Fjell, A. M., Westlye, L. T., Due-Tonnessen, P. & Walhovd, K. B. (2009). Heterogeneity in subcortical brain development: A structural magnetic resonance imaging study of brain maturation from 8 to 30 years. *J Neurosci* 29, 11772-82.
57. Porter, J. N., Roy, A. K., Benson, B., Carlisi, C., Collins, P. F., Leibenluft, E., Pine, D. S., Luciana, M. & Ernst, M. (2015). Age-related changes in the intrinsic functional connectivity of the human ventral vs. dorsal striatum from childhood to middle age. *Developmental Cognitive Neuroscience* 11, 83-95.
58. Pujol, J., Soriano-Mas, C., Ortiz, H., Sebastian-Galles, N., Losilla, J. M. & Deus, J. (2006). Myelination of language-related areas in the developing brain. *Neurology* 66, 339-43.
59. Qiu, A., Crocetti, D., Adler, M., Mahone, E. M., Denckla, M. B., Miller, M. I. & Mostofsky, S. H. (2009). Basal ganglia volume and shape in children with attention deficit hyperactivity disorder. *Am J Psychiatry* 166, 74-82.
60. Robertson, Caroline E., Ratai, E.-M. & Kanwisher, N. (2015). Reduced GABAergic Action in the Autistic Brain. *Current Biology.*
61. Robertson, F. C., Narr, K. L., Molteno, C. D., Jacobson, J. L., Jacobson, S. W. & Meintjes, E. M. (2016). Prenatal Alcohol Exposure is Associated with Regionally Thinner Cortex During the Preadolescent Period. *Cerebral Cortex* 26, 3083-3095.
62. Sebastian, C., Viding, E., Williams, K. D. & Blakemore, S. J. (2010). Social brain development and the affective consequences of ostracism in adolescence. *Brain and Cognition* 72, 134-45.

63. Sebastian, C. L., Tan, G. C., Roiser, J. P., Viding, E., Dumontheil, I. & Blakemore, S.-J. (2011). Developmental influences on the neural bases of responses to social rejection: implications of social neuroscience for education. *Neuroimage* 57, 686-694.
64. Shaw, P., Gilliam, M., et al. (2011). Cortical development in typically developing children with symptoms of hyperactivity and impulsivity: support for a dimensional view of attention deficit hyperactivity disorder. *Am J Psychiatry* 168, 143-51.
65. Shulman, E. P., Smith, A. R., Silva, K., Icenogle, G., Duell, N., Chein, J. & Steinberg, L. (2016). The dual systems model: Review, reappraisal, and reaffirmation. *Dev Cogn Neurosci* 17, 103-17.
66. Sousa, S. S., Amaro, E., Jr., Crego, A., Goncalves, O. F. & Sampaio, A. (2018). Developmental trajectory of the prefrontal cortex: a systematic review of diffusion tensor imaging studies. *Brain imaging and behavior* 12, 1197-1210.
67. Sperry, R. W. (1963). Chemoaffinity in the orderly growth of nerve fiber patterns and connections. *Proceedings of the National Academy of Sciences* 50, 703-710.
68. Steinberg, L. (2008). A social neuroscience perspective on adolescent risk-taking. *Dev Rev* 28, 78-106.
69. Steinberg, L. (2009). Should the science of adolescent brain development inform public policy? *American psychologist* 64, 739-750.
70. Steinberg, L. (2013). Does recent research on adolescent brain development inform the mature minor doctrine? *The Journal of medicine and philosophy* 38, 256-67.
71. Steinberg, L., Cauffman, E., Woolard, J., Graham, S. & Banich, M. (2009). Are adolescents less mature than adults?: minors' access to abortion, the juvenile death penalty, and the alleged APA "flip-flop". *Am Psychol* 64, 583-94.
72. Steinberg, L., Cauffman, E., Woolard, J., Graham, S. & Banich, M. (2009). Reconciling the complexity of human development with the reality of legal policy: Reply to Fischer, Stein, and Heikkinen (2009). *American Psychologist* 64, 601-604.
73. Steinberg, L. & Monahan, K. C. (2007). Age differences in resistance to peer influence. *Dev Psychol* 43, 1531-43.
74. Steinberg, L. & Scott, E. S. (2003). Less guilty by reason of adolescence: developmental immaturity, diminished responsibility, and the juvenile death penalty. *Am Psychol* 58, 1009-18.
75. Szeszko, P. R., Ardekani, B. A., Ashtari, M., Malhotra, A. K., Robinson, D. G., Bilder, R. M. & Lim, K. O. (2005). White matter abnormalities in obsessive-compulsive disorder: a diffusion tensor imaging study. *Arch Gen Psychiatry* 62, 782-90.
76. Tamnes, C. K., Fjell, A. M., Westlye, L. T., Ostby, Y. & Walhovd, K. B. (2012). Becoming consistent: developmental reductions in intraindividual variability in reaction time are related to white matter integrity. *The Journal of Neuroscience* 32, 972-82.
77. Tamnes, C. K., Herting, M. M., et al. (2017). Development of the Cerebral Cortex across Adolescence: A Multisample Study of Inter-Related Longitudinal Changes in Cortical Volume, Surface Area, and Thickness. *The Journal of Neuroscience* 37, 3402-3412.
78. Tamnes, C. K., Østby, Y., Fjell, A. M., Westlye, L. T., Due-Tønnessen, P. & Walhovd, K. B. (2010). Brain Maturation in Adolescence and Young Adulthood: Regional Age-Related Changes in Cortical Thickness and White Matter Volume and Microstructure. *Cerebral Cortex* 20, 534--548.
79. Teicher, M. H. & Samson, J. A. (2013). Childhood maltreatment and psychopathology: A case for ecophenotypic variants as clinically and neurobiologically distinct subtypes. *Am J Psychiatry* 170, 1114-33.
80. Teicher, M. H. & Samson, J. A. (2016). Annual Research Review: Enduring neurobiological effects of childhood abuse and neglect. *J Child Psychol Psychiatry* 57, 241-66.
81. Teicher, M. H., Samson, J. A., Anderson, C. M. & Ohashi, K. (2016). The effects of childhood maltreatment on brain structure, function and connectivity. *Nature reviews neuroscience* 17, 652-666.
82. Teicher, M. H., Tomoda, A. & Andersen, S. L. (2006). Neurobiological consequences of early stress and childhood maltreatment: are results from human and animal studies comparable? *Ann N Y Acad Sci* 1071, 313-23.

83. Wahlstrom, D., Collins, P., White, T. & Luciana, M. (2010). Developmental changes in dopamine neurotransmission in adolescence: behavioral implications and issues in assessment. *Brain Cogn* 72, 146-59.
84. Wahlstrom, D., White, T., Hooper, C. J., Vrshek-Schallhorn, S., Oetting, W. S., Brott, M. J. & Luciana, M. (2007). Variations in the catechol O-methyltransferase polymorphism and prefrontally guided behaviors in adolescents. *Biol Psychiatry* 61, 626-32.
85. Wahlstrom, D., White, T. & Luciana, M. (2010). Neurobehavioral evidence for changes in dopamine system activity during adolescence. *Neurosci Biobehav Rev* 34, 631-48.
86. Weinberger, D. R., Elvevag, B. & Giedd, J. (2005). *The Adolescent Brain: A Work in Progress.*
87. Whittle, S., Dennison, M., et al. (2013). Childhood maltreatment and psychopathology affect brain development during adolescence. *Journal of the American Academy of Child and Adolescent Psychiatry* 52, 940-952.e1.
88. Whittle, S., Simmons, J. G., Dennison, M., Vijayakumar, N., Schwartz, O., Yap, M. B. H., Sheeber, L. & Allen, N. B. (2014). Positive parenting predicts the development of adolescent brain structure: a longitudinal study. *Developmental cognitive neuroscience* 8, 7-17.
89. Whittle, S., Vijayakumar, N., Simmons, J. G. & et al. (2017). Role of positive parenting in the association between neighborhood social disadvantage and brain development across adolescence. *JAMA Psychiatry* 74, 824-832.
90. Willoughby, T., Good, M., Adachi, P. J., Hamza, C. & Tavernier, R. (2013). Examining the link between adolescent brain development and risk taking from a social–developmental perspective. *Brain and cognition* 83, 315-323.
91. Yakovlev, P. I. & Lecours, A.-R. (1967). The myelogenetic cycles of regional maturation in the brain. In *Regional development of the brain in early life* (Minkowski, A., ed.), pp. 3-70. Blackwell, Oxford.
92. Ziol-Guest, K. M., Duncan, G. J., Kalil, A. & Boyce, W. T. (2012). Early childhood poverty, immune-mediated disease processes, and adult productivity. *Proc Natl Acad Sci U S A* 109 Suppl 2, 17289-93.

This is Exhibit "C" to the affidavit of Sidney Segalowitz, sworn before me this 9th day of January, 2020

A Commissioner for taking Affidavits etc.

Spencer Wesley Alexander Chalmers, a Commissioner etc., Province of Ontario, for Clarke Child and Family Law. Expires September 4, 2021.

Cerebral Cortex January 2016;26:257–267
doi: 10.1093/cercor/bhu214
Advance Access publication September 21, 2014

Organizing Principles of Human Cortical Development—Thickness and Area from 4 to 30 Years: Insights from Comparative Primate Neuroanatomy

Inge K. Amlien[1], Anders M. Fjell[1,2], Christian K. Tamnes[1], Håkon Grydeland[1], Stine K. Krogsrud[1], Tristan A. Chaplin[3,4,5], Marcello G. P. Rosa[3,4,5] and Kristine B. Walhovd[1,2]

[1]Research Group for Lifespan Changes in Brain and Cognition, Department of Psychology, University of Oslo, Oslo, Norway, [2]Department of Physical Medicine and Rehabilitation, Unit of Neuropsychology, Oslo University Hospital, Oslo, Norway, [3]Department of Physiology, [4]Monash Vision Group, Monash University, Clayton, VIC, Australia and [5]ARC Centre of Excellence for Integrative Brain Function, Clayton, VIC, Australia

Address correspondence to Inge K. Amlien, Department of Psychology, PO Box 1094 Blindern, 0317 Oslo, Norway.
Email: inge.amlien@psykologi.uio.no

The human cerebral cortex undergoes a protracted, regionally heterogeneous development well into young adulthood. Cortical areas that expand the most during human development correspond to those that differ most markedly when the brains of macaque monkeys and humans are compared. However, it remains unclear to what extent this relationship derives from allometric scaling laws that apply to primate brains in general, or represents unique evolutionary adaptations. Furthermore, it is unknown whether the relationship only applies to surface area (SA), or also holds for cortical thickness (CT). In 331 participants aged 4 to 30, we calculated age functions of SA and CT, and examined the correspondence of human cortical development with macaque to human expansion, and with expansion across nonhuman primates. CT followed a linear negative age function from 4 to 30 years, while SA showed positive age functions until 12 years with little further development. Differential cortical expansion across primates was related to regional maturation of SA and CT, with age trajectories differing between high- and low-expanding cortical regions. This relationship adhered to allometric scaling laws rather than representing uniquely macaque–human differences: regional correspondence with human development was as large for expansion across nonhuman primates as between humans and macaque.

Keywords: area, cortex, development, evolution, thickness

Introduction

The human brain undergoes a protracted development, which is traceable postnatally well into the third decade (Tamnes et al. 2010; Lebel and Beaulieu 2011; Petanjek et al. 2011; Raznahan, Shaw, et al. 2011; Grydeland et al. 2013). This is unparalleled in comparison with other primates (Rilling 2014). Human cortical development is highly heterogeneous across regions (Shaw et al. 2008), with structural maturation proceeding in a coordinated manner across large-scale neural networks (Raznahan, Lerch, et al. 2011; Raznahan et al. 2012; Alexander-Bloch et al. 2013; Walhovd et al. 2014). These coordinated changes are related to development of cognitive abilities (Shaw et al. 2006), and evolutionary adaptation has been suggested as one principle governing the changes (Shaw et al. 2008), but limited evidence exists. Intriguingly, Hill et al. (2010) showed that cortical surface area (SA) in regions that appear expanded in humans, relative to the macaque monkey, tend to be those that change the most between human infancy and adulthood. It is unclear whether these relationships can be found for surface expansion alone, or also apply to cortical thickness (CT) (Gogtay et al. 2004), as these measures are shaped by independent genes (Rakic 1988; Panizzon et al. 2009) and neurobiological events (Rakic et al. 2009) and may even be negatively correlated in adults (Hogstrom et al. 2013).

It also remains to be established whether the overlap between human cortical development and interspecific cortical expansion, assessed based on macaque–human comparisons, is a result of human-specific evolutionary adaptations, or can be explained largely due to allometric scaling laws—i.e., that regional differences in cortical size can be predicted from increases in brain size (Rilling 2014). For example, it has been suggested that the relative immaturity of high-expanding areas at birth reflects evolutionary pressure for these areas to develop postnatally, taking advantage of interactions with the environment (Hill et al. 2010; Petanjek and Kostović 2012; Raznahan et al. 2012).

If regional differences in cortical size from a smaller to a larger brained nonhuman primate can predict regional differences in brain growth in humans, then the "evo–devo" relationship can be said to adhere to more general allometric scaling laws. Alternatively, the observed relationship between macaque–human differential cortical expansion and cortical development could represent more specific adaptations, which evolved relatively late in human evolution in parallel with the evolution of a larger complement of higher order association areas (Hill et al. 2010).

In the present study, we calculated age functions across development from 4 to 30 years based on cross-sectional brain scans from 331 participants. We then tested how the estimated developmental trajectories of CT, SA and cortical volume (CV) varied across the cortex as a function of cortical expansion in humans relative to interspecific expansion, namely comparisons between multiple primates—macaque vs. humans, marmoset vs. macaque, and marmoset vs. capuchin (Van Essen and Dierker 2007; Hill et al. 2010; Chaplin et al. 2013). We hypothesized that regions that are selectively larger in humans compared with nonhuman primates would show more protracted developmental curves for SA, and to a lesser degree CT.

We further tested whether the relationship between interspecific cortical expansion and human cortical development changed as a function of age, and hypothesized that the relationship would be strongest in younger children, when cortical development proceeds at a higher pace, and when the proportion of cortical variability stemming from early events during neurogenesis may be greater (Rakic 2009).

Finally, by examining the relationships between human cortical development and interspecific cortical expansion, we

Cerebral Cortex Advance Access published January 5, 2010

Cerebral Cortex
doi:10.1093/cercor/bhp282

White Matter Development in Adolescence: A DTI Study

M. R. Asato[1,2], R. Terwilliger[2], J. Woo[2] and B. Luna[2,3]

Laboratory of Neurocognitive Development, Departments of, [1]Pediatrics, [2]Psychiatry and [3]Psychology, University of Pittsburgh, Pittsburgh, PA, USA

Address correspondence to Miya R. Asato, Division of Child Neurology, 6th floor Faculty Pavilion, Children's Hospital of Pittsburgh, 4401 Penn Avenue, Pittsburgh, PA 15224, USA. Email: asatomr@upmc.edu.

Adolescence is a unique period of physical and cognitive development that includes concurrent pubertal changes and sex-based vulnerabilities. While diffusion tensor imaging (DTI) studies show white matter maturation throughout the lifespan, the state of white matter integrity specific to adolescence is not well understood as are the contributions of puberty and sex. We performed whole-brain DTI studies of 114 children, adolescents, and adults to identify age-related changes in white matter integrity that characterize adolescence. A distinct set of regions across the brain were found to have decreasing radial diffusivity across age groups. Region of interest analyses revealed that maturation was attained by adolescence in broadly distributed association and projection fibers, including those supporting cortical and brain stem integration that may underlie known enhancements in reaction time during this period. Maturation after adolescence included association and projection tracts, including prefrontal–striatal connections, known to support top-down executive control of behavior and interhemispheric connectivity. Maturation proceeded in parallel with pubertal changes to the postpubertal stage, suggesting hormonal influences on white matter development. Females showed earlier maturation of white matter integrity compared with males. Together, these findings suggest that white matter connectivity supporting executive control of behavior is still immature in adolescence.

Keywords: diffusion tensor imaging, gender, myelination, puberty

Introduction

Adolescence is a unique period of development characterized by immature brain processes and limitations in decision making. While the gross morphology of the brain is in place by this time as are core cognitive abilities, there are significant refinements to brain processes (Yakovlev and Lecours 1967; Huttenlocher 1990) that continue into adulthood as cognitive control continues to improve (Demetriou et al. 2002; Luna et al. 2004; Luciana et al. 2005). This period in development is recognized for brain-based vulnerabilities that affect behavior, including the emergence of psychopathology (Everling and Fischer 1998; Chau et al. 2004; Sweeney et al. 2004; Paus et al. 2008) and increases in overall mortality rate due to risk-taking behavior (Spear 2000). Adolescence is also characterized by important pubertal changes that can influence behavior and brain processing. Puberty is a period of development intrinsically related to the timing and exposure to gonadal hormones on the brain (McEwen 2001) and through these mechanisms exerts unique effects on brain and behavior processes during adolescence (Spear 2000; Sisk and Zehr 2005). Finally, during this period there are important sex-based differences that emerge, including the increased incidence of mood disorders in females (Giaconia et al. 1994; Nolen-Hoeksema and Girgus 1994), higher mortality in males due to risk-taking behavior and conduct disorders (Arnett 1992; Zahn-Waxler et al. 2008), and sex-based disparities in visuospatial versus verbal abilities (Delgado and Prieto 1996; Collins and Kimura 1997). Understanding structural brain changes that are unique to adolescence can better inform us regarding the inherent vulnerabilities of this period of development.

Developmental vulnerabilities in adolescence occur in the context of immature ability to voluntarily control our behavior in a planned fashion compared with adults. Overall improvements in cognitive control and reaction time show a nonlinear developmental trajectory with a sharp increase in performance from childhood to adolescence supporting increased speed of information processing that may be supported by enhanced white matter connectivity. This pattern changes from adolescence to adulthood as developmental progressions are less steep, and performance then attains a relative plateau (Kail 1993; Luna et al. 2004). Functional neuroimaging studies of voluntary control also demonstrate that differences during childhood may be qualitatively different from those that occur during adolescence. Functional magnetic resonance imaging (MRI) studies show differential recruitment of prefrontal regions in childhood, adolescence, and adulthood during tasks requiring cognitive control (Luna et al. 2000, 2001; Tamm et al. 2002; Crone et al. 2006; Velanova et al. 2008; Geier et al. 2009). Functional connectivity analyses, which may be independent from structural connectivity, also show distinct patterns in childhood and adolescence indicating protracted integration of long range connectivity supporting cognitive control (Fair et al. 2007, 2009). Whether the supporting white matter circuitry also demonstrates stage-like developmental patterns has not yet been well understood.

Myelination, which speeds neuronal transmission by the elaboration of a concentric phospholipid layer of insulation around axons by oligodendrocytes, continues to occur through adolescence (Yakovlev and Lecours 1967; Huttenlocher 1990), particularly in association areas into adulthood (Yakovlev and Lecours 1967; Benes 1989). Histologically based findings are supported by structural MRI studies (Pfefferbaum et al. 1994; Giedd, Blumenthal, Jeffries, Castellanos, et al. 1999; Sowell et al. 2003), which also show decreases in cortical gray matter in the context of white matter development (Giedd, Blumenthal, Jeffries, Castellanos, et al. 1999; Sowell et al. 2001; Gogtay et al. 2004; Giorgio et al. 2009). The concurrent changes in gray and white matter may not represent a simple reciprocal relationship and may be influenced by other neurobiological processes and tissue properties related to MRI (Paus et al. 2008; Tamnes et al. 2009). While histological studies of myelination emphasize a posterior to anterior gradient (Yakovlev and Lecours 1967), these findings have been extended to include prolonged development in other regions such as the hippocampus (Benes et al. 1994) and temporal regions (Giedd, Blumenthal, Jeffries,

Development of structure–function coupling in human brain networks during youth

Graham L. Baum[a,b], Zaixu Cui[a,b], David R. Roalf[a,b], Rastko Ciric[c], Richard F. Betzel[d], Bart Larsen[a,b], Matthew Cieslak[a,b], Philip A. Cook[e], Cedric H. Xia[a,b], Tyler M. Moore[a,b], Kosha Ruparel[a,b], Desmond J. Oathes[a], Aaron F. Alexander-Bloch[f], Russell T. Shinohara[g,h], Armin Raznahan[i], Raquel E. Gur[a,b,e,j], Ruben C. Gur[a,b,e,j], Danielle S. Bassett[a,j,k,l,m,n], and Theodore D. Satterthwaite[a,b,1]

[a]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104; [b]Lifespan Brain Institute, Children's Hospital of Philadelphia, Philadelphia, PA 19104; [c]Department of Bioengineering, Stanford University, Stanford, CA 94305; [d]Department of Psychological and Brain Sciences, Indiana University Bloomington, Bloomington, IN 47405; [e]Department of Radiology, University of Pennsylvania, Philadelphia, PA 19104; [f]Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06510; [g]Penn Statistics in Imaging and Visualization Center, Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA 19104; [h]Center for Biomedical Image Computing and Analytics, University of Pennsylvania, Philadelphia, PA 19104; [i]Developmental Neurogenomics Unit, National Institute of Mental Health, Bethesda, MD 20814; [j]Department of Neurology, University of Pennsylvania, Philadelphia, PA 19104; [k]Department of Bioengineering, University of Pennsylvania, Philadelphia, PA 19104; [l]Department of Electrical and Systems Engineering, University of Pennsylvania, Philadelphia, PA 19104; [m]Department of Physics and Astronomy, University of Pennsylvania, Philadelphia, PA 19104; and [n]Santa Fe Institute, Santa Fe, NM 87501

Edited by Marcus E. Raichle, Washington University in St. Louis, St. Louis, MO, and approved November 27, 2019 (received for review July 12, 2019)

The protracted development of structural and functional brain connectivity within distributed association networks coincides with improvements in higher-order cognitive processes such as executive function. However, it remains unclear how white-matter architecture develops during youth to directly support coordinated neural activity. Here, we characterize the development of structure–function coupling using diffusion-weighted imaging and *n*-back functional MRI data in a sample of 727 individuals (ages 8 to 23 y). We found that spatial variability in structure–function coupling aligned with cortical hierarchies of functional specialization and evolutionary expansion. Furthermore, hierarchy-dependent age effects on structure–function coupling localized to transmodal cortex in both cross-sectional data and a subset of participants with longitudinal data ($n = 294$). Moreover, structure–function coupling in rostrolateral prefrontal cortex was associated with executive performance and partially mediated age-related improvements in executive function. Together, these findings delineate a critical dimension of adolescent brain development, whereby the coupling between structural and functional connectivity remodels to support functional specialization and cognition.

brain development | MRI | connectome | cortical organization | structure–function

The human cerebral cortex is organized along a functional hierarchy extending from unimodal sensory cortex to transmodal association cortex (1, 2). This macroscale functional hierarchy is anchored by an anatomical backbone of white-matter pathways that coordinate synchronized neural activity and cognition. Both primate cortical evolution and human brain development have been characterized by the targeted expansion and remodeling of transmodal association areas (3, 4), which underpin the integration of sensory representations and abstract rules for executing goals. The protracted development of transmodal association cortex in humans provides an extended window for activity-dependent myelination (5) and synaptic pruning (6). This period of cortical plasticity sculpts functional specialization in transmodal association cortex and may be critical for developing higher-order executive functions such as working memory, mental flexibility, and inhibitory control (7).

Characterizing the functional specialization of cortical areas based on their patterns of connectivity has been central to understanding hierarchies of brain organization (8, 9). Network theory has provided a parsimonious framework for modeling structure–function mappings in neurobiological systems across species and spatial scales (10). Convergent evidence has highlighted the strong correspondence between measures of structural and functional brain connectivity at different spatiotemporal scales, including neural populations (11), specialized cortical regions (12), and large-scale brain networks (13–15). However, only sparse data exist regarding how the maturation of white-matter architecture during human brain development supports coordinated fluctuations in neural activity underlying cognition. Furthermore, aberrant development of structural constraints on functional communication could contribute to deficits in executive function and the emergence of neuropsychiatric disorders during adolescence (16–18).

Structure–function coupling describes structural support for functional communication and occurs when a cortical region's profile of interregional white-matter connectivity predicts the strength of interregional functional connectivity. Here, we describe the cortical topography of structure–function coupling and delineate how it evolves with development. To do this, we tested three related hypotheses. First, we hypothesized that structure–function coupling would reflect the functional specialization of a

Significance

The human brain is organized into a hierarchy of functional systems that evolve in childhood and adolescence to support the dynamic control of attention and behavior. However, it remains unknown how developing white-matter architecture supports coordinated fluctuations in neural activity underlying cognition. We document marked remodeling of structure–function coupling in youth, which aligns with cortical hierarchies of functional specialization and evolutionary expansion. Further, we demonstrate that structure–function coupling in rostrolateral prefrontal cortex supports age-related improvements in executive ability. These findings have broad relevance for accounts of experience-dependent plasticity in healthy development and abnormal development associated with neuropsychiatric illness.

Author contributions: G.L.B., R.E.G., R.C.G., D.S.B., and T.D.S. designed research; G.L.B. performed research; Z.C., D.R.R., R.C., R.F.B., B.L., M.C., P.A.C., C.H.X., T.M.M., K.R., D.J.O., A.F.A.-B., R.T.S., A.R., D.S.B., and T.D.S. contributed new reagents/analytic tools; G.L.B., Z.C., R.C., and T.M.M. analyzed data; and G.L.B. and T.D.S. wrote the paper.

The authors declare no competing interest.

This article is a PNAS Direct Submission.

Data deposition: The data reported in this paper have been deposited in the database of Genotypes and Phenotypes (accession no. dbGaP: phs000607.v2.p2).

[1]To whom correspondence may be addressed. Email: sattertt@pennmedicine.upenn.edu.

This article contains supporting information online at https://www.pnas.org/lookup/suppl/doi:10.1073/pnas.1912034117/-/DCSupplemental.

doi:10.1093/scan/nsm009 SCAN (2007) 2, 130–139

Adolescent development of the neural circuitry for thinking about intentions

Sarah-Jayne Blakemore,[1] Hanneke den Ouden,[1,2] Suparna Choudhury,[3] and Chris Frith[2]
[1]Institute of Cognitive Neuroscience, University College London, 17 Queen Square, London WC1N 3AR, UK, [2]Wellcome Centre for Neuroimaging, University College London, 12 Queen Square, London WC1N 3BG, UK, and [3]Brain and Behavioural Sciences, Institute of Child Health, University College London, 30 Guilford Street, London WC1N 1EH, UK

In this fMRI study, we investigated the development during adolescence of the neural network underlying thinking about intentions. A total of 19 adolescent participants (aged 12.1–18.1 years), and 11 adults (aged 22.4–37.8 years), were scanned using fMRI. A factorial design was employed with between-subjects factor *age group* and within-subjects factor *causality* (intentional or physical). In both adults and adolescents, answering questions about intentional causality *vs* physical causality activated the medial prefrontal cortex (PFC), superior temporal sulcus (STS), temporal poles and precuneus bordering with posterior cingulate cortex. In addition, there was a significant interaction between group and task in the medial PFC. During intentional relative to physical causality, adolescents activated part of the medial PFC more than did adults and adults activated part of the right STS more than did adolescents. These results suggest that the neural strategy for thinking about intentions changes between adolescence and adulthood. Although the same neural network is active, the relative roles of the different areas change, with activity moving from anterior (medial prefrontal) regions to posterior (temporal) regions with age.

Keywords: adolescence; theory of mind; mentalising; social cognition; development; intentional stance

INTRODUCTION

Adolescence is a time characterised by marked behavioural, hormonal and physical changes (Feldman and Elliott, 1990; Coleman and Hendry, 1999). Adolescents develop a capacity to hold in mind more multidimensional concepts and are thus able to think in a more strategic manner (Peterson, 1988). In addition to improvements in such 'executive functions' (Anderson *et al.*, 2001), during adolescence there seems to be a qualitative shift in the nature of social thinking such that adolescents are more self-aware and self-reflective (Elkind, 1967; Steinberg, 2005). In this study, we investigated the development of the neural circuitry underlying the ability to predict the actions that result from self-related intentions during adolescence.

Recent structural MRI studies have demonstrated that the brain undergoes considerable development during adolescence. In particular, the prefrontal cortex (PFC) undergoes the most pronounced course of structural development, while development of superior temporal cortex, including the superior temporal sulcus (STS), is most protracted (Sowell *et al.*, 2003; Gogtay *et al.*, 2004; Toga *et al.*, 2006). These MRI studies demonstrate that in PFC, there is an increase in grey matter up to the onset of puberty and a subsequent rapid decrease in grey matter density from just after puberty and throughout adolescence, continuing into early adulthood. While grey matter development in the PFC follows a sharp inverted U-curve, grey matter in the superior temporal cortex/STS steadily declines during adolescence and well into adulthood, reaching maturity relatively late (Gogtay *et al.*, 2004; Toga *et al.*, 2006). At the same time, there is an increase in cortical white matter density from puberty, throughout adolescence and into adulthood (Giedd *et al.*, 1996; 1999; Reiss *et al.*, 1996; Sowell *et al.*, 2001; Barnea-Goraly *et al.*, 2005). Results of earlier post-mortem investigations of human brain development suggest that the cortical changes detected using MRI, especially in PFC, mainly reflect two cellular processes occurring during adolescence: (i) synaptogenesis, which is followed by synaptic pruning, and (ii) axonal myelination (Yakovlev and Lecours, 1967; Huttenlocher, 1979; Huttenlocher *et al.*, 1983). It has been hypothesised that these maturational processes fine-tune neural circuitry in the PFC and other cortical regions, and thus increase efficiency of the cognitive systems they subserve (see Blakemore and Choudhury, 2006a for review)

Based on the finding that PFC and superior temporal cortex/STS undergo structural development during adolescence, it was hypothesised that the functioning within these regions would also show developmental change during this time period. Many high-level cognitive

Received 12 March 2007; Accepted 21 March 2007

This study was supported by the Wellcome Trust, MRC and the Royal Society, UK. S.J.B. is supported by a Royal Society Dorothy Hodgkin Fellowship. S.C. is supported by an MRC PhD studentship. H.d.O. is supported by the Wellcome Trust Four Year PhD Programme in Neuroscience at UCL. We thank Erin Hope Thompson for her help with this manuscript and Emily Jacobs for help with stimuli and pilot testing.

Correspondence should be addressed to Dr. Sarah-Jayne Blakemore, Institute of Cognitive Neuroscience, Alexandra House, 17 Queen Square, London WC1N 3AR. E-mail: s.blakemore@ucl.ac.uk.

Neuroscience and Biobehavioral Reviews 35 (2011) 1654–1664

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review

The social brain in adolescence: Evidence from functional magnetic resonance imaging and behavioural studies

Stephanie Burnett[a,*], Catherine Sebastian[b], Kathrin Cohen Kadosh[c], Sarah-Jayne Blakemore[c]

[a] Department of Brain Rehabilitation and Repair, Institute of Neurology, University College London, Queen Square, London WC1N 3BG, United Kingdom
[b] Clinical, Educational and Health Psychology, Division of Psychology and Language Sciences, University College London, 26 Bedford Way, London WC1H 0AP, United Kingdom
[c] Institute of Cognitive Neuroscience, University College London, 17 Queen Square, London WC1N 3AR, United Kingdom

ARTICLE INFO

Article history:
Received 23 April 2010
Received in revised form 1 October 2010
Accepted 20 October 2010

Keywords:
Adolescence
fMRI
Social brain
Development
Mentalising
Face processing
Emotion regulation

ABSTRACT

Social cognition is the collection of cognitive processes required to understand and interact with others. The term 'social brain' refers to the network of brain regions that underlies these processes. Recent evidence suggests that a number of social cognitive functions continue to develop during adolescence, resulting in age differences in tasks that assess cognitive domains including face processing, mental state inference and responding to peer influence and social evaluation. Concurrently, functional and structural magnetic resonance imaging (MRI) studies show differences between adolescent and adult groups within parts of the social brain. Understanding the relationship between these neural and behavioural observations is a challenge. This review discusses current research findings on adolescent social cognitive development and its functional MRI correlates, then integrates and interprets these findings in the context of hypothesised developmental neurocognitive and neurophysiological mechanisms.

Contents

1. Introduction

Humans are an intensely social species. Humans show a repertoire of social abilities – from rapidly and automatically detecting the presence of another human in our environment, to making inferences about their emotions, beliefs and enduring character traits, and finally using this knowledge to guide interactions (Frith and Frith, 2008, 2010). The last two decades have seen significant progress in understanding the neural underpinnings of

Abbreviations: ACC, anterior cingulate cortex; ATC, anterior temporal cortex; BOLD, blood oxygenation level-dependent; DLPFC, dorsolateral prefrontal cortex; FA, fractional anisotropy; FFA, fusiform face area; fMRI, functional magnetic resonance imaging; MPFC, medial prefrontal cortex; MRI, magnetic resonance imaging; MTR, magnetisation-transfer ratio; OFA, occipital face area; OFC, orbitofrontal cortex; PFC, prefrontal cortex; pSTS, posterior superior temporal sulcus; RPI, resistance to peer influence; STS, superior temporal sulcus; TPJ, temporo-parietal junction; VMPFC, ventromedial prefrontal cortex.

* Corresponding author. Tel.: +44 2076795434.
E-mail address: burstephanie@gmail.com (S. Burnett).

0149-7634/$ – see front matter.
doi:10.1016/j.neubiorev.2010.10.011

ELSEVIER

BIOLOGICAL PSYCHOLOGY

Biological Psychology 54 (2000) 241–257

www.elsevier.com/locate/biopsycho

Structural and functional brain development and its relation to cognitive development

B.J. Casey [a,*], Jay N. Giedd [b], Kathleen M. Thomas [a]

[a] *Department of Psychiatry, The Sackler Institute for Developmental Psychobiology, Weill Medical College of Cornell University, 525 East 68th Street, Box 171, New York, NY10021, USA*

[b] *Child Psychiatry Branch, National Institute for Mental Health, New York, NY10021, USA*

Abstract

Despite significant gains in the fields of pediatric neuroimaging and developmental neurobiology, surprisingly little is known about the developing human brain or the neural bases of cognitive development. This paper addresses MRI studies of structural and functional changes in the developing human brain and their relation to changes in cognitive processes over the first few decades of human life. Based on post-mortem and pediatric neuroimaging studies published to date, the prefrontal cortex appears to be one of the last brain regions to mature. Given the prolonged physiological development and organization of the prefrontal cortex during childhood, tasks believed to involve this region are ideal for investigating the neural bases of cognitive development. A number of normative pediatric fMRI studies examining prefrontal cortical activity in children during memory and attention tasks are reported. These studies, while largely limited to the domain of prefrontal functioning and its development, lend support for continued development of attention and memory both behaviorally and physiologically throughout childhood and adolescence. Specifically, the magnitude of activity observed in these studies was greater and more diffuse in children relative to adults. These findings are consistent with the view that increasing cognitive capacity during childhood may coincide with a gradual loss rather than formation of new synapses and presumably a strengthening of remaining synaptic connections. It is clear that innovative methods like fMRI together with MRI-based morphometry and nonhuman primate studies will transform our current understanding of human brain development and its relation to behavioral development.

Keywords: Brain development; Neuroimaging; Prefrontal functioning; Magnetic resonance imaging

* Corresponding author. Fax: + 1-212-7465755.

E-mail address: bjc2002@mail.med.cornell.edu (B.J. Casey).

0301-0511/00/$ - see front matter

PII: S0301-0511(00)00058-2

Developmental Science

Developmental Science (2010), pp F1–F10 DOI: 10.1111/j.1467-7687.2010.01035.x

FAST-TRACK REPORT

Peers increase adolescent risk taking by enhancing activity in the brain's reward circuitry

Jason Chein, Dustin Albert, Lia O'Brien, Kaitlyn Uckert and Laurence Steinberg

Department of Psychology, Temple University, USA

Abstract

The presence of peers increases risk taking among adolescents but not adults. We posited that the presence of peers may promote adolescent risk taking by sensitizing brain regions associated with the anticipation of potential rewards. Using fMRI, we measured brain activity in adolescents, young adults, and adults as they made decisions in a simulated driving task. Participants completed one task block while alone, and one block while their performance was observed by peers in an adjacent room. During peer observation blocks, adolescents selectively demonstrated greater activation in reward-related brain regions, including the ventral striatum and orbitofrontal cortex, and activity in these regions predicted subsequent risk taking. Brain areas associated with cognitive control were less strongly recruited by adolescents than adults, but activity in the cognitive control system did not vary with social context. Results suggest that the presence of peers increases adolescent risk taking by heightening sensitivity to the potential reward value of risky decisions.

Introduction

Teenagers are known to engage in more risky behavior than children or adults: adolescents are more likely than older or younger individuals to binge drink, smoke cigarettes, have casual sex partners, engage in violent and other criminal behavior, and to be involved in fatal or serious automobile crashes, the majority of which are caused by risky driving or driving under the influence of alcohol (Steinberg, 2008). Many experts agree that these preventable behaviors present the greatest threat to the well-being of young people in industrialized societies.

Significantly, adolescent risk taking differs from that of adults in its social context as well as its incidence. One of the hallmarks of adolescent risk taking is that it is much more likely than that of adults to occur in the presence of peers, as evidenced in studies of reckless driving (Simons-Morton, Lerner & Singer, 2005), substance abuse (Chassin, Hussong & Beltran, 2009), and crime (Zimring, 1998). Relatively greater adolescent risk taking in the presence of peers could be explained simply by the fact that adolescents spend more time with friends than do adults. However, recent experimental evidence (Gardner & Steinberg, 2005; O'Brien, Albert, Chein & Steinberg, in press) indicates that adolescents' decisions are directly influenced by the mere presence of peers. Gardner and Steinberg (2005), for instance, examined risk taking in adolescents, college undergraduates, and adults who were randomly assigned to engage in a simulated driving task alone or in the presence of two friends. They found that adolescents (and undergraduates to a lesser extent), but not adults, took a substantially greater number of risks when observed by peers.

Many research groups (Casey, Getz & Galvan, 2008; Luna, Padmanabhan & O'Hearn, 2010; Somerville, Jones & Casey, 2010; Steinberg, 2008; Van Leijenhorst, Moor, de Macks, Rombouts, Westenberg & Crone, 2010a; see also Ernst, Pine & Hardin, 2006) have posited that adolescents' relatively greater propensity toward risky behavior reflects the joint contribution of two brain systems that affect decision-making: (i) an *incentive processing* system involving the ventral striatum (VS; including the nucleus accumbens, NAcc) and the orbitofrontal cortex (OFC), among other regions, which biases decision-making based on the valuation and prediction of potential rewards and punishments; and (ii) a *cognitive control* system, including the lateral prefrontal cortex (LPFC), which supports goal-directed decision-making by keeping impulses in check and by providing the mental machinery needed for deliberation regarding alternative choices.

Neuroimaging studies conducted in both adult and adolescent populations show that these systems contribute to decision-making in an interactive fashion, with impulsive or risky choices often coinciding with the increased engagement of incentive processing regions

Address for correspondence: Jason M. Chein, Temple University, Department of Psychology, 6th Fl. Weiss Hall, 1701 N. 13th Street, Philadelphia, PA 19122, USA; e-mail: jchein@temple.edu

THE JOURNAL OF COMPARATIVE NEUROLOGY 453:116–130 (2002)

Amygdalo-Cortical Sprouting Continues Into Early Adulthood: Implications for the Development of Normal and Abnormal Function During Adolescence

MILES GREGORY CUNNINGHAM, SUJOY BHATTACHARYYA, AND FRANCINE MARY BENES*
Laboratory of Structural Neuroscience, McLean Hospital; Program in Neuroscience and Department of Psychiatry, Harvard Medical School, Boston, Massachusetts 02478

ABSTRACT

Adolescence is a critical stage for the development of emotional maturity and diverse forms of psychopathology. The posterior basolateral nucleus of the amygdala is known to mediate fear and anxiety and is important in assigning emotional valence to cognitive processes. The medial prefrontal cortex, a homologue of the human anterior cingulate cortex, mediates emotional, attentional, and motivational behaviors at the cortical level. We postulate that the development of connectivity between these two corticolimbic regions contributes to an enhanced integration of emotion and cognition during the postnatal period. In order to characterize the development of this relay, injections of the anterograde tracer biocytin were stereotaxically placed within the posterior basolateral nucleus of the amygdala of rats at successive postnatal time points (postnatal days 6–120). Labeled fibers in the medial prefrontal cortex were evaluated using a combination of brightfield, confocal, and electron microscopy. We found that the density of labeled fibers originating from the posterior basolateral nucleus shows a sharp curvilinear increase within layers II and V of the anterior cingulate cortex and the infralimbic subdivisions of medial prefrontal cortex during the late postweanling period. This increase was paralleled by a linear rise in the number of axospinous and axodendritic synapses present in the neuropil. Based on these results, we propose that late maturation of amygdalo-cortical connectivity may provide an anatomical basis for the development and integration of normal and possibly abnormal emotional behavior during adolescence and early adulthood. J. Comp. Neurol. 453:116–130, 2002.

Indexing terms: medial prefrontal cortex; basolateral nucleus; postnatal; biocytin;anterograde tracing

The most rapid biopsychosocial growth occurs during adolescence, a period of social adaptation, emotional turmoil, impulsivity, and stress (Spear, 2000). This period is also associated with the appearance of diverse psychopathologic states, including psychosis, depression, substance abuse, violence, and suicide (Besseghini, 1997; Safer, 1997; Beasley and Beardslee, 1998; Kools, 1998; Albright, 1999; Kaminer, 1999; Pratt and Greydanus, 2000). Although changes within the brain during adolescence may establish the foundation for the maturation of normal, adaptive behaviors, they may also serve as "triggers" for the onset of abnormal forms of behavior (Huttenlocher, 1984; Benes, 1995, 1997). Historically, theorists have emphasized the importance of adolescence in the emergence of adult personality features (Ewen, 1980), although the substrates for such changes have only recently begun to be explored. This research is now benefiting from a paradigmatic shift toward viewing postnatal brain de-

Grant sponsor: NIMH; Grant numbers: MH00423 and MH42261; Grant sponsor: the Stanley Foundation.

*Correspondence to: Francine M. Benes, M.D., Ph.D., McLean Hospital, 115 Mill Street, Belmont, MA 02478. E-mail: benesf@mclean.harvard.edu

Received 2 July 2001; Revised 29 January 2002; Accepted 21 June 2002
DOI 10.1002/cne.10376

Developmental Science

Developmental Science 13:6 (2010), pp 886–899

DOI: 10.1111/j.1467-7687.2009.00940.x

PAPER

Neurodevelopmental changes in the circuits underlying empathy and sympathy from childhood to adulthood

Jean Decety and Kalina J. Michalska

Center for Cognitive and Social Neuroscience, Department of Psychology and Psychiatry, University of Chicago, USA

Abstract

Empathy and sympathy play crucial roles in much of human social interaction and are necessary components for healthy coexistence. Sympathy is thought to be a proxy for motivating prosocial behavior and providing the affective and motivational base for moral development. The purpose of the present study was to use functional MRI to characterize developmental changes in brain activation in the neural circuits underpinning empathy and sympathy. Fifty-seven individuals, whose age ranged from 7 to 40 years old, were presented with short animated visual stimuli depicting painful and non-painful situations. These situations involved either a person whose pain was accidentally caused or a person whose pain was intentionally inflicted by another individual to elicit empathic (feeling as the other) or sympathetic (feeling concern for the other) emotions, respectively. Results demonstrate monotonic age-related changes in the amygdala, supplementary motor area, and posterior insula when participants were exposed to painful situations that were accidentally caused. When participants observed painful situations intentionally inflicted by another individual, age-related changes were detected in the dorsolateral prefrontal and ventromedial prefrontal cortex, with a gradual shift in that latter region from its medial to its lateral portion. This pattern of activation reflects a change from a visceral emotional response critical for the analysis of the affective significance of stimuli to a more evaluative function. Further, these data provide evidence for partially distinct neural mechanisms subserving empathy and sympathy, and demonstrate the usefulness of a developmental neurobiological approach to the new emerging area of moral neuroscience.

Introduction

The ability to perceive, appreciate and respond to the affective states of another, and predict the subsequent events that will result, is an important and valuable interpersonal phenomenon (Decety & Batson, 2007). Among the psychological processes that are the basis for most of social perception and interaction, empathy and sympathy play key roles. Empathy is one of the higher-order emotions that typically emerge as the child comes to a greater awareness of the experience of others, during the second and third years of life, and that arises in the context of someone else's emotional experience (Robinson, 2008). Here, we distinguish between empathy (the ability to appreciate the emotions and feelings of others with a minimal distinction between self and other) and sympathy (feelings of concern about the welfare of others). While empathy and sympathy are often conflated, the two can be dissociated, and although sympathy may stem from the apprehension of another's emotional state, it does not have to be congruent with the affective state of the other.

Empathy and sympathy are thought to play a central role in moral development and prosocial behavior (Smetana & Killen, 2008). Individuals who experience another's emotion and feel concern for them are expected to be motivated to help and not hurt other people (Eisenberg & Eggum, 2009; Zahn-Waxler & Radke-Yarrow, 1990). Sympathy is viewed by developmental psychologists as contributing to the development and elicitation of higher levels of moral reasoning (Eisenberg, 1986; Grusec, Davidov & Lundell, 2004; Hoffman, 2000; Knafo, Zahn-Waxler, Van Hulle, Robinson & Rhee, 2008).

The complex construct of empathy can be decomposed in a model that includes bottom-up processing of affective sharing and top-down processing in which the perceiver's motivation, intentions, and self-regulation influence the extent of an empathic experience (Decety, 2007; Decety & Jackson, 2004; Decety & Meyer, 2008; Eisenberg & Eggum, 2009; Hodges & Wegner, 1997). Recent cognitive neuroscience empirical research with adult participants indicates that the affective, cognitive, and regulatory aspects of empathy involve interacting, yet partially non-overlapping neural circuits (Lamm, Batson & Decety, 2007a; Lamm, Nusbaum, Meltzoff & Decety, 2007b; Lamm, Meltzoff & Decety, 2009). There is, to our knowledge, no study that has explored the

Address for correspondence: Jean Decety, Center for Cognitive and Social Neuroscience, Department of Psychology and Psychiatry, University of Chicago, 5848 S. University Avenue, Chicago, IL 60637, USA; e-mail: decety@uchicago.edu

Mini Review 16

Developmental Neuroscience

Dev Neurosci 2010;32:257–267
DOI: 10.1159/000317771

Received: March 22, 2010
Accepted after revision: June 14, 2010
Published online: August 31, 2010

The Neurodevelopment of Empathy in Humans

Jean Decety

Center for Cognitive and Social Neuroscience, Departments of Psychology and Psychiatry, University of Chicago, Chicago, Ill., USA

Key Words
Affective neuroscience · Amygdala · Empathy · Theory of mind · Neurodevelopment · Orbitofrontal cortex · Ventromedial prefrontal cortex

Abstract
Empathy, which implies a shared interpersonal experience, is implicated in many aspects of social cognition, notably prosocial behavior, morality and the regulation of aggression. The purpose of this paper is to critically examine the current knowledge in developmental and affective neuroscience with an emphasis on the perception of pain in others. It will be argued that human empathy involves several components: affective arousal, emotion understanding and emotion regulation, each with different developmental trajectories. These components are implemented by a complex network of distributed, often recursively connected, interacting neural regions including the superior temporal sulcus, insula, medial and orbitofrontal cortices, amygdala and anterior cingulate cortex, as well as autonomic and neuroendocrine processes implicated in social behaviors and emotional states. Decomposing the construct of empathy into subcomponents that operate in conjunction in the healthy brain and examining their developmental trajectory provides added value to our current approaches to understanding human development. It can also benefit our understanding of both typical and atypical development.

Introduction

Among the psychological processes that are the basis for much of social perception and smooth social interaction, empathy plays a key role. Empathy-related responding, including caring and sympathetic concern, is thought to motivate prosocial behavior, inhibit aggression and pave the way to moral reasoning [Eisenberg and Eggum, 2009]. On the other hand, children suffering from certain developmental disorders such as conduct disorder and disruptive behavior disorders are considered to have little empathy and concern for the feelings and wellbeing of others, as well as a lack of remorse and guilt, all of which are regarded as risk factors in developing hostile, aggressive or even violent behavior [de Wied et al., 2006].

This paper critically examines our current knowledge about the development of the mechanisms that support the experience of empathy and associated behavioral responses such as sympathy in the human brain. I begin by clarifying some definitional issues of empathy and associated phenomena. Next I address the neurodevelopment of empathy in relation to a model that distinguishes (a) bottom-up processing of affective communication, (b) emotion understanding, (c) top-down reappraisal processing in which the perceiver's motivation, intentions and attitudes moderate the extent of an empathic experience, and (d) an awareness of a self-other differentiation. I argue that studying subcomponents of more complex sociopsychological constructs like empathy can be par-

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

Accessible online at:
www.karger.com/dne

Jean Decety
Center for Cognitive and Social Neuroscience
Departments of Psychology and Psychiatry, University of Chicago
5848 South University Avenue, Chicago, IL 60637 (USA)
E-Mail decety@uchicago.edu

NeuroImage 64 (2013) 671–684

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Development of brain structural connectivity between ages 12 and 30: A 4-Tesla diffusion imaging study in 439 adolescents and adults

Emily L. Dennis [a], Neda Jahanshad [a], Katie L. McMahon [b], Greig I. de Zubicaray [c], Nicholas G. Martin [d], Ian B. Hickie [e], Arthur W. Toga [a], Margaret J. Wright [c,d], Paul M. Thompson [a,*]

[a] Imaging Genetics Center, Laboratory of Neuro Imaging, UCLA School of Medicine, Los Angeles, CA, USA
[b] Center for Advanced Imaging, University of Queensland, Brisbane, Australia
[c] School of Psychology, University of Queensland, Brisbane, Australia
[d] Queensland Institute of Medical Research, Brisbane, Australia
[e] Brain and Mind Research Institute, University of Sydney, Australia

ARTICLE INFO

Article history:
Accepted 3 September 2012
Available online 14 September 2012

Keywords:
HARDI
Structural connectivity
Graph theory
Development

ABSTRACT

Understanding how the brain matures in healthy individuals is critical for evaluating deviations from normal development in psychiatric and neurodevelopmental disorders. The brain's anatomical networks are profoundly re-modeled between childhood and adulthood, and diffusion tractography offers unprecedented power to reconstruct these networks and neural pathways *in vivo*. Here we tracked changes in structural connectivity and network efficiency in 439 right-handed individuals aged 12 to 30 (211 female/126 male adults, mean age = 23.6, SD = 2.19; 31 female/24 male 12 year olds, mean age = 12.3, SD = 0.18; and 25 female/22 male 16 year olds, mean age = 16.2, SD = 0.37). All participants were scanned with high angular resolution diffusion imaging (HARDI) at 4 T. After we performed whole brain tractography, 70 cortical gyral-based regions of interest were extracted from each participant's co-registered anatomical scans. The proportion of fiber connections between all pairs of cortical regions, or nodes, was found to create symmetric fiber density matrices, reflecting the structural brain network. From those 70 × 70 matrices we computed graph theory metrics characterizing structural connectivity. Several key global and nodal metrics changed across development, showing increased network integration, with some connections pruned and others strengthened. The increases and decreases in fiber density, however, were not distributed proportionally across the brain. The frontal cortex had a disproportionate number of decreases in fiber density while the temporal cortex had a disproportionate number of increases in fiber density. This large-scale analysis of the developing structural connectome offers a foundation to develop statistical criteria for aberrant brain connectivity as the human brain matures.

Introduction

The human brain changes profoundly, both functionally and structurally, between childhood and adulthood (Dosenbach et al., 2010; Gogtay et al., 2004; Lenroot et al., 2007; Shaw et al., 2008; Sowell et al., 2003). Following the massive growth in the number of synapses after birth, anatomical studies show a decline in synaptic density, as short-range connections are pruned in favor of long-range ones (Huttenlocher, 1979, 1990). Studies of structural connectivity using diffusion imaging show that the fractional anisotropy of water along white matter tracts – an index of myelination and axonal coherence – increases in childhood, plateaus in adulthood, and declines in old age (Kochunov et al., 2010). Studies of functional connectivity have employed resting-state fMRI data to estimate the "developmental ages" or relative maturity of participants, finding that chronological age accounts for over half of the variance in functional brain connectivity in developmental samples (Dosenbach et al., 2010). Defining the developmental trajectory for various measures of brain structure and function is critical for understanding the general principles of neural network development. Determining the normal developmental trajectory will also help to identify deviations in structural circuitry implicated in neuropsychiatric disorders such as autism or schizophrenia (Scott-Van Zeeland et al., 2010).

Graph theory is a branch of mathematics developed to describe and analyze networks, offering a variety of metrics that have become popular for characterizing networks in the brain. By modeling the brain as a collection of nodes (hubs) and edges (connections between them), graph theory quantifies network topology through a number of standard parameters (Sporns et al., 2004). One of these is path length, a measure of the distance, in edges, between one brain region (node) and another (Rubinov and Sporns, 2010). Global efficiency is

* Corresponding author at: Laboratory of Neuro Imaging, Department of Neurology, UCLA School of Medicine, 635 Charles Young Drive South, Suite 225, Los Angeles, CA 90095-7334, USA. Fax: +1 310 206 5518.
E-mail address: thompson@loni.ucla.edu (P.M. Thompson).

1053-8119/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.neuroimage.2012.09.004

Developmental Science

Developmental Science 13:6 (2010), pp F15–F24 DOI: 10.1111/j.1467-7687.2010.01014.x

12

FAST-TRACK ARTICLE

Development of relational reasoning during adolescence

Iroise Dumontheil,[1,2] Rachael Houlton,[1] Kalina Christoff[3] and Sarah-Jayne Blakemore[1]

1. *Institute of Cognitive Neuroscience, University College London, UK*
2. *Neuroscience Department, Karolinska Institute, Sweden*
3. *Department of Psychology, University of British Columbia, Canada*

Abstract

*Non-linear changes in behaviour and in brain activity during adolescent development have been reported in a variety of cognitive tasks. These developmental changes are often interpreted as being a consequence of changes in brain structure, including non-linear changes in grey matter volumes, which occur during adolescence. However, very few studies have attempted to combine behavioural, functional and structural data. This multi-method approach is the one we took in the current study, which was designed to investigate developmental changes in behaviour and brain activity during relational reasoning, the simultaneous integration of multiple relations. We used a relational reasoning task known to recruit rostrolateral prefrontal cortex (RLPFC), a region that undergoes substantial structural changes during adolescence. The task was administered to female participants in a behavioural (*N = *178, 7–27 years) and an fMRI study (*N = *37, 11–30 years). Non-linear changes in accuracy were observed, with poorer performance during mid-adolescence. fMRI and VBM results revealed a complex picture of linear and possibly non-linear changes with age. Performance and structural changes partly accounted for changes with age in RLPFC and medial superior frontal gyrus activity but not for a decrease in activation in the anterior insula/frontal operculum between mid-adolescence and adulthood. These functional changes might instead reflect the maturation of neurocognitive strategies.*

Introduction

Previous studies have reported non-linear developmental changes in performance on cognitive tasks, including face processing and match-to-sample tasks, during adolescence (e.g. Carey, Diamond & Woods, 1980; Diamond, Carey & Back, 1983; McGivern, Andersen, Byrd, Mutter & Reilly, 2002). Typically, a dip in performance is observed around the start of puberty (age 11–12 years old) and its timing can differ between genders (McGivern *et al.*, 2002). Non-linear developmental changes in brain structure, in particular grey matter volumes (Giedd, Blumenthal, Jeffries, Castellanos, Zijdenbos, Paus, Evans & Rapoport, 1999; Shaw, Kabani, Lerch, Eckstrand, Lenroot, Gogtay, Greenstein, Clasen, Evans, Rapoport & Giedd, 2008), and in brain function during face processing and go-nogo tasks (Hare, Tottenham, Galvan, Voss, Glover & Casey, 2008; Uhlhaas, Roux, Singer, Haenschel, Sireteanu & Rodriguez, 2009) have also been reported. Behavioural and functional changes are often interpreted as being a consequence of the structural changes (Horská, Kaufmann, Brant, Naidu, Harris & Barker, 2002; Lewis, 1997; Tseng & O'Donnell, 2005, 2007; see Spear, 2000, for review). However, very few studies to date have attempted to combine behavioural, functional and structural data to better understand non-linear developmental changes. This multi-method approach is the one we took in the current study. We first carried out a large-scale behavioural study to evaluate development in performance on a specific cognitive control task, and then a functional magnetic resonance imaging (fMRI) study to investigate the relationship between functional and structural neural changes with age in this task.

The rostrolateral prefrontal cortex (RLPFC), corresponding to the lateral portion of Brodmann area 10 (BA10), undergoes substantial structural changes during adolescence (see Dumontheil, Burgess & Blakemore, 2008, for review). RLPFC is involved in the elaboration, evaluation and maintenance of abstract rules and information (Burgess, Dumontheil & Gilbert, 2007; Christoff & Gabrieli, 2000; Christoff, Keramatian, Gordon, Smith & Mädler, 2009; Koechlin, Ody & Kouneiher, 2003; Ramnani & Owen, 2004) and has been particularly implicated in relational reasoning (Christoff, Prabhakaran, Dorfman, Zhao, Kroger, Holyoak &

Address for correspondence: Iroise Dumontheil, Institute of Cognitive Neuroscience, UCL, 17 Queen Square, London WC1N 3AR, UK; e-mail: i.dumontheil@gmail.com

Childhood poverty, chronic stress, and adult working memory

Gary W. Evans[1] and Michelle A. Schamberg

Departments of Design and Environmental Analysis and Human Development, Cornell University, Ithaca, NY 14853-4401

Edited by Bruce S. McEwen, The Rockefeller University, New York, NY, and approved February 24, 2009 (received for review November 22, 2008)

The income–achievement gap is a formidable societal problem, but little is known about either neurocognitive or biological mechanisms that might account for income-related deficits in academic achievement. We show that childhood poverty is inversely related to working memory in young adults. Furthermore, this prospective relationship is mediated by elevated chronic stress during childhood. Chronic stress is measured by allostatic load, a biological marker of cumulative wear and tear on the body that is caused by the mobilization of multiple physiological systems in response to chronic environmental demands.

A large, robust literature demonstrates a pervasive income–achievement gap. Family income is a strong and consistent predictor of multiple indices of achievement, including standardized test scores, grades in school, and educational attainment. Family income matters to children's cognitive development (1–3), with more enduring economic hardship particularly harmful (4, 5). The income–achievement gap is already present by kindergarten and accelerates over time (6, 7). The longer the duration of childhood exposure to poverty, the worse achievement levels become. Achievement test scores and school performance, however, do not inform us about what neurocognitive processes are influenced by childhood poverty. Furthermore, the voluminous income–achievement gap literature is silent on underlying biological explanations.

Here, we test 2 hypotheses. One is that childhood poverty will interfere with working memory in young adults. Working memory is the temporary storage mechanism that enables us to hold a small amount of information active over a short interval and to manipulate it. Working memory is essential to language comprehension, reading, and problem solving, and it is a critical prerequisite for long-term storage of information. The second hypothesis we test is that the prospective relationship between childhood poverty and adult working memory will be mediated by chronic stress exposure, (i.e., poverty → chronic stress → working memory). Farah and colleagues (8) found significant deficits in working memory between low- and middle-socioeconomic status (SES) kindergarten children and, in a second sample, between low- and middle-SES 11-year-olds (9). In a third study of first-graders, SES was a significant predictor of working memory (10). An important, missing component of this groundbreaking work is the underlying biological mechanisms to account for the SES–neurocognitive link.

Both animal and human studies reveal that working memory resides in the prefrontal cortex, although it is clearly influenced by hippocampal, and possibly amygdala, interactions with the prefrontal cortex as well (11–14). The human hippocampus and prefrontal cortex are each disrupted by chronic physiological stress (14–17). Chronically elevated physiological stress is a plausible model for how poverty could get into the brain and eventually interfere with achievement.

We measure chronic physiological stress by using allostatic load. Allostatic load is an index of cumulative wear and tear on the body caused by repeated mobilizations of multiple physiological systems over time in response to environmental demands (16, 18–24). Allostasis is a dynamic and interactive set of multiple physiological systems of bodily equilibrium maintenance. According to allostasis theory, the body continuously adjusts its normal operating range in response to external requirements. These dynamic adjustments reflect downward regulation to maintain the organism's internal stability, but at levels more congruent with environmental conditions. The active, ongoing maintenance of internal equilibrium increases allostatic load, which reflects chronic wear and tear caused by the mobilization of resources to meet changing environmental exigencies. Overexposure to a combination of multiple, activated bodily response systems (e.g., neuronal, endocrine, cardiovascular) alters the ability of the body to respond efficiently to environmental demands. Longer, more frequent exposure to environmental stressors accelerates bodily wear and tear. Chronic and more intensive environmental stressors cause the body to mobilize multiple physiological systems to meet those demands, but at higher levels of activity. Conversely, when environmental demands are low, individuals who have had a higher allostatic load burden will be less efficient in turning off the multiple physiological resources marshaled to deal with chronic demands.

Interest in allostasis has risen primarily for 2 reasons. First, whereas singular physiological markers of adaptation to environmental demands (e.g., blood pressure) are modestly linked to various disease endpoints (e.g., coronary heart disease), the combined effect of singular physiological changes across multiple biological systems captured by allostatic load is substantially more predictive of disease outcomes (18–24). Second, in addition to contributing to physical morbidity, chronically elevated allostatic load also influences neurological processes, particularly in the hippocampus and prefrontal cortex, that are capable of disrupting cognitive functioning. These neurological processes include altered neurotransmitter activity (e.g., dopamine, norepinephrine, glutamate), suppression of neurogenesis as well as elevated neurotoxicity, alterations in receptor binding sites (e.g., mineral corticoid, glucocorticoid), and morphological changes, such as dendritic remodeling and smaller hippocampal and prefrontal cortex volumes (14–17). Thus, chronically elevated allostatic load could lead to disturbances in working memory in human beings. To date, however, this has not been tested.

Thus, in this paper we bring together 2 separate research literatures, neurocognition and physiological stress, to address a major societal problem, namely, the income–achievement gap. Numerous investigators employing a wide array of study designs have uncovered consistent evidence of an income–achievement gap. Missing in this voluminous literature is evidence of underlying neurocognitive and biological mechanisms. We hypothesize that a plausible contributor to the income–achievement gap

Author contributions: G.W.E. designed research; M.A.S. performed research; G.W.E. and M.A.S. analyzed data; and G.W.E. and M.A.S. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

Freely available online through the PNAS open access option.

[1]To whom correspondence should be addressed. E-mail: gwe1@cornell.edu.

BRAIN RESEARCH 1114 (2006) 166–174

available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

BRAIN RESEARCH

Research Report

Childhood poverty: Specific associations with neurocognitive development

Martha J. Farah[a,*], *David M. Shera*[b], *Jessica H. Savage*[a], *Laura Betancourt*[a], *Joan M. Giannetta*[c], *Nancy L. Brodsky*[c], *Elsa K. Malmud*[c], *Hallam Hurt*[c]

[a]*Department of Psychology and Center for Cognitive Neuroscience, University of Pennsylvania, USA*
[b]*Division of Biostatistics and Epidemiology, Department of Pediatrics Children's Hospital of Philadelphia and Department of Epidemiology and Biostatistics, University of Pennsylvania, USA*
[c]*Division of Neonatology, Department of Pediatrics, University of Pennsylvania and Children's Hospital of Philadelphia, USA*

ARTICLE INFO

Article history:
Accepted 21 June 2006
Available online 1 August 2006

Keywords:
Socioeconomic status
Prefrontal cortex
Development
Executive function
Memory
Environment

ABSTRACT

Growing up in poverty is associated with reduced cognitive achievement as measured by standardized intelligence tests, but little is known about the underlying neurocognitive systems responsible for this effect. We administered a battery of tasks designed to tax-specific neurocognitive systems to healthy low and middle SES children screened for medical history and matched for age, gender and ethnicity. Higher SES was associated with better performance on the tasks, as expected, but the SES disparity was significantly nonuniform across neurocognitive systems. Pronounced differences were found in Left perisylvian/Language and Medial temporal/Memory systems, along with significant differences in Lateral/Prefrontal/Working memory and Anterior cingulate/Cognitive control and smaller, nonsignificant differences in Occipitotemporal/Pattern vision and Parietal/Spatial cognition.

1. Introduction

Beginning as early as preschool and persisting throughout childhood and beyond, individuals of low socioeconomic status (SES) perform below their middle class counterparts on tests of intelligence and school achievement (e.g., Bradley and Corwyn, 2002). Measured in standard deviation, SES gradients for cognitive achievement are even steeper than those for physical health (Duncan et al., 1998) and are likely to play a role in the persistence of poverty across generations.

Little is known about the underlying mental systems that mediate the SES disparities in cognitive performance. IQ tests and school achievement are valuable in that they have well-understood psychometric properties and predictive power concerning future life trajectory. However, they do not correspond in any straightforward way to the current scientific "parse" of cognitive function into underlying components. In the present investigation, we attempt to characterize the cognitive outcomes of childhood poverty in terms of the framework of cognitive neuroscience.

How and why might a sociological construct, SES, be associated with brain function? The answer lies in the nature of SES itself. Although SES is generally estimated by measuring parental education and occupational status, it encompasses far more than these simple indices, including associated differences in physical and mental health (Adler et al., 1994) and in physical and psychosocial aspects of the environment (Evans, 2004). Important psychosocial factors

* *Corresponding author.* Center for Cognitive Neuroscience, 3720 Walnut St., Philadelphia, PA 19104, USA. Fax: +1 215 898 1982.
E-mail address: mfarah@psych.upenn.edu (M.J. Farah).

0006-8993/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.brainres.2006.06.072

Journal of Experimental Psychology:
Learning, Memory, and Cognition
2009, Vol. 35, No. 3, 709–730

15

0278-7393/09/$12.00 DOI: 10.1037/a0014983

Affective and Deliberative Processes in Risky Choice: Age Differences in Risk Taking in the Columbia Card Task

Bernd Figner
Columbia University

Rachael J. Mackinlay and Friedrich Wilkening
University of Zurich

Elke U. Weber
Columbia University

The authors investigated risk taking and underlying information use in 13- to 16- and 17- to 19-year-old adolescents and in adults in 4 experiments, using a novel dynamic risk-taking task, the Columbia Card Task (CCT). The authors investigated risk taking under differential involvement of affective versus deliberative processes with 2 versions of the CCT, constituting the most direct test of a dual-system explanation of adolescent risk taking in the literature so far. The "hot" CCT was designed to trigger more affective decision making, whereas the "cold" CCT was designed to trigger more deliberative decision making. Differential involvement of affective versus deliberative processes in the 2 CCT versions was established by self-reports and assessment of electrodermal activity. Increased adolescent risk taking, coupled with simplified information use, was found in the hot but not the cold condition. Need-for-arousal predicted risk taking only in the hot condition, whereas executive functions predicted information use in the cold condition. Results are consistent with recent dual-system explanations of risk taking as the result of competition between affective processes and deliberative cognitive-control processes, with adolescents' affective system tending to override the deliberative system in states of heightened emotional arousal.

Keywords: risk taking, adolescence, affective and deliberative decision making, dual system, cognitive control

Supplemental materials: http://dx.doi.org/10.1037/a0014983.supp

Everyday risk taking shows a typical developmental trajectory. Comparatively low during childhood, risk taking increases when individuals reach puberty, peaks in adolescence and early adulthood, and decreases again during adulthood. This age pattern has been documented in different risk-taking behaviors, such as the use of licit and illicit substances, dangerous behavior in traffic, unsafe sexual practices, delinquent behaviors, and risky recreational sports (Boyer, 2006; Casey, Getz, & Galvan, 2008; Reyna & Farley, 2006; Rivers, Reyna, & Mills, 2008; Steinberg, 2008). Although for many adolescents increased risk taking is a transient phenomenon, it can have a negative impact on adult life. For example, adolescent alcohol, nicotine, or drug use is a powerful predictor for later substance use and other behavioral problems (e.g., Ellickson, D'Amico, Collins, & Klein, 2005; Grant et al., 2006). It is therefore important to explore the causes and mechanisms of risk taking in adolescents, which are currently not well understood.

Psychological research has investigated risk taking with different methods. Most common have been risky decision-making tasks in the laboratory and self-report questionnaires of everyday risk-taking behaviors. Results from studies using these methods have sometimes observed the typical age (and gender[1]) patterns, but other times not (Boyer, 2006; Reyna & Farley, 2006). Shedding some light on this inconsistency, Byrnes, Miller, and Schafer (1999) found that the kind of measure used to assess risk taking

Bernd Figner and Elke U. Weber, Center for the Decision Sciences and Department of Psychology, Columbia University; Rachael J. Mackinlay and Friedrich Wilkening, Department of Psychology, University of Zurich, Zurich, Switzerland.

This research was supported by a fellowship from the Swiss National Science Foundation (Grants Nos. PA001-115327 and PBZH1-110268) awarded to Bernd Figner, two grants by the U.S. National Science Foundation (Grant No. SES–0720932 awarded to Bernd Figner and Elke U. Weber; Grant No. SES–0452932 awarded to Elke U. Weber), and a grant by the Jacobs Center for Productive Youth Development awarded to Rachael J. Mackinlay.

We thank Carl Hart for helpful comments on earlier versions of the article and our research assistants for their help in various aspects of the study.

Correspondence concerning this article should be addressed to Bernd Figner, Center for the Decision Sciences and Department of Psychology, Columbia University, 406 Schermerhorn Hall, Mail Code 5501, 1190 Amsterdam Avenue, New York, NY 10027. E-mail: bf2151@columbia.edu

[1] When gender differences are observed, male adolescents typically take even greater risks than do female adolescents (e.g., Elander, West, & French, 1993; Gullone, Moore, Moss, & Boyd, 2000; Turner & McClure, 2003; Wilson & Daly, 1985). However, this pattern is not consistent across domains, and gender differences have been reported to have grown smaller over the last decades (Byrnes et al., 1999).

OXFORD

16 Cerebral Cortex, 2018; 1–12

doi: 10.1093/cercor/bhy266
Original Article

ORIGINAL ARTICLE

Continuity and Discontinuity in Human Cortical Development and Change From Embryonic Stages to Old Age

Anders M. Fjell [1,2], Chi-Hua Chen[3], Donatas Sederevicius[1], Markus H. Sneve [1], Håkon Grydeland [1], Stine K. Krogsrud[1], Inge Amlien[1], Lia Ferschmann[1], Hedda Ness[1], Line Folvik[1], Dani Beck[1], Athanasia M. Mowinckel[1], Christian K. Tamnes[1], René Westerhausen[1], Asta K. Håberg[4,5], Anders M. Dale[3,6] and Kristine B. Walhovd[1,2]

[1]Department of Psychology, Center for Lifespan Changes in Brain and Cognition, University of Oslo, 0317 Oslo, Norway, [2]Department of Radiology and Nuclear Medicine, Oslo University Hospital, 0372 Oslo, Norway, [3]Department of Radiology, University of California, San Diego, La Jolla, CA 92093, USA, [4]Department of Medical Imaging, St. Olav's Hospital, 7491 Trondheim, Norway, [5]Department of Neuroscience, Norwegian University of Science and Technology (NTNU), N-7491 Trondheim, Norway and [6]Department of Neurosciences, University of California, San Diego, La Jolla, CA 92093, USA

Address correspondence to Anders M. Fjell, Department of Psychology, Center for Lifespan Changes in Brain and Cognition, University of Oslo, Pb. 1094 Blindern, 0317 Oslo, Norway. Email: andersmf@psykologi.uio.no orcid.org/0000-0003-2502-8774

Abstract

The human cerebral cortex is highly regionalized, and this feature emerges from morphometric gradients in the cerebral vesicles during embryonic development. We tested if this principle of regionalization could be traced from the embryonic development to the human life span. Data-driven fuzzy clustering was used to identify regions of coordinated longitudinal development of cortical surface area (SA) and thickness (CT) (n = 301, 4–12 years). The principal divide for the developmental SA clusters extended from the inferior–posterior to the superior–anterior cortex, corresponding to the major embryonic morphometric anterior–posterior (AP) gradient. Embryonic factors showing a clear AP gradient were identified, and we found significant differences in gene expression of these factors between the anterior and posterior clusters. Further, each identified developmental SA and CT clusters showed distinguishable life span trajectories in a larger longitudinal dataset (4–88 years, 1633 observations), and the SA and CT clusters showed differential relationships to cognitive functions. This means that regions that developed together in childhood also changed together throughout life, demonstrating continuity in regionalization of cortical changes. The AP divide in SA development also characterized genetic patterning obtained in an adult twin sample. In conclusion, the development of cortical regionalization is a continuous process from the embryonic stage throughout life.

Key words: aging, cognition, cortical development, magnetic resonance imaging, protomap theory

Cerebral Cortex July 2010;20:1613-1629
doi:10.1093/cercor/bhp225
Advance Access publication October 29, 2009

Immaturities in Reward Processing and Its Influence on Inhibitory Control in Adolescence

C.F. Geier, R. Terwilliger, T. Teslovich, K. Velanova and B. Luna

Laboratory of Neurocognitive Development, Department of Psychiatry and Psychology, Center for the Neural Basis of Cognition, University of Pittsburgh, Pittsburgh, PA 15213, USA

The nature of immature reward processing and the influence of rewards on basic elements of cognitive control during adolescence are currently not well understood. Here, during functional magnetic resonance imaging, healthy adolescents and adults performed a modified antisaccade task in which trial-by-trial reward contingencies were manipulated. The use of a novel fast, event-related design enabled developmental differences in brain function underlying temporally distinct stages of reward processing and response inhibition to be assessed. Reward trials compared with neutral trials resulted in faster correct inhibitory responses across ages and in fewer inhibitory errors in adolescents. During reward trials, the blood oxygen level–dependent signal was attenuated in the ventral striatum in adolescents during cue assessment, then overactive during response preparation, suggesting limitations during adolescence in reward assessment and heightened reactivity in anticipation of reward compared with adults. Importantly, heightened activity in the frontal cortex along the precentral sulcus was also observed in adolescents during reward-trial response preparation, suggesting reward modulation of oculomotor control regions supporting correct inhibitory responding. Collectively, this work characterizes specific immaturities in adolescent brain systems that support reward processing and describes the influence of reward on inhibitory control. In sum, our findings suggest mechanisms that may underlie adolescents' vulnerability to poor decision-making and risk-taking behavior.

Keywords: adolescence, antisaccade, fMRI, response inhibition, reward

Introduction

Negative outcomes associated with risky or reckless behaviors are a major contributor to sharp increases (~200%) in morbidity and mortality rates observed during adolescence (Arnett 1992; Spear 2000; Dahl 2004). Risk taking can be defined as engaging, often impulsively, in behaviors that are high in subjective desirability or excitement but which expose the individual to potential injury or loss (e.g., driving extremely fast and engaging in unprotected sex) (Irwin 1990). Adolescents' propensity to engage in risk taking provides compelling behavioral evidence for immaturities in decision-making abilities. However, our understanding of the neural basis of risk taking remains limited. Although multiple functional circuitries are expected to contribute to behavioral risk taking, 2 likely primary systems are reward processing and inhibitory control (Steinberg 2004). Immature detection and appraisal of rewards coupled with limitations in endogenous impulse control could result in poor decision making that may then set the stage for engaging in risk taking. In order to inform the neural basis of risk-taking behavior, in this paper, we compare reward processing and its effects on inhibitory control in adolescents compared with adults.

An extensive literature has delineated the neural circuitry supporting reward processing in mature adults (Schultz 2000; Breiter et al. 2001; O'Doherty et al. 2001; Roesch and Olson 2004; Hikosaka et al. 2006). In particular, the orbitofrontal cortex (OFC), dorsal and ventral striatum (VS), and medial prefrontal cortex (PFC) have been identified as key components (Schultz 2000; McClure et al. 2004). Importantly, the temporal resolution of single-unit and event-related functional magnetic resonance imaging (fMRI) studies has shown that reward processing is not a monolithic function but rather a dynamic suite of interrelated computations. Distinct signals occurring before ("anticipatory" signals) and after reward delivery ("consummatory" signals) have been identified (Schultz 2000; Hare et al. 2008). Anticipatory signals are associated with the initial detection and determination of the valence of reward-predicting cues, as well as with assessment of the anticipated value of a future reward (Knutson et al. 2001; O'Doherty et al. 2002). Consummatory signals include those related to the magnitude of the received reward (Delgado et al. 2000, 2003; Rolls 2000; O'Doherty et al. 2001) and whether or not the received reward matched up with predictions ("prediction-error" signals) (Schultz 2000; Schultz et al. 2000).

Comparatively, our understanding of the development of reward processing through adolescence remains quite limited. Anatomical studies indicate that primary reward regions show persistent immaturities through adolescence, including continued thinning of gray matter in basal ganglia and OFC (Giedd et al. 1996; Sowell et al. 1999; Gogtay et al. 2004; Toga et al. 2006), which in part are likely due to the loss of weak or unused synapses via synaptic pruning (Gogtay et al. 2004). During adolescence, an increased number of underspecified synapses could result in limitations in the identification of reward cues and value representations relative to adults. In parallel with synaptic pruning, myelination increases linearly throughout development (Yakovlev and Lecours 1967). Myelination enhances the efficiency of information processing by increasing the speed and fidelity of distal neuronal transmission, aiding the functional integration of the widely distributed brain circuitry critical for the emergence of complex higher-order behavior (Goldman-Rakic et al. 1992; Luna and Sweeney 2004). A comparative undermyelination of the adolescent brain could contribute to a limited ability to efficiently integrate reward signals with efferent motor systems necessary for motivated behavior (Roesch and Olson 2003, 2004).

Along with persistent microstructural maturation, converging data from human and animal models indicate that dopamine (DA) neurotransmission in striatal and cortical systems

Structural Magnetic Resonance Imaging of the Adolescent Brain

JAY N. GIEDD

National Institute of Mental Health, National Institutes of Health, Department of Health and Human Services, Bethesda, Maryland 20892, USA

ABSTRACT: **Magnetic resonance imaging (MRI) provides accurate anatomical brain images without the use of ionizing radiation, allowing longitudinal studies of brain morphometry during adolescent development. Results from an ongoing brain imaging project being conducted at the Child Psychiatry Branch of the National Institute of Mental Health indicate dynamic changes in brain anatomy throughout adolescence. White matter increases in a roughly linear pattern, with minor differences in slope in the four major lobes (frontal, parietal, temporal, occipital). Cortical gray matter follows an inverted U-shape developmental course with greater regional variation than white matter. For instance, frontal gray matter volume peaks at about age 11.0 years in girls and 12.1 years in boys, whereas temporal gray matter volume peaks at about age at 16.7 years in girls and 16.2 years in boys. The dorsal lateral prefrontal cortex, important for controlling impulses, is among the latest brain regions to mature without reaching adult dimensions until the early 20s. The details of the relationships between anatomical changes and behavioral changes, and the forces that influence brain development, have not been well established and remain a prominent goal of ongoing investigations.**

KEYWORDS: **magnetic resonance imaging (MRI); adolescence; gray matter; white matter**

INTRODUCTION

It comes as no surprise to parents of teens that the brain of an 8 year old is different than the brain of a 13 year old. Yet to pin down these differences in a scientific way has been elusive. Nature has gone to great extremes to protect this most vital organ. It is wrapped in a leathery case, surrounded by a protective moat of fluid, and completely encased in bone. This has shielded the brain from falls or attacks from predators, but it has also shielded the brain from scientists. Even after the availability of X rays or CT scans, the study of the healthy teen brain remained indirect, because such techniques use ionizing radiation, which ethically precludes their use in non-ill populations.

Address for correspondence: Jay N. Giedd, M.D., National Institute of Mental Health, National Institutes of Health, Department of Health and Human Services, Room 4C110, 10 Center Dr. MSC 1367, Bethesda, MD 20892-1367. Voice: 301-435-4517; fax: 301-480-8898.
jg@nih.gov

Ann. N.Y. Acad. Sci. 1021: 77–85 (2004).
doi: 10.1196/annals.1308.009

Dynamic mapping of human cortical development during childhood through early adulthood

Nitin Gogtay*†, Jay N. Giedd*, Leslie Lusk*, Kiralee M. Hayashi‡, Deanna Greenstein*, A. Catherine Vaituzis*, Tom F. Nugent III*, David H. Herman*, Liv S. Clasen*, Arthur W. Toga‡, Judith L. Rapoport*, and Paul M. Thompson‡

*Child Psychiatry Branch, National Institutes of Mental Health, National Institutes of Health, Bethesda, MD 20892; and ‡Laboratory of Neuro Imaging, Department of Neurology, University of California School of Medicine, Los Angeles, CA 90095-1769

Communicated by Leslie G. Ungerleider, National Institutes of Health, Bethesda, MD, April 15, 2004 (received for review January 7, 2004)

We report the dynamic anatomical sequence of human cortical gray matter development between the age of 4–21 years using quantitative four-dimensional maps and time-lapse sequences. Thirteen healthy children for whom anatomic brain MRI scans were obtained every 2 years, for 8–10 years, were studied. By using models of the cortical surface and sulcal landmarks and a statistical model for gray matter density, human cortical development could be visualized across the age range in a spatiotemporally detailed time-lapse sequence. The resulting time-lapse "movies" reveal that (*i*) higher-order association cortices mature only after lower-order somatosensory and visual cortices, the functions of which they integrate, are developed, and (*ii*) phylogenetically older brain areas mature earlier than newer ones. Direct comparison with normal cortical development may help understanding of some neurodevelopmental disorders such as childhood-onset schizophrenia or autism.

Human brain development is structurally and functionally a nonlinear process (1–3), and understanding normal brain maturation is essential for understanding neurodevelopmental disorders (4, 5). The heteromodal nature of cognitive brain development is evident from studies of neurocognitive performance (6, 7), functional imaging (functional MRI or positron-emission tomography) (8–10), and electroencephalogram coherence studies (1, 2, 10). Prior imaging studies show regional nonlinear changes in gray matter (GM) density during childhood and adolescence with prepubertal increase followed by postpubertal loss (11–14). The GM density on MRI is an indirect measure of a complex architecture of glia, vasculature, and neurons with dendritic and synaptic processes. Studies of GM maturation show a loss in cortical GM density over time (15, 16), which temporally correlates with postmortem findings of increased synaptic pruning during adolescence and early adulthood (17–19). Here we present a study of cortical GM development in children and adolescents by using a brain-mapping technique and a prospectively studied sample of 13 healthy children (4–21 years old), who were scanned with MRI every 2 years for 8–10 years. Because the scans were obtained repeatedly on the same subjects over time, statistical extrapolation of points in between scans enabled construction of an animated time-lapse sequence ("movie") of pediatric brain development. We hypothesized that GM development in childhood through early adulthood would be nonlinear as described before and would progress in a localized, region-specific manner coinciding with the functional maturation. We also predicted that the regions associated with more primary functions (e.g., primary motor cortex) would develop earlier compared with the regions that are involved with more complex and integrative tasks (e.g., temporal lobe).

The result is a dynamic map of GM maturation in the pre- and postpubertal period. Our results, while highlighting the remarkable heterogeneity, show that the cortical GM development appears to follow the functional maturation sequence, with the primary sensorimotor cortices along with frontal and occipital poles maturing first, and the remainder of the cortex developing in a parietal-to-frontal (back-to-front) direction. The superior temporal cortex, which contains association areas that integrate information from several sensory modalities, matured last. Furthermore, the maturation of the cortex also appeared to follow the evolutionary sequence in which these regions were created.

Methods

Subjects. Sample demographics are shown in Table 1. All subjects were recruited from the community for an ongoing National Institute of Mental Health study of human brain development (20). Briefly, each subject was given a structured diagnostic interview to rule out any psychiatric diagnoses at each visit. Subjects returned every 2 years for a follow-up MRI together with psychiatric and neurocognitive reassessment. A subset of all children who had three or more usable MRI scans and were between the ages of 4 and 21 years was chosen to be included in this study. The study was approved by the National Institute of Mental Health institutional review board, and an informed consent was obtained from subjects >18 years old or from parents of minor subjects, and an additional written assent was obtained from each minor subject.

Image Processing and Analysis. MRI images were acquired at the National Institute of Mental Health on the same 1.5-T General Electric scanner. The MRI sequence was consistent throughout the study. T1-weighted images with contiguous 1.5-mm slices in the axial plane and 2.0-mm slices in the coronal plane were obtained by using 3D spoiled-gradient recalled echo in the steady state. Imaging parameters were: echo time, 5 ms; repetition time, 24 ms; flip angle, 45°; acquisition matrix, 256 × 192; number of excitations, 1; and field of view, 24 cm. With each major software/hardware upgrade, the reliability of the data before and after the upgrade was tested by scanning a set of subjects before and after the upgrade (20). Briefly, for each scan, a radio-frequency bias field-correction algorithm was applied. Baseline images were normalized, transforming them to a standard 3D stereotaxic space (21). Follow-up scans were then aligned to the baseline scan from the same subject, and mutually registered scans for each subject were linearly mapped into the International Consortium for Brain Mapping (ICBM) space (22). An extensively validated tissue classifier generated detailed maps of GM, white matter, and cerebrospinal fluid by using a Gaussian mixture distribution to generate a maximum *a posteriori* segmentation of the data (23, 24), and a surface model of the cortex was then automatically extracted for each subject and time point as described (25).

An image-analysis technique known as cortical pattern matching (25–27) was used to better localize cortical differences over time and increase the power to detect systematic changes (25). This approach matches gyral features of cortical

Abbreviations: GM, gray matter; STG, superior temporal gyrus.

†To whom correspondence should be addressed at: Child Psychiatry Branch, National Institute of Mental Health, Building 10, Room 3N 202, Bethesda, MD 20892. E-mail: nitin@codon.nih.gov.

www.pnas.org/cgi/doi/10.1073/pnas.0402680101

Brain and Cognition 72 (2010) 6–15

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Review Article

Mapping gray matter development: Implications for typical development and vulnerability to psychopathology

Nitin Gogtay [a,*], Paul M. Thompson [b]

[a] Child Psychiatry Branch, NIMH, NIH, Building 10, Rm 3N202, 10 Center Drive, MSC-1600, Bethesda, MD 20892, USA
[b] Laboratory of Neuroimaging, Department of Neurology, UCLA School of Medicine, LA, CA 90095, USA

ARTICLE INFO

Article history:
Available online 30 September 2009

Keywords:
Brain
Imaging
Development
Psychopathology

ABSTRACT

Recent studies with brain magnetic resonance imaging (MRI) have scanned large numbers of children and adolescents repeatedly over time, as their brains develop, tracking volumetric changes in gray and white matter in remarkable detail. Focusing on gray matter changes specifically, here we explain how earlier studies using lobar volumes of specific anatomical regions showed how different lobes of the brain matured at different rates. With the advent of more sophisticated brain mapping methods, it became possible to chart the dynamic trajectory of cortical maturation using detailed 3D and 4D (dynamic) models, showing spreading waves of changes evolving through the cortex. This led to a variety of time-lapse films revealing characteristic deviations from normal development in schizophrenia, bipolar illness, and even in siblings at genetic risk for these disorders. We describe how these methods have helped clarify how cortical development relates to cognitive performance, functional recovery or decline in illness, and ongoing myelination processes. These time-lapse maps have also been used to study effects of genotype and medication on cortical maturation, presenting a powerful framework to study factors that influence the developing brain.

Published by Elsevier Inc.

1. Introduction

Human brain development is a structurally and functionally non-linear process (Johnson, 2001; Thatcher, 1992; Thatcher, Walker, & Giudice, 1987) and most major neuropsychiatric disorders are now thought to arise out of deviations from normal brain development, suggesting a neurodevelopmental basis for these disorders. It is therefore important to study both normal and abnormal brain changes with age in order to understand how major neuropsychiatric disorders emerge (Schlaggar et al., 2002; Stiles, 2000). Postmortem studies provide information at molecular and cellular levels, but are limited by the scarcity of human brain tissue, inability to provide information during life, and the inability to use longitudinal designs. Noninvasive brain imaging, with recent advances in the resolution of MRI and in mapping methodology, provides a unique alternative to study brain development *during life*, allowing studies that assess the same individual or group of subjects repeatedly. This allows the dynamic trajectory of an illness, or the profile of cortical development throughout childhood and adolescence, to be visualized as a time-lapse map, presenting statistics on the 3D profiles of brain changes at different ages (Gogtay, Giedd et al., 2004; Gogtay, Greenstein et al., 2007; Gogtay et al., 2008; Thompson, Mega, Vidal, Rapoport, & Toga, 2001; Thompson, Vidal et al., 2001).

Earlier brain imaging studies using prospective anatomic MRI scans measured gray and white matter changes that were summarized for individual lobes of the brain. While providing new insights, these lobar volume measures were limited by the lack of fine-scale details at sub-regional levels. These region-of-interest measures, for example, could not generally establish whether the functionally distinct sub-regions within a cortical lobe had structurally distinct developmental trajectories. They could not detect sweeping waves of dynamic changes that spread across the cortex, and were relatively insensitive to effects that did not coincide neatly with lobar boundaries. These limitations were overcome by more recent techniques that allow the measurement of cortical thickness or gray matter density at individual voxel locations in the image (e.g., voxel-based morphometry, VBM) (Ashburner et al., 2003) or across surface models of the entire cortex (Luders et al., 2005; Thompson et al., 2004, 2005). Thus, ideally, using both global/lobar measures and GM density/thickness measures in a complementary way can provide clearer understanding of brain development.

By aligning images from multiple subjects to a common reference brain or coordinate system, statistical maps can be made to show the evidence for group differences in gray matter at each location in the co-registered images. Additional detailed maps can

* Corresponding author. Fax: +1 301 402 0296.
E-mail addresses: gogtayn@mail.nih.gov (N. Gogtay), thompson@loni.ucla.edu (P.M. Thompson).

0278-2626/$ - see front matter Published by Elsevier Inc.
doi:10.1016/j.bandc.2009.08.009

Prevention Science, Vol. 5, No. 4, December 2004 (© 2004)

How Early Experience Matters in Intellectual Development in the Case of Poverty[1]

Gilbert Gottlieb[2,4] and Clancy Blair[3]

Experiments with rodents indicate that severe early psychological and social deprivation has lasting detrimental effects on learning ability that are not remedied by exposure to enriching experiences in adulthood. Findings indicate that environmental adversity early in life works to limit the development of intelligence with consequences for later functioning. Animal experiments are best viewed as supplying a rationale for early intervention in disadvantaged infants and children who would otherwise be likely to evince low intellectual capabilities later in life. Animal experiments conducted to date do not support an interpretation that early enrichment necessarily boosts later intellectual performance beyond the normal or species-typical range. They indicate that early intervention promotes normative development by preventing adverse early rearing conditions from leading to negative consequences for cognitive ability and self-regulation. The Abecedarian Project, an early enrichment intervention with infants from economically deprived backgrounds, is presented as an example of how early experience matters in terms of human intellectual development in disadvantaged populations. The results of that program reflect what one would expect from the rodent studies mentioned above.

KEY WORDS: early intervention; intelligence; animal models.

The evidence to be reviewed in the first section of the paper indicates that rodents reared in "enriched" psychological environments show better learning ability than animals reared under psychologically and socially impoverished circumstances. However, there is no evidence that animals reared in so-called enriched laboratory environments show learning abilities beyond the normal or species-typical range. Rather, the rodent research indicates that the enriched early experience averts the deterioration of learning ability that is seen when animals are reared under impoverished conditions early in life. Exposure to enriched conditions later in life is without effect in rodents that have been severely deprived early in life. These findings suggest that interventions with impoverished human populations should be instigated as early as possible with a view to preventing intellectual deterioration in such populations.

The earliest systematic study of the role of early experience in influencing the later learning abilities of rodents was done by Bernard Hymovitch (1952), a doctoral student of Donald Hebb. Hymovitch reared young rats under four conditions and then later tested them in the very challenging Hebb-Williams maze. The maze test consists of a series of twelve problems in which the path between the start and finish (food) boxes is altered from problem to problem by rearranging the internal walls of the maze. This maze is considerably more difficult than a Y- or T-maze, so it taxes the animal's learning ability to a much greater degree than usual maze tasks.

Hymovitch's animals were housed individually in (1) a stovepipe cage (which permitted little motor or

[1]This article is based, in part, on an invited presentation by the first author at the 2002 meeting of the American Psychological Association, in Chicago.

[2]Center for Developmental Science, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.

[3]Human Development and Family Studies, Pennsylvania State University, Pennsylvania.

[4]Correspondence should be directed to Gilbert Gottlieb, Center for Developmental Science, CB# 8115, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-8115; e-mail: gottlieb@email.unc.edu.

1389-4986/04/1200-0245/1

22

VIEWPOINT

Neglected Infections of Poverty in the United States and Their Effects on the Brain

Peter J. Hotez, MD, PhD
National School of Tropical Medicine, Baylor College of Medicine, Houston, Texas; Sabin Vaccine Institute, Texas Children's Hospital Center for Vaccine Development, Houston; and Department of Biology, Baylor University, Waco, Texas.

A group of neglected infections are emerging as important causes of psychiatric and mental illness among vulnerable populations living in extreme poverty in the United States. These chronic infections may partially account for the achievement gap noted among socioeconomically disadvantaged students.

The neglected tropical diseases (NTDs) are a group of chronic parasitic and related infections that can last decades or even the lifetime of an individual. During this time, they produce long-lasting and debilitating effects that impair productive capacity and child development. Indeed, the NTDs have actually been shown to trap people in poverty through these adverse effects.

The NTDs are not rare diseases. Quite the opposite—the NTDs are now recognized as the most common afflictions of impoverished people living in low- and middle-income countries of Africa, Asia, and Latin America. The NTDs are also considered a major reason why the "bottom billion" (ie, the 1.3 billion) people living below the poverty level cannot escape poverty.

In 2008, I identified a group of neglected parasitic and related infections of poverty among the extreme poor in the United States that closely resemble the NTDs in terms of their ability to produce chronic, debilitating, and poverty-promoting effects.[1] A new review reveals that these neglected infections remain widespread and disproportionately affect selected vulnerable populations, including African American and Hispanic populations living in poverty and the homeless.[2] Texas, the Gulf Coast region, and other parts of the southern United States represent the major affected areas, most likely because of their association with the extreme poverty in these regions.[2]

Now, additional information has determined that the neglected infections of poverty also cause important psychiatric and neurological effects on vulnerable populations in the southern United States (**Table**). Toxocariasis is a larval parasitic worm infection of the brain and viscera that results from accidental ingestion of *Toxocara* species eggs shed by dogs and cats. The eggs are nearly ubiquitous in disadvantaged urban and rural environments—the seroprevalence among disadvantaged African American populations exceeds 20%.[1,2] An estimated 2.8 million African American individuals have toxocariasis.[1] In a large survey of the US population,[3] it was recently found that children who are seropositive for *Toxocara* infection (a marker of exposure and infection) scored significantly lower on the Wechsler Intelligence Scale for Children-Revised and the Wide Range Achievement Test-Revised than did seronegative children. Toxocariasis is also associated with epilepsy and may be an important cause of epilepsy among African American children.[2]

Persons with toxocariasis are also more likely to be co-infected with *Toxoplasma gondii*, a parasitic protozoan that causes toxoplasmosis. Both of these zoonotic infections can be acquired from cats. Like toxocariasis, toxoplasmosis also disproportionately occurs among non-Hispanic black individuals and is linked to poverty.[4] Approximately 1 million new cases occur annually in the United States.[2] A recent body of literature has identified provocative associations between toxoplasmosis and adult psychiatric illness, possibly a long-term consequence from congenital *Toxoplasma* infection and the resulting disruptions in fetal neurodevelopment.[5,6] Specifically, seropositivity for toxoplasmosis has been strongly linked to bipolar mood disorder and schizophrenia.[5,6] Still another congenital infection that causes intellectual disabilities (as well as losses in hearing and vision) and disproportionately affects African American children is congenital cytomegalovirus (CMV) infection.[1] In pregnancy, non-Hispanic black women are at substantially increased risk of acquiring primary CMV infection compared with non-Hispanic white women, especially during teen pregnancies.[1] An estimated 27 000 new cases of congenital CMV infection occur annually.[1]

Beyond African American individuals, 2 neglected infections of poverty also affect other vulnerable populations in the United States. Neurocysticercosis, a larval pork tapeworm infection, is an important cause of epilepsy and chronic headaches in mostly Hispanic individuals.[2] My previous estimate indicates that between 41 000 and 169 000 people are living with cysticercosis in the United States.[1] Several studies have identified cognitive impairments in patients with neurocysticercosis and even dementia. In addition, the largest numbers of new cases of West Nile virus (WNV) infection are currently found in Texas—during a 2012 WNV outbreak there, almost 2000 cases were reported. Homeless populations are considered at risk for acquiring WNV infection. Neuroinvasive WNV infection has now been linked to chronic depression in a high proportion of patients.[7]

The links between these neglected infections of poverty and psychiatric and neurologic illnesses have potentially important implications for mental health care providers. The neglected infections outlined here are not rare diseases in the United States, and millions of people in this country are estimated to be living with chronic toxocariasis, toxoplasmosis, CMV infection, neurocysticercosis, and WNV infection. Together, they likely account for a substantial yet hidden burden of mental illness in the United States. These infections can be extremely challenging to diagnose, manage, treat, or prevent. A national awareness program should be imple-

Corresponding Author: Peter J. Hotez, MD, PhD, National School of Tropical Medicine, Baylor College of Medicine, 1 Baylor Plaza, Ste 164a, Houston, TX 77030 (hotez@bcm.edu).

23

Table. Summary of the Effect of Neglected Infections of Poverty on the Mental Health of the US Population

Disease	Vulnerable Population Living in Poverty	Estimated No. of Cases	Neurocognitive or Psychiatrics Effects
Toxocariasis	African American	Up to 2.8 million	Diminished cognitive function, epilepsy
Toxoplasmosis	African American	~1 Million new cases annually	Bipolar and other mood disorders, schizophrenia, vision loss
Congenital cytomegalovirus infection	African American	>6000 of Almost 30 000 new cases annually	Intellectual disabilities, hearing and vision loss
Neurocysticercosis	Hispanic American	Tens of thousands	Epilepsy, headache, cognitive impairments, dementia
West Nile virus infection	Homeless	1868 Cases reported in Texas in 2012	Depression

mented that would include specific commitments to the training of psychiatrists and mental health care professionals, with opportunities for joint patient management with experts in infectious and tropical diseases.

Yet another untapped aspect of the neglected infections of poverty is their potential contribution to the achievement gap that has been noted between wealthy suburban populations and socioeconomically disadvantaged minority populations. Specific programs of treatment and prevention could represent a major step toward improving the mental health of African American and Hispanic children affected by the neglected infections of poverty. Today in developing countries, low-cost programs of mass drug administration are being used to reduce or control the major NTDs affecting the cognitive development and mental health of children, including hookworm and other intestinal helminth infections and schistosomiasis. Although this approach would need to be modified to take on neglected infections specific to the United States, it could similarly produce important mental health benefits. The neglected infections of poverty represent a substantial yet hidden burden of mental illness that may require an unprecedented collaboration between psychiatrists, neurologists, and infectious and tropical disease experts.

ARTICLE INFORMATION

Published Online: August 6, 2014. doi:10.1001/jamapsychiatry.2014.1045.

Conflict of Interest Disclosures: None reported.

REFERENCES

1. Hotez PJ. Neglected infections of poverty in the United States of America. *PLoS Negl Trop Dis*. 2008;2(6):e256.

2. Hotez PJ. Neglected parasitic infections of poverty in the United States. *PLoS Negl Trop Dis*. In press.

3. Walsh MG, Haseeb MA. Reduced cognitive function in children with toxocariasis in a nationally representative sample of the United States. *Int J Parasitol*. 2012;42(13-14):1159-1163.

4. Jones JL, Kruszon-Moran D, Sanders-Lewis K, Wilson M. Toxoplasma gondii infection in the United States, 1999 2004, decline from the prior decade. *Am J Trop Med Hyg*. 2007;77(3):405-410.

5. Hamdani N, Daban-Huard C, Lajnef M, et al. Relationship between Toxoplasma gondii infection and bipolar disorder in a French sample. *J Affect Disord*. 2013;148(2-3):444-448.

6. Torrey EF, Bartko JJ, Yolken RH. Toxoplasma gondii and other risk factors for schizophrenia: an update. *Schizophr Bull*. 2012;38(3):642-647.

7. Nolan MS, Hause AM, Murray KO. Findings of long-term depression up to 8 years post infection from West Nile virus. *J Clin Psychol*. 2012;68(7):801-808.

Cerebral Cortex March 2009;19:640-657
doi:10.1093/cercor/bhn117
Advance Access publication July 24, 2008

24

Development of Anterior Cingulate Functional Connectivity from Late Childhood to Early Adulthood

A.M. Clare Kelly[1], Adriana Di Martino[1,2], Lucina Q. Uddin[1], Zarrar Shehzad[1], Dylan G. Gee[1], Philip T. Reiss[3], Daniel S. Margulies[1,4], F. Xavier Castellanos[1,5] and Michael P. Milham[1]

[1]Phyllis Green and Randolph Cowen Institute for Pediatric Neuroscience at the NYU Child Study Center, New York, NY, USA, [2]Division of Child and Adolescent Neuropsychiatry, Department of Neuroscience, University of Cagliari, Italy, [3]NYU Child Study Center, Division of Biostatistics, New York, NY, USA, [4]Berlin School of Mind and Brain, Humboldt Universität, Berlin, Germany and [5]Nathan Kline Institute for Psychiatric Research, Orangeburg, NY, USA

Human cerebral development is remarkably protracted. Although microstructural processes of neuronal maturation remain accessible only to morphometric post-mortem studies, neuroimaging tools permit the examination of macrostructural aspects of brain development. The analysis of resting-state functional connectivity (FC) offers novel possibilities for the investigation of cerebral development. Using seed-based FC methods, we examined the development of 5 functionally distinct cingulate-based intrinsic connectivity networks (ICNs) in children (n = 14, 10.6 ± 1.5 years), adolescents (n = 12, 15.4 ± 1.2) and young adults (n=14, 22.4 ± 1.2). Children demonstrated a more diffuse pattern of correlation with voxels proximal to the seed region of interest (ROI) ("local FC"), whereas adults exhibited more focal patterns of FC, as well as a greater number of significantly correlated voxels at long distances from the seed ROI. Adolescents exhibited intermediate patterns of FC. Consistent with evidence for different maturational time courses, ICNs associated with social and emotional functions exhibited the greatest developmental effects. Our findings demonstrate the utility of FC for the study of developing functional organization. Moreover, given that ICNs are thought to have an anatomical basis in neuronal connectivity, measures of FC may provide a quantitative index of brain maturation in healthy subjects and those with neurodevelopmental disorders.

Keywords: anterior cingulate, BA 25, development, functional connectivity, self-regulation

Introduction

Neuronal Maturation and Cerebral Development

Histological and stereological post-mortem studies of human and nonhuman primate brain have provided profound insights into the microstructural processes of neuronal maturation and the development of cerebral functional organization. These studies suggest that postnatal cerebral development is marked by a period of "exuberant" and redundant synaptic connectivity, likely reflecting an overproduction of dendrites, dendritic spines, and axons during the perinatal period (Huttenlocher et al. 1982; LaMantia and Rakic 1994; Petanjek et al. 2008). This superabundant connectivity is maintained throughout childhood, such that synaptic density remains at higher-than-adult levels until about the onset of puberty, from which time there is a net elimination of synapses. As a result of such "pruning," the density of synapses declines by ~40% during adolescence, before reaching a plateau in adulthood (Huttenlocher 1979; Huttenlocher et al. 1982; Rakic et al. 1986; Bourgeois and Rakic 1993; Bourgeois et al. 1994; Rakic et al. 1994). The rate at which pruning occurs varies across the cerebrum: the decline in synaptic density appears to begin earlier in visual and somatosensory cortex than in prefrontal cortex (Bourgeois et al. 1994; Huttenlocher and Dabholkar 1997). Neuronal myelination, another key process in postnatal neuronal maturation, appears to follow a similarly protracted and regionally specific time course. Though few studies have examined this process in human brain, post-mortem analyses suggest that myelination begins near the end of the second trimester of fetal life, increases intensely during the first 2 decades of life, then continues at a slower rate into middle adulthood, with the most protracted development in the frontal and temporal lobes (Yakovlev and Lecours 1967; Brody et al. 1987; Benes et al. 1994).

That the nonlinear developmental pattern of synaptogenesis and synaptic elimination is associated with concurrent functional development of neuronal networks is suggested by the observation that neurotransmitter innervation and receptor density follow a similar developmental trajectory throughout the cortex (Goldman-Rakic and Brown 1982; Lidow et al. 1991; Lidow and Rakic 1992; Rosenberg and Lewis, 1995; Lambe et al. 2000). Early synaptic redundancy has been suggested as the basis for the emergence of cognitive function in the infant (Goldman-Rakic 1987; Petanjek et al. 2008), as well as the synaptic plasticity that characterizes children's ability for learning and recovery from injury (Changeux and Danchin 1976). Though associated with the loss of this superabundant plasticity, synaptic pruning may enable more efficient information transfer across spatially distal regions in the brain, and may therefore underlie the development of mature cognitive function (Changeux and Danchin 1976; Goldman-Rakic 1987; Huttenlocher 1990; Paus et al. 1999).

Magnetic Resonance Imaging Studies of Cerebral Development

The emergence of magnetic resonance imaging (MRI) and more recently, diffusion tensor imaging (DTI) have permitted the noninvasive examination of age-related structural changes in vivo (e.g., Giedd et al. 1999; Paus et al. 1999; Sowell et al. 1999; Sowell et al. 2003; Gogtay et al. 2004). These studies have been largely consistent with the human and nonhuman morphometric data: the observed age-related increases in white matter (WM) are primarily thought to reflect progressive myelination, whereas age-related decreases in gray matter are thought to reflect both synaptic pruning and myelination (Bartzokis et al. 2001; Giedd 2004; Gogtay et al. 2004; Sowell et al. 2004). Specifically, studies have observed that global WM volume increases linearly between the ages of 4 and 22 years (Giedd et al. 1999), with continued increases observed up to the fifth decade of life (Bartzokis et al. 2001; Sowell et al. 2003).

Effects of childhood poverty and chronic stress on emotion regulatory brain function in adulthood

Pilyoung Kim[a,1], Gary W. Evans[b], Michael Angstadt[c], S. Shaun Ho[c], Chandra S. Sripada[c], James E. Swain[c,d], Israel Liberzon[c], and K. Luan Phan[e,f]

[a]Department of Psychology, University of Denver, Denver, CO 80208; [b]Departments of Design and Environmental Analysis and Human Development, Bronfenbrenner Center for Translational Research, Cornell University, Ithaca, NY 14853; [c]Department of Psychiatry, University of Michigan, Ann Arbor, MI 48109; [d]Child Study Center, Yale University, New Haven, CT 06520-7900; [e]Department of Psychiatry, University of Illinois at Chicago, Chicago, IL 60608; and [f]Mental Health Service Line, Jesse Brown Veterans Affairs Medical Center, Chicago, IL 60612

Edited* by Bruce S. McEwen, The Rockefeller University, New York, NY, and approved August 21, 2013 (received for review May 2, 2013)

Childhood poverty has pervasive negative physical and psychological health sequelae in adulthood. Exposure to chronic stressors may be one underlying mechanism for childhood poverty–health relations by influencing emotion regulatory systems. Animal work and human cross-sectional studies both suggest that chronic stressor exposure is associated with amygdala and prefrontal cortex regions important for emotion regulation. In this longitudinal functional magnetic resonance imaging study of 49 participants, we examined associations between childhood poverty at age 9 and adult neural circuitry activation during emotion regulation at age 24. To test developmental timing, concurrent, adult income was included as a covariate. Adults with lower family income at age 9 exhibited reduced ventrolateral and dorsolateral prefrontal cortex activity and failure to suppress amygdala activation during effortful regulation of negative emotion at age 24. In contrast to childhood income, concurrent adult income was not associated with neural activity during emotion regulation. Furthermore, chronic stressor exposure across childhood (at age 9, 13, and 17) mediated the relations between family income at age 9 and ventrolateral and dorsolateral prefrontal cortex activity at age 24. The findings demonstrate the significance of childhood chronic stress exposures in predicting neural outcomes during emotion regulation in adults who grew up in poverty.

fMRI | childhood adversity | socioeconomic status | reappraisal

Childhood poverty is related to increased risk of psychopathology (1–3) and physical illness in adulthood (4, 5). Furthermore, childhood poverty predicts adult morbidity irrespective of adult poverty (5–7). One possible mechanism to explain the far-reaching effects of childhood poverty on health is chronic stress (8). Chronic exposure to stressors associated with living in low-income families has long-term negative effects on physiological stress regulatory systems (9–12), eventually resulting in pathology (13, 14). Growing evidence suggests exposure to chronic stress and socioeconomic adversity produces lasting neurobiological changes (15, 16). However, little is known about whether childhood poverty is prospectively associated with central nervous system mechanisms involved in emotion regulation. Such knowledge may provide insights into identifying neural patterns for emotion regulatory dysfunction among adults who grew up in childhood poverty.

The amygdala and prefrontal cortex (PFC) play a critical role for stress and emotion regulation. The amygdala detects and responds to threats from the environment, activating physiological stress responses (17). The PFC is widely considered as a top-down region that regulates the amygdala (18, 19). More specifically, the ventrolateral PFC (VLPFC), dorsolateral PFC (DLPFC), and medial PFC (mPFC) implement cognitive strategies such as cognitive reappraisal involved in emotion regulation (18–20). During reappraisal of negative stimuli, increased activity in the VLPFC, DLPFC, and mPFC regions is associated with diminished amygdala reactivity to negative stimuli as well as decreased perceived negative affect (21). Amygdala and PFC dysregulation has also been observed in populations with mood dysregulation, including depression (22), anxiety disorders (23, 24) including posttraumatic stress disorder (25), impulsive aggression (26), and substance abuse (27). Aberrant amygdala reactivity and inefficient or blunted PFC regulatory function are considered a neurobiological mechanism involved in impaired emotion regulation in these psychiatric disorders.

Amygdala and PFC functions have also been shown to be affected by socioeconomic disparities (28, 29). In children, low socioeconomic status (SES) has been related to greater amygdala volume (30) and reduced PFC activity during cognitive tasks (31). In adults, retrospective reports of childhood SES were associated with elevated amygdala activity while processing negative facial expressions independently of adult SES (32) and reduced VLPFC activity while experiencing social exclusion (33). However, whether the amygdala and PFC functions associated with childhood poverty are directly related to effortful emotion regulation has never been examined.

At present, little is known about underlying mechanisms that account for the relation between childhood SES and neural functioning. Chronic stress is one hypothetical mediator of the negative link between childhood poverty and adult health outcomes (8, 10). For example, children living in poverty are more likely to be exposed to multiple chronic stressors including violence, family turmoil, separation from family members, and substandard living environments (34, 35). In our previous studies, poverty exposure at age 9 prospectively predicted physiological stress dysregulation (34) and emotion dysregulation

Significance

Childhood poverty has been linked to emotion dysregulation, which is further associated with negative physical and psychological health in adulthood. The current study provides evidence of prospective associations between childhood poverty and adult neural activity during effortful attempts to regulate negative emotion. Adults with lower family income at age 9 exhibited reduced ventrolateral and dorsolateral prefrontal cortex activity and failure to suppress amygdala activation at age 24. Chronic stressor exposure across childhood mediated the relations between family income at age 9 and prefrontal cortex activity. The concurrent adult income, on the other hand, was not associated with neural activity. The information on the developmental timing of poverty effects and neural mechanisms may inform early interventions aimed at reducing health disparities.

Author contributions: P.K., G.W.E., S.S.H., J.E.S., I.L., and K.L.P. designed research; M.A., S.S.H., and J.E.S. performed research; P.K., G.W.E., M.A., C.S.S., I.L., and K.L.P. analyzed data; and P.K., G.W.E., M.A., S.S.H., C.S.S., J.E.S., I.L., and K.L.P. wrote the paper.

The authors declare no conflict of interest.

*This Direct Submission article had a prearranged editor.

[1]To whom correspondence should be addressed. E-mail: pilyoung.kim@du.edu.

This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1308240110/-/DCSupplemental.

THEME ARTICLE

Brain Plasticity and Behaviour in the Developing Brain

Bryan Kolb PhD[1]; Robbin Gibb PhD[1]

Abstract

Objective: To review general principles of brain development, identify basic principles of brain plasticity, and discuss factors that influence brain development and plasticity. **Method:** A literature review of relevant English-language manuscripts on brain development and plasticity was conducted. **Results:** Brain development progresses through a series of stages beginning with neurogenesis and progressing to neural migration, maturation, synaptogenesis, pruning, and myelin formation. Eight basic principles of brain plasticity are identified. Evidence that brain development and function is influenced by different environmental events such as sensory stimuli, psychoactive drugs, gonadal hormones, parental-child relationships, peer relationships, early stress, intestinal flora, and diet. **Conclusions:** The development of the brain reflects more than the simple unfolding of a genetic blueprint but rather reflects a complex dance of genetic and experiential factors that shape the emerging brain. Understanding the dance provides insight into both normal and abnormal development.

Key words: *brain development, cerebral plasticity, environmental stimulation, epigenetics*

Résumé

Objectifs: Présenter les grandes lignes du développement cérébral; expliquer le principe de la plasticité du cerveau; exposer les facteurs qui influencent son développement et sa plasticité. **Méthodologie:** Analyse de la littérature publiée en anglais sur le développement et la plasticité du cerveau. **Résultats:** Le cerveau se développe par étapes, la première étant la neurogénèse, suivie de la migration des neurones, de la maturation, de la synaptogénèse, de l'élagage synaptique et de la myélinisation. Les auteurs présentent huit principes fondamentaux de la plasticité du cerveau. Ils constatent que le développement et le fonctionnement du cerveau sont influencés par divers facteurs environnementaux comme les stimuli sensoriels, les substances psychoactives, les hormones gonadales, les relations parent-enfant, les relations avec les pairs, le stress dans la petite enfance, la flore intestinale et le régime alimentaire. **Conclusion:** Le développement du cerveau va au-delà de la construction de la carte génétique; certaines interactions complexes entre facteurs génétiques et expérimentaux agissent sur le cerveau en formation. Comprendre ces interactions permettra d'étudier le développement normal ou anormal du cerveau.

Mots clés: *développement cerebral, plasticité du cerveau, environnementaux comme les stimuli, épigénétique*

The development of the brain reflects more than the simple unfolding of a genetic blueprint but rather reflects a complex dance of genetic and experiential factors that shape the emerging brain. Brains exposed to different environmental events such as sensory stimuli, drugs, diet, hormones, or stress thus may develop in very different ways. The goal of the current article is to review the ways the developing brain can be sculpted by a wide range of pre- and postnatal factors. We begin with an overview of brain development, followed by a brief review of principles of brain plasticity and finally a consideration of how factors influence brain development and adult behaviour. Because most of what we know about brain plasticity and behaviour in development comes from studies of the laboratory rat our discussion will focus on the rat but will consider humans when possible. In addition, the discussion will be biased towards plasticity in cerebral structures because most of what we know about modulation of brain development is based upon studies of cerebral development. There is little

[1]Department of Neuroscience, Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, Alberta

Corresponding Email: kolb@uleth.ca

Submitted: March 16, 2011; Accepted: June 29, 2011

Pediatr Blood Cancer 2014;61:1720–1723

REVIEW

Brain Development, Experience, and Behavior

Bryan Kolb, PhD,* Richelle Mychasiuk, PhD, and Robbin Gibb, PhD

Brain development progresses through a series of stages beginning with neurogenesis and progressing to neural migration, maturation, synaptogenesis, pruning, and myelin formation. This review examines the literature on how early experiences alter brain development, including environmental events such as sensory stimuli, early stress, psychoactive drugs, parent-child relationships, peer relationships, intestinal flora, diet, and radiation. This sensitivity of the brain to early experiences has important implications for understanding neurodevelopmental disorders as well as the effect of medical interventions in children. Pediatr Blood Cancer 2014;61:1720–1723.

Key words: brain development; cerebral plasticity; environmental stimulation; epigenetics

INTRODUCTION

Brain development is a prolonged process that reflects more than the simple unfolding of a genetic blueprint but rather reflects a complex interaction of genetic and experiential factors that shape the emerging brain and ultimately behavior. Brains exposed to different environmental events or perturbations thus may develop in very different ways. The goal of the current article is to review the ways the developing brain can be sculpted by a wide range of pre- and postnatal factors. We begin with an overview of brain development, followed by a consideration of how factors influence brain development and adult behavior. Because most of what we know about brain plasticity and behavior in development comes from studies of the laboratory rat our discussion will focus on the rat but will consider humans when possible.

BRAIN DEVELOPMENT

Brain development can be divided loosely into two phases. In most mammals the first reflects a genetically determined sequence of events *in utero* that can be modulated by maternal environment and pre-conceptual events. The second phase, which is both pre- and postnatal in humans, is a time when the connectivity of the brain is very sensitive not only to the environment but also to the patterns of brain activity produced by experiences. More importantly, however, it is now recognized that epigenetic changes, which can be defined as changes in developmental outcomes, including regulation of gene expression, are based upon mechanisms other than DNA itself [1]. For example, gene expression can be altered by specific experiences, including pre-conceptual experiences, and this in turn can lead to organizational changes in the nervous system.

Figure 1 outlines the general stages characteristic of brain development in all mammals. Cells that are destined to produce the nervous system begin to form about 3 weeks after fertilization in humans. Once formed, the presumptive neurons must migrate to their eventual correct location, differentiate into the appropriate phenotype, form connections, and then are pruned based upon experience. Pruning is an important stage: the number of excitatory synapses is 2-to-3 times greater in children than in adults and that spine density begins to decrease during puberty, stabilizing at the adult level around age 30 [2].

Not all brain regions mature at the same rate. In particular, the prefrontal cortex is very slow to develop, finally reaching maturity at about 30 years [2]. The plasticity and prolonged development of the brain provides an opportunity for continual modification of cognitive function but, in addition, creates a potential susceptibility to the formation of abnormal circuitry leading to compromised behavioral function. The brain is especially vulnerable to experiences at the onset of puberty when the frontal lobe is massively pruning synapses. Thus, the peak age of onset for most mental disorders is estimated at 14 years [3], including anxiety disorders, psychoses (including schizophrenia), bipolar disorder, depression, eating disorders, and substance abuse most commonly emerge by or during adolescence.

FACTORS INFLUENCING BRAIN DEVELOPMENT

Over the past 20 years it has become clear that even fairly innocuous-looking experiences can profoundly affect brain development and that the range of experiences that can alter brain development is much larger than had been once believed. We will highlight some of the most well studied effects.

The simplest way to manipulate experience across ages is to compare brain structure in animals living in standard laboratory caging to animals placed either in so-called enriched environments or in severely impoverished environments. When animals are placed in complex environments in which there is an opportunity for animals to interact with a changing sensory and social environment and to engage in far more motor activity than regular caging. There are many of neural changes associated with this form of enrichment including increases in brain size, cortical thickness, neuron size, dendritic branching, spine density, synapses per neuron, glial numbers and complexity, and vascular arborization [4]. In contrast, impoverishment produces changes in the opposite direction, as well as cell loss [5].

Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, Canada

Grant sponsor: Natural Science and Engineering Research Council of Canada (B.K. and R.G.)

Conflict of interest: Nothing to declare.

*Correspondence to: Bryan Kolb, Department of Neuroscience, Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, Alberta, Canada T1K 3M4. E-mail: kolb@uleth.ca

Received 14 August 2013; Accepted 25 November 2013

DOI 10.1002/pbc.24908
Published online 24 December 2013 in Wiley Online Library (wileyonlinelibrary.com).

Cognitive Development xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Cognitive Development

Stress and prefrontal cortical plasticity in the developing brain

Bryan Kolb[a,b,*], Allonna Harker[a], Richelle Mychasiuk[c], Silvana R. de Melo[d], Robbin Gibb[a]

[a] Department of Neuroscience, University of Lethbridge, Lethbridge, AB, T1K 3M4 Canada
[b] Canadian Institute for Advanced Research, 180 Dundas St W, Toronto, ON, M5G 1Z8 Canada
[c] Alberta Children's Hospital Research Institute, HMRB233,3330 Hospital Drive, Calgary, AB, T2N 4N1, Canada
[d] Department of C. Morfológicas – DCM, University of Estadual de Maringá, Maringá, Paraná, Brazil

ARTICLE INFO

Article history:
Received 30 April 2016
Received in revised form 31 October 2016
Accepted 5 January 2017
Available online xxx

Keywords:
Prefrontal cortex
Cerebral development
Stress
Brain plasticity
Epigenetics

ABSTRACT

There is a large literature showing that stress in adulthood induces the production of stress hormones leading to a modulation of brain function, which is accomplished, in part, by changing the structure of neurons, especially in the hippocampus and prefrontal cortex, and these changes are correlated with behavioral change. Here we review the effects of preconception, gestational, and bystander gestational stress, as well as maternal separation on prefrontal cortex and behavioral development, largely in animal models. The general conclusion is that developmental stressors modify the organization of the prefrontal cortex in adulthood with results varying according to age at stress and region measured. It is likely that all of these stress effects are mediated by (re)programming of later gene activity in the brains of the offspring.

Contents

* Corresponding author at: Department of Neuroscience, University of Lethbridge, Lethbridge, AB, T1K 3M4, Canada.
E-mail address: kolb@uleth.ca (B. Kolb).

http://dx.doi.org/10.1016/j.cogdev.2017.01.001
0885-2014/

Please cite this article in press as: Kolb, B., et al. Stress and prefrontal cortical plasticity in the developing brain. *Cognitive Development* (2017), http://dx.doi.org/10.1016/j.cogdev.2017.01.001

The Journal of Neuroscience, April 4, 2018 • 38(14):3559–3570 • 3559

Development/Plasticity/Repair

The Integration of Functional Brain Activity from Adolescence to Adulthood

Prantik Kundu,[1] Brenda E. Benson,[3] Dana Rosen,[4] Sophia Frangou,[2] Ellen Leibenluft,[3] Wen-Ming Luh,[6] Peter A. Bandettini,[5] Daniel S. Pine,[3] and Monique Ernst[4]

[1]Section on Advanced Functional Neuroimaging, Brain Imaging Center, [2]Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, New York 10029, [3]Emotion and Development Branch, [4]Section on Neurobiology of Fear and Anxiety, [5]Section on Functional Imaging Methods, National Institute of Mental Health, Bethesda, Maryland 20892, and [6]Cornell MRI Facility, Cornell University, Ithaca, New York 14853

Age-related changes in human functional neuroanatomy are poorly understood. This is partly due to the limits of interpretation of standard fMRI. These limits relate to age-related variation in noise levels in data from different subjects, and the common use of standard adult brain parcellations for developmental studies. Here we used an emerging MRI approach called multiecho (ME)-fMRI to characterize functional brain changes with age. ME-fMRI acquires blood oxygenation level-dependent (BOLD) signals while also quantifying susceptibility-weighted transverse relaxation time (T_2^*) signal decay. This approach newly enables reliable detection of BOLD signal components at the subject level as opposed to solely at the group-average level. In turn, it supports more robust characterization of the variability in functional brain organization across individuals. We hypothesized that BOLD components in the resting state are not stable with age, and would decrease in number from adolescence to adulthood. This runs counter to the current assumptions in neurodevelopmental analyses of brain connectivity that the number of BOLD signal components is a random effect. From resting-state ME-fMRI of 51 healthy subjects of both sexes, between 8.3 and 46.2 years of age, we found a highly significant ($r = -0.55, p \ll 0.001$) exponential decrease in the number of BOLD components with age. The number of BOLD components were halved from adolescence to the fifth decade of life, stabilizing in middle adulthood. The regions driving this change were dorsolateral prefrontal cortices, parietal cortex, and cerebellum. The functional network of these regions centered on the cerebellum. We conclude that an age-related decrease in BOLD component number concurs with the hypothesis of neurodevelopmental integration of functional brain activity. We show evidence that the cerebellum may play a key role in this process.

Key words: complexity; development; fMRI; multiecho; resting state

Significance Statement

Human brain development is ongoing from childhood to at least 30 years of age. Functional MRI (fMRI) is key for characterizing changes in brain function that accompany development. However, developmental fMRI studies have relied on reference maps of adult brain organization in the analysis of data from younger subjects. This approach may limit the characterization of functional activity patterns that are particular to children and adolescents. Here we used an emerging fMRI approach called multi-echo fMRI that is not susceptible to such biases when analyzing the variation in functional brain organization over development. We hypothesized an integration of the components of brain activity over development, and found that the number of components decreases exponentially, halving from 8 to 35 years of age. The brain regions most affected underlie executive function and coordination. In summary, we show major changes in the organization and integration of functional networks over development into adulthood, with both methodological and neurobiological implications for future lifespan and disease studies on brain connectivity.

Introduction

Characterizing brain development from adolescence to adulthood is critical for understanding neuropsychiatric disease and healthy brain function. However, the trajectories of changes in functional organization during brain development are not yet well characterized. Developmental studies of white matter structural change based on diffusion weighted MRI report nonlinear trajectories involving faster changes at earlier ages, followed by stabilization at later ages (Wallace et al., 2006). Microstructural changes in white matter are also known to be

Received June 27, 2017; revised Jan. 21, 2018; accepted Jan. 25, 2018.

Author contributions: P.K., B.E.B., S.F., E.L., W.-M.L., P.A.B., D.S.P., and M.E. designed research; P.K., B.E.B., D.R., W.-M.L., D.S.P., and M.E. performed research; P.K. contributed unpublished reagents/analytic tools; P.K., B.E.B., E.L., W.-M.L., and M.E. analyzed data; P.K., B.E.B., S.F., E.L., W.-M.L., P.A.B., D.S.P., and M.E. wrote the paper.

Correspondence should be addressed to Prantik Kundu, Section on Advanced Functional Neuroimaging, Brain Imaging Center, Icahn School of Medicine at Mount Sinai, New York, NY 10029. E-mail: prantikk@gmail.com or prantik.kundu@mssm.edu.

DOI:10.1523/JNEUROSCI.1864-17.2018

 0270-6474/18/383559-12$15.00/0

The Journal of Neuroscience, December 1, 2000, 20(23):8780–8787

Differential Postnatal Development of Catecholamine and Serotonin Inputs to Identified Neurons in Prefrontal Cortex of Rhesus Monkey

Evelyn K. Lambe, Leonid S. Krimer, and Patricia S. Goldman-Rakic

Section of Neurobiology, Yale University School of Medicine, New Haven, Connecticut 06520

The monoaminergic innervation of cerebral cortex has long been implicated in its development. Methods now exist to examine catecholamine and serotonin inputs to identified neurons in the cerebral cortex. We have quantified such inputs on pyramidal and nonpyramidal cells in prefrontal cortex of rhesus monkeys ranging in age from 2 weeks to 10 years. Individual layer III neurons were filled with Lucifer yellow and double-immunostained with axons containing either tyrosine hydroxylase (TH) or 5-hydroxytryptamine (5-HT). The filled cells were reconstructed, and putative appositions between the axons and dendritic spines and shafts were quantified at high magnification using light microscopy.

The density of catecholamine appositions on pyramidal neurons matures slowly, reaching only half the adult level by 6 months of age and thereafter rising gradually to adult levels by 2 years of age. By contrast, the density of serotonin appositions on pyramidal cells reaches the adult level before the second week after birth. The average adult pyramidal neuron in layer III of area 9m receives three times stronger input from catecholaminergic than from serotoninergic axons. The overall density of both inputs to interneurons does not appear to change during postnatal development. Selective changes in the TH innervation of pyramidal cells against a backdrop of constant TH innervation of interneurons suggest that the balance between excitation and inhibition may change developmentally in the prefrontal cortex. By contrast, 5-HT innervation of both types of neurons remains relatively constant over the age range studied.

Key words: tyrosine hydroxylase; dopamine; serotonin; 5-hydroxytryptamine; pyramidal neuron; interneuron; rhesus monkey; nonhuman primate; prefrontal cortex

Monoaminergic systems of the brain modulate excitatory transmission in cortical circuits that are critical for normal adult function of prefrontal cortex (Williams and Goldman-Rakic, 1995; Vollenweider et al., 1998). The same neurotransmitters have been implicated directly and indirectly in several aspects of neurodevelopment (Mattson, 1988; Levitt et al., 1997), in the pathophysiology of schizophrenia (Lieberman, 1999), and in the psychotomimetic effects of certain hallucinogens (Breier, 1995; Farber et al., 1999; Gouzoulis-Mayfrank et al., 1999). There are timing similarities among the attainment of peak working memory performance (Diamond and Goldman-Rakic, 1989), the typical age of onset of schizophrenia (Lieberman, 1999), and the age at which certain drugs begin to trigger psychosis (Farber et al., 1999). These developmental parallels suggest that a detailed understanding of the postnatal changes in monoaminergic input to cortical neurons may shed light on the changes in circuitry needed for mature working memory performance, as well as on how this circuitry may become disrupted in psychosis.

Monoamines have been extensively studied during embryonic development (Lauder and Bloom, 1974; Coyle and Molliver, 1977; Buznikov, 1984; Mattson, 1988; Verney et al., 1993; Levitt, 1997), yet relatively few studies *in vitro* have addressed postnatal changes in monoaminergic innervation of frontal cortex. Over the prepubertal period, serotonin and dopamine levels appear to fluctuate before rising to adult levels at puberty (Goldman-Rakic and Brown, 1982). However, differences exist between these two neurotransmitters. From birth to adulthood, there is a protracted and dramatic increase in the synthetic capacity for dopamine, whereas that for serotonin stays at a constant low level (Goldman-Rakic and Brown, 1982). Furthermore, the length of axons that contain tyrosine hydroxylase (TH), an enzyme critical for the production of dopamine, continues to increase until puberty (Rosenberg and Lewis, 1995). In addition, adult TH density in area 9 of frontal cortex is much greater than that for 5-hydroxytryptamine (5-HT) (Lewis et al., 1992).

These differences in axonal density during postnatal development raise the question of how they affect individual neurons in prefrontal cortex. Anatomical work in the adult has shown a predominance of TH innervation onto pyramidal cells relative to interneurons (Krimer et al., 1997). Functional studies in the adult have shown that dopamine modulates the ability of prefrontal neurons to maintain activity during the delay period of working memory tasks (Sawaguchi et al., 1990; Williams and Goldman-Rakic, 1995). In view of pronounced differences in working memory ability across postnatal development (Diamond and Goldman-Rakic, 1989), understanding of the developmental changes in monoaminergic innervation of single neurons in frontal cortex may provide insight into the anatomical underpinning of cognitive maturation.

In summary, this study presents findings using infrared differential interference contrast (IR-DIC) videomicroscopy to fill selected individual neurons in rhesus monkeys, followed by double-immunostaining and quantification of contacts between monoaminergic axons and labeled cortical neurons. The pattern of TH and 5-HT innervation to identified pyramidal cells and interneurons shows changes over the first 10 postnatal years. The relevance of these findings in regard to changes in dopamine-dependent properties of prefrontal function, including its vulnerability during adolescence to schizophrenia and ketamine-induced psychosis, is discussed.

MATERIALS AND METHODS

Tissue preparation. Twelve monkeys between the ages of 2 weeks and 10 years were administered ketamine (5–10 mg/kg) and atropine (0.2 mg/kg) and placed under deep surgical anesthesia with sodium pentobarbitol (100 mg/kg). They were then perfused transcardially with a solution of 4% paraformaldehyde, 15% picric acid, and 0.2% gluteraldehyde in 0.1 M phosphate buffer (PB) for 4–7 min, depending on the age and the size of the animal. The ages of the monkeys are shown in Tables 1 and 2. Two animals were included at the following ages: 2 weeks, 2 months, and 2 years. Tissue blocks from dorsomedial area 9 in the left hemisphere were excised and sectioned with a microtome into 400 μm slices. These slices were maintained in ice-cold PB until injection.

Injection of fluorescent dye. Layers within the cortex were visualized

Received July 11, 2000; revised Aug. 31, 2000; accepted Sept. 12, 2000.

We thank Terri Beattie and Heather Findlay for expert assistance with animal care.

Correspondence should be addressed to Patricia Goldman-Rakic, Section of Neurobiology, Yale University School of Medicine, P.O. Box 208001, New Haven, CT 06520-8001. E-mail: patricia.goldman-rakic@yale.edu.

ELSEVIER

31

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 40 (2008) 1044–1055

Microstructural maturation of the human brain from childhood to adulthood

C. Lebel,[a,1] L. Walker,[a,1] A. Leemans,[b,c] L. Phillips,[d] and C. Beaulieu[a,*]

[a]*Department of Biomedical Engineering, Faculty of Medicine and Dentistry, Room 1098 Research Transition Facility, University of Alberta, Edmonton, Alberta, Canada T6G 2V2*
[b]*School of Psychology (CUBRIC), Cardiff University, Cardiff, UK*
[c]*Department of Physics (Visionlab), Antwerp University, Antwerp, Belgium*
[d]*Canadian Centre for Research on Literacy, University of Alberta, Edmonton, Alberta, Canada*

Received 8 May 2007; revised 14 September 2007; accepted 23 December 2007
Available online 11 January 2008

Brain maturation is a complex process that continues well beyond infancy, and adolescence is thought to be a key period of brain rewiring. To assess structural brain maturation from childhood to adulthood, we charted brain development in subjects aged 5 to 30 years using diffusion tensor magnetic resonance imaging, a novel brain imaging technique that is sensitive to axonal packing and myelination and is particularly adept at virtually extracting white matter connections. Age-related changes were seen in major white matter tracts, deep gray matter, and subcortical white matter, in our large ($n=202$), age-distributed sample. These diffusion changes followed an exponential pattern of maturation with considerable regional variation. Differences observed in developmental timing suggest a pattern of maturation in which areas with fronto-temporal connections develop more slowly than other regions. These *in vivo* results expand upon previous postmortem and imaging studies and provide quantitative measures indicative of the progression and magnitude of regional human brain maturation.

Introduction

Brain development is a complex process linked with behavioral, emotional, cognitive, and overall maturation that progresses throughout childhood, adolescence, and into adulthood. A thorough knowledge of structural brain development during adolescence is crucial for understanding the extensive cognitive and behavioral advances that occur during the same period, and for linking brain structure with brain function in both healthy and disease states. Postmortem studies can and have provided valuable insight into white matter development, demonstrating continued myelination of white matter tracts into the second and third decades of life (Yakovlev and Lecours, 1967; Benes, 1989). However, these studies are limited by the availability of young, previously healthy subjects.

Magnetic resonance imaging (MRI) is a powerful tool that has made it possible to investigate healthy brain development *in vivo*, demonstrating both global brain development, as well as more specific brain maturation. MRI has been used extensively to study brain and tissue volume changes, and has demonstrated that though total brain volume remains approximately constant after early childhood, the volume of the individual tissue components changes throughout the life span (Giedd et al., 1999; Good et al., 2001). Studies of cortical gray matter development have shown regional patterns of brain maturation, with distinct areas developing at different rates (Sowell et al., 2004; Lerch et al., 2006; Whitford et al., 2007).

Despite the fact that adolescence is considered a crucial period of brain rewiring, relatively little is known about the development of the white matter tracts that form this wiring or the deep gray matter structures that provide the relay stations. Previous studies using T1-weighted anatomical MRI have shown various brain white matter changes during adolescence, including an overall volume increase (Giedd et al., 1999), and increases of "white matter density" in the internal capsule and the left arcuate fasciculus (Paus et al., 1999). Diffusion tensor MRI (DTI) is a non-invasive tool that provides unique information about tissue microstructure, including indirect measures of myelination and axonal growth, and may be more sensitive than conventional imaging (Basser et al., 1994; Beaulieu, 2002; Le Bihan, 2003). DTI has demonstrated more widespread white matter and deep gray matter development with age during childhood and adolescence (Mukherjee et al., 2001; Schmithorst et al., 2002; Barnea-Goraly et al., 2005; Ben Bashat et al., 2005; Snook et al., 2005; Ashtari et al., 2007) than is observed on T1-weighted scans. However, previous DTI studies of adolescence were limited by small sample sizes (Morriss et al., 1999; Eluvathingal et al., 2007), limited brain regions analyzed (Ben Bashat et al., 2005;

* Corresponding author. Fax: +1 780 492 8259.
E-mail address: christian.beaulieu@ualberta.ca (C. Beaulieu).
[1] These authors contributed equally to this work.
Available online on ScienceDirect (www.sciencedirect.com).

1053-8119/$ - see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2007.12.053

Developmental Science 5:3 (2002), pp 293–300

Mapping the development of white matter tracts with diffusion tensor imaging

Tie-Qiang Li[1] and Michael D. Noseworthy[2]

1. Department of Radiology, Indiana University School of Medicine, USA
2. Department of Diagnostic Imaging, The Hospital for Sick Children, Toronto, Canada

Abstract

In this study, the development of white matter was studied using an optimized diffusion tensor imaging (DTI) protocol in 20 normal subjects (10–40 years old). The normal development of white matter tracts was addressed by comparing the diffusion anisotropy results between two sub-groups: eight adults (26–38 years old) and eight adolescents (13–15 years old). The difference in myelination extent between these two groups as indexed by the fractional anisotropy was identified by conducting a student t-test of the measured diffusion anisotropy maps. Significant differences ($p < 0.01$) were detected in the gyrus frontalis medialis (GFM), gyrus temporalis medialis (GTM) and gyrus cinguli (GC), in addition to the developmental changes in corpus callosum. A brief overview of previous published DTI studies in developmental science and current progress in DTI techniques is also given at the end of this paper. It may be useful for readers interested in using DTI to study developmental problems but who are not familiar with the various technical aspects.

Introduction

The measurement of the diffusion coefficient with nuclear magnetic resonance (NMR) has long been exploited as a method for investigating molecular motions in complex biological systems (Callaghan, 1991; Cory & Garroway, 1990; Li, Haggkvist & Odberg, 1997; Stejskal & Tanner, 1965; Tanner, 1983). Diffusion-weighted contrast was subsequently applied in MR imaging with the acquisition of diffusion-weighted images along three orthogonal gradients. However, robust methods for the characterization of the full diffusion tensor were not developed until more recently. The power of DTI to reveal the details of microstructure in biological tissues relies on the fact that the random, three-dimensional, diffusion-driven molecular motion is sensitive to the tissue structure at a microscopic scale. The molecular mobility in tissues may not be the same in all directions, because of either a peculiar physical arrangement of the medium, or the presence of obstacles that may limit molecular movement in some directions. Diffusion in a heterogeneous system has the characteristics of a second order symmetric tensor rather than a scalar, as would be appropriate for an isotropic system with Gaussian diffusion.

The diffusion tensor can be fully determined by diffusion-weighted MRI with diffusion-weighting gradients applied in at least six non-collinear directions. As shown in Figure 1, with DTI the average diffusitivity, diffusion anisotropy and directionality can be fully extracted, characterized and exploited to provide even more exquisite details of tissue microstructure well beyond the usual image resolution. DTI provides a great opportunity to study the development of myelination in the brain, map white matter tracts connecting different brain regions and relate these changes with the development of normal cognitive ability and disorders. A typical DTI study entails three steps: (1) determination of six independent diffusion tensor elements in the laboratory frame with diffusion-weighted imaging measurements; (2) evaluation of eigenvalues and eigenvectors of the diffusion tensor; and (3) calculation and display of diffusion anisotropy and directionality. Due to the requirement for pulse sequence programming and post-processing techniques, this procedure, until more recently, was limited to experimental and research settings with MRI physics support. However, the number of DTI capable facilities is growing and is therefore being applied in the study of numerous brain pathologies including demyelinating disorders (e.g. multiple sclerosis), epilepsy, brain tumours, ischemia and psychological problems (e.g. schizophrenia, dyslexia). In addition to neuropathological processes, the normal development of the brain can also be

Address for correspondence: Tie-Qiang Li, Department of Radiology, Indiana University School of Medicine, 541 Clinical Drive, Room 112, Indianapolis, Indiana 46202-5111, USA; e-mail: tili@iupui.edu

33

Available online at www.sciencedirect.com

ScienceDirect

Brain and Cognition 65 (2007) 209–237

Brain and Cognition

www.elsevier.com/locate/b&c

The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition

S.J. Lupien [a,*], F. Maheu [b], M. Tu [c], A. Fiocco [a], T.E. Schramek [a]

[a] *Center for Studies on Human Stress, Douglas Hospital Research Center, McGill University, Montreal, Que., Canada*
[b] *Mood and Anxiety Disorders Program, Emotional Development and Affective Neuroscience Branch, National Institute of Mental Health, NIH, Bethesda, MD 20892, USA*
[c] *University of British Columbia, Centre for Community Child Health Research, 480 Oak Street, L408, Vancouver, BC, Canada V6H 3V4*

Accepted 21 February 2007
Available online 26 April 2007

Abstract

In this review, we report on studies that have assessed the effects of exogenous and endogenous increases in stress hormones on human cognitive performance. We first describe the history of the studies on the effects of using exogenous stress hormones such as glucocorticoids as anti-inflammatory medications on human cognition and mental health. Here, we summarize the cases that led to the diagnosis of glucocorticoid-induced 'steroid psychosis' in human populations and which demonstrated that these stress hormones could thus cross the blood–brain barrier and access the brain where they could influence cognition and mental health. We then summarize studies that assessed the effects of the exogenous administration of glucocorticoids on cognitive performance supported by the hippocampus, the frontal lobes and amygdala. In the second section of the paper, we summarize the effects of the endogenous release of glucocorticoids induced by exposure to a stressful situation on human cognition and we further dissociate the effects of emotion from those of stress on human learning and memory. Finally, in the last section of the paper, we discuss the potential impact that the environmental context to which we expose participants when assessing their memory could have on their reactivity to stress and subsequent cognitive performance. In order to make our point, we discuss the field of memory and aging and we suggest that some of the 'age-related memory impairments' observed in the literature could be partly due to increased stress reactivity in older adults to the environmental context of testing. We also discuss the inverse negative correlations reported between hippocampal volume and memory for young and older adults and suggest that these inverse correlations could be partly due to the effects of contextual stress in young and older adults, as a function of age-related differences in hippocampal volume.

Keywords: Stress; Glucocorticoids; Catecholamines; Memory; Aging; Hippocampus

1. Introduction

Stress is a popular topic these days. A week seldom passes without hearing or reading about stress and its deleterious effects on health. Given this negative impact of stress on human health, many types of stress management therapies have been put forward to decrease stress and thus, promote health. However, there is a great paradox in the field of stress research, and it relates to the fact that the popular definition of stress is very different from the scientific definition of stress. This has left a multitude of people and experts talking about, and working on, very different aspects of the stress response.

In popular terms, stress is mainly defined as time pressure. We feel stressed when we do not have the time to perform the tasks we want to perform within a given period of time. This time pressure usually triggers a set of physiological reactions that give us the indication that we are stressed. Although this definition is certainly accurate in terms of one component of the stress response, it is

* Corresponding author. Fax: +1 514 888 4064.
E-mail address: sonia.lupien@mcgill.ca (S.J. Lupien).

0278-2626/$ - see front matter © 2007 Published by Elsevier Inc.
doi:10.1016/j.bandc.2007.02.007

Brain on stress: How the social environment gets under the skin

Bruce S. McEwen[1]

Laboratory of Neuroendocrinology, The Rockefeller University, New York, NY 10065

Edited by Gene E. Robinson, University of Illinois at Urbana-Champaign, Urbana, IL, and approved May 11, 2012 (received for review January 11, 2012)

Stress is a state of the mind, involving both brain and body as well as their interactions; it differs among individuals and reflects not only major life events but also the conflicts and pressures of daily life that alter physiological systems to produce a chronic stress burden that, in turn, is a factor in the expression of disease. This burden reflects the impact of not only life experiences but also genetic variations and individual health behaviors such as diet, physical activity, sleep, and substance abuse; it also reflects stable epigenetic modifications in development that set lifelong patterns of physiological reactivity and behavior through biological embedding of early environments interacting with cumulative change from experiences over the lifespan. Hormones associated with the chronic stress burden protect the body in the short run and promote adaptation (allostasis), but in the long run, the burden of chronic stress causes changes in the brain and body that can lead to disease (allostatic load and overload). Brain circuits are plastic and remodeled by stress to change the balance between anxiety, mood control, memory, and decision making. Such changes may have adaptive value in particular contexts, but their persistence and lack of reversibility can be maladaptive. However, the capacity of brain plasticity to effects of stressful experiences in adult life has only begun to be explored along with the efficacy of top-down strategies for helping the brain change itself, sometimes aided by pharmaceutical agents and other treatments.

brain structural plasticity | adverse childhood experiences | interventions

The brain is the central organ of stress and adaptation (Fig. 1). The social environment as well as the physical environment have powerful effects on the body and the brain through the neuroendocrine, autonomic, and immune systems (1–3). Two important processes are evident: The first process is the biological embedding of early experiences, the subject of this symposium, that determines operating ranges of physiological systems for the effects of later experiences, and the second process is the cumulative wear and tear of the physical and social environment on the brain and body acting through the neuroendocrine, autonomic, metabolic, and immune systems. This review focuses on the central role of the brain in both processes (2, 3) and the interaction of biological embedding with cumulative wear and tear over the life course; it considers the nature of interventions that can alter the predispositions and risks created by biological embedding as well as those interventions caused by life experiences and the health-damaging and -promoting behaviors by which individuals live their lives. In particular, increasing understanding of the plasticity of the mature brain offers some hope for finding better strategies to help those individuals whose lives have been burdened by adverse early-life experiences. At the same time, this view presents an encouraging and broader message as to the potential for experience—and pharmacologically regulated brain plasticity. Our current understanding in this area has been facilitated by advances in neuroendocrinology and neuroscience.

Historical Background

Neuroendocrinology, which developed and flourished beginning in the 1950s through the pioneering work of Geoffrey W. Harris (4) and many others (5) and led to the Nobel Prize recognition of Roger Guillemin (6) and Andrew V. Schally (7), focused on the hypothalamus and its connection with the pituitary gland. Hormonal feedback on these organs was part of the negative and positive feedback regulation of pituitary hormone secretion. Work on estradiol feedback (8, 9) called attention to hormone effects on mating behavior and defense of territory and brought in structures like the amygdala in addition to the hypothalamus. Glucocorticoid actions were focused on the hypothalamus until the discovery of glucocorticoid and mineralocorticoid receptors in the hippocampus (10) began to shift the focus from the feedback regulation of neuroendocrine function to other aspects of behavior, including cognition, mood, and self-regulatory behaviors.

Robert M. Sapolsky (11), studying the aging brain, developed the "glucocorticoid-cascade hypothesis" of stress and aging in the work by Sapolsky et al. (11), which focused on the deleterious effects of glucocorticoid feedback on the hippocampus, and this finding was reinforced by the elegant studies of Landfield et al. (12). Other than damage, however, there are now known to be many beneficial, adaptive actions of adrenal steroids on memory and immune function (13–15). Moreover, adrenal steroids do not work in a vacuum, but rather, they work in concert with other mediators of the autonomic, immune, and metabolic hormone systems (1); this work, together with the adaptive as well as potentially damaging aspects of these mediators, became part of the concepts of allostasis and allostatic load (16).

This notion of protection and damage as ends of possible outcomes of the actions of the mediators of allostasis was extended back to the brain by the finding of structural plasticity not only in hippocampus but in other brain regions, such as amygdala, prefrontal cortex, and nucleus accumbens (2). The concept of the plasticity of the adult brain is traceable to the enriched environment studies of the 1960s (17). Indeed, acute and chronic stress-induced plasticity is reversible, at least in young adult brains (18), and it does not constitute brain damage per se; however, the overstimulation of these systems (e.g., by seizures, head trauma, and ischemia) does cause permanent irreversible damage (19). Moreover, there is evidence that the aging brain loses its resilience [that is, its ability to recover from stress-induced changes (18) as well as those changes caused by isolation and an unhealthy lifestyle], which can be ameliorated by top-down interventions, such as physical activity and positive social interactions (20, 21). In this connection and others, modern imaging methods are enabling translation from animal models to the human brain.

This paper results from the Arthur M. Sackler Colloquium of the National Academy of Sciences, "Biological Embedding of Early Social Adversity: From Fruit Flies to Kindergartners," held December 9–10, 2011, at the Arnold and Mabel Beckman Center of the National Academies of Sciences and Engineering in Irvine, CA. The complete program and audio files of most presentations are available on the NAS Web site at www.nasonline.org/biological-embedding.

Author contributions: B.S.M. wrote the paper.

The author declares no conflict of interest.

This article is a PNAS Direct Submission.

[1]E-mail: mcewen@mail.rockefeller.edu.

www.pnas.org/cgi/doi/10.1073/pnas.1121254109

Development/Plasticity/Repair

Heterogeneity in Subcortical Brain Development: A Structural Magnetic Resonance Imaging Study of Brain Maturation from 8 to 30 Years

Ylva Østby,[1] Christian K. Tamnes,[1] Anders M. Fjell,[1,2] Lars T. Westlye,[1] Paulina Due-Tønnessen,[3] and Kristine B. Walhovd[1,2]

[1]Center for the Study of Human Cognition, Department of Psychology, University of Oslo, N-0317 Oslo, Norway, [2]Department of Neuropsychology, Ullevaal University Hospital, N-0407 Oslo, Norway, and [3]Department of Radiology, Rikshospitalet University Hospital, N-0027 Oslo, Norway

Brain development during late childhood and adolescence is characterized by decreases in gray matter (GM) and increases in white matter (WM) and ventricular volume. The dynamic nature of development across different structures is, however, not well understood, and the present magnetic resonance imaging study took advantage of a whole-brain segmentation approach to describe the developmental trajectories of 16 neuroanatomical volumes in the same sample of children, adolescents, and young adults (n = 171; range, 8–30 years). The cerebral cortex, cerebral WM, caudate, putamen, pallidum, accumbens area, hippocampus, amygdala, thalamus, brainstem, cerebellar GM, cerebellar WM, lateral ventricles, inferior lateral ventricles, third ventricle, and fourth ventricle were studied. The cerebral cortex was further analyzed in terms of lobar thickness and surface area. The results revealed substantial heterogeneity in developmental trajectories. GM decreased nonlinearly in the cerebral cortex and linearly in the caudate, putamen, pallidum, accumbens, and cerebellar GM, whereas the amygdala and hippocampus showed slight, nonlinear increases in GM volume. WM increased nonlinearly in both the cerebrum and cerebellum, with an earlier maturation in cerebellar WM. In addition to similarities in developmental trajectories within subcortical regions, our results also point to differences between structures within the same regions: among the basal ganglia, the caudate showed a weaker relationship with age than the putamen and pallidum, and in the cerebellum, differences were found between GM and WM development. These results emphasize the importance of studying a wide range of structural variables in the same sample, for a broader understanding of brain developmental principles.

Introduction

Subcortical structures are important in developmental disorders (Krain and Castellanos, 2006), and we need a better understanding of the dynamics of differential subcortical brain development. However, few magnetic resonance imaging (MRI) studies cover normal brain development in multiple subcortical regions in childhood and adolescence. The aim of the present study was to describe and compare the developmental trajectories of several subcortical structures in the same sample of participants, thereby shedding light on the dynamic interplay between different brain structures in development.

It is generally acknowledged that gray matter (GM) volume increases in early childhood and decreases during adolescence (Jernigan et al., 1991; Reiss et al., 1996; Giedd et al., 1999; Sowell et al., 1999, 2002; Lenroot et al., 2007; Wilke et al., 2007; Shaw et al., 2008). This may, in part, reflect early synaptic arborization and later pruning (Huttenlocher, 1990). Results indicate that subcortical GM structures show differential developmental trajectories (Giedd et al., 1996b; Sowell et al., 2002; Toga et al., 2006). Because most studies have quantified only one or a few structures, the relative development of the subcortical structures is still unclear, however. For instance, different emphasis has been put on either the caudate or lenticular nuclei in development in various reports, sometimes because of methodological constraints (Jernigan et al., 1991; Giedd et al., 1996a; Sowell et al., 1999, 2002; Wilke et al., 2007). There has been some focus on structural development of the cerebellum (Sowell et al., 2002; Liu et al., 2003; Mackie et al., 2007) and accumbens (Sowell et al., 2002), but cerebellar development is still not characterized in terms of separate WM and GM development. Furthermore, there is a need for a broader understanding of the development of hippocampus and amygdala, as these structures often appear to increase during development, although discrepancies exist (Giedd et al., 1996b; Sowell et al., 2002; Gogtay et al., 2006; Toga et al., 2006; Guo et al., 2007). It is not clear how this is to be understood within a (proposed) framework of arborization/pruning as general principles of GM development. White matter (WM) volume has been shown to increase, often linearly, probably driven by increased myelination during adolescence and early adulthood (Reiss et al., 1996; Giedd et al., 1999; Sowell et al., 2002;

Received March 13, 2009; revised July 7, 2009; accepted Aug. 3, 2009.

This work was supported by the Norwegian Research Council (177404/W50 and 186092/V50 to K.B.W., 170837/V50 to Ivar Reinvang); the University of Oslo (K.B.W.); and the Department of Psychology, University of Oslo (A.M.F.). We thank Mari Torstveit, Victoria Torp Sells, and Vivi Agnete Larsen for contributing to the data acquisition; Dag Erik Eilertsen for assistance in statistical analyses; and Inge Amlien and Tonje Østby for help with preparation of the figures. We also thank all participants and their parents for taking part in this study.

Correspondence should be addressed to Ylva Østby, Department of Psychology, University of Oslo, P.O. Box 1094 Blindern, N-0317 Oslo, Norway. E-mail: ylva.ostby@psykologi.uio.no.

DOI:10.1523/JNEUROSCI.1242-09.2009

 0270-6474/09/2911772-11$15.00/0

Developmental Cognitive Neuroscience 11 (2015) 83–95

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn

Age-related changes in the intrinsic functional connectivity of the human ventral vs. dorsal striatum from childhood to middle age

James N. Porter[a], Amy K. Roy[d], Brenda Benson[e], Christina Carlisi[e], Paul F. Collins[b], Ellen Leibenluft[e], Daniel S. Pine[e], Monica Luciana[b,c], Monique Ernst[e,*]

[a] University of Iowa Hospitals and Clinics Department of Neurology, USA
[b] University of Minnesota Department of Psychology, USA
[c] University of Minnesota Center for Neurobehavioral Development, USA
[d] Fordham University, Department of Psychology, USA
[e] Section on Development and Affective Neuroscience, National Institute of Mental Health, National Institutes of Health, USA

ARTICLE INFO

Article history:
Received 10 April 2014
Received in revised form 22 July 2014
Accepted 21 August 2014
Available online 30 August 2014

Keywords:
Resting-state
Adolescence
Development
Functional-connectivity
Striatum
Prefrontal-cortex

ABSTRACT

The striatum codes motivated behavior. Delineating age-related differences within striatal circuitry can provide insights into neural mechanisms underlying ontogenic behavioral changes and vulnerabilities to mental disorders. To this end, a dual ventral/dorsal model of striatal function was examined using resting state intrinsic functional connectivity (iFC) imaging in 106 healthy individuals, ages 9–44. Broadly, the dorsal striatum (DS) is connected to prefrontal and parietal cortices and contributes to cognitive processes; the ventral striatum (VS) is connected to medial orbitofrontal and anterior cingulate cortices, and contributes to affective valuation and motivation. Findings revealed patterns of age-related changes that differed between VS and DS iFCs. We found an age-related increase in DS iFC with posterior cingulate cortex (pCC) that stabilized after the mid-twenties, but a decrease in VS iFC with anterior insula (aIns) and dorsal anterior cingulate cortex (dACC) that persisted into mid-adulthood. These distinct developmental trajectories of VS vs. DS iFC might underlie adolescents' unique behavioral patterns and vulnerabilities to psychopathology, and also speaks to changes in motivational networks that extend well past 25 years old.

1. Introduction

The basal ganglia, at the intersection of the midbrain and forebrain, are implicated in a wide range of motor, cognitive, and affective functions that are subserved by cortical–striatal–thalamic–cortical loops (Alexander et al., 1986; Haber, 2003; Selemon and Goldman-Rakic, 1985). Accordingly, the striatum, the major input component of the basal ganglia, receives connections from all cortical regions in a parallel, segregated fashion. Five parallel networks were originally proposed in the classic paper by Alexander et al. (1986); more recent accounts add the notion of a functional gradient within the striatum (Haber, 2003). Specifically, a ventral to dorsal schema has been linked with an affective/motivational to cognitive/motor

* Corresponding author at: Head of Neurodevelopment of Reward Systems, Emotional Development and Affective Neuroscience Branch (EDAN), Section on Neurobiology of Fear and Anxiety (NFA), National Institute of Mental Health/NIH, 15K North Drive, Bethesda, MD 20892, USA. Tel.: +1 301 402 9355; fax: +301 402 2010; mobile: +1 301 675 4525.
E-mail address: ernstm@mail.nih.gov (M. Ernst).

http://dx.doi.org/10.1016/j.dcn.2014.08.011

Myelination of language-related areas in the developing brain

J. Pujol, MD; C. Soriano-Mas, PhD; H. Ortiz, MSc; N. Sebastián-Gallés, PhD; J.M. Losilla, PhD; and J. Deus, PhD

Abstract—*Background:* The rapid development of language abilities in early childhood coincides with a similarly accelerated progression in brain maturation. *Objective:* To quantitate myelination in the lateral part of the verbal left hemisphere from birth to 3 years in the living human brain. *Methods:* One hundred children (mean age 16.6 months) were examined using three-dimensional MRI, and a subgroup of 40 children were also evaluated behaviorally. The volume of myelinated white matter was measured in language-related temporal and frontal regions and in the central sensorimotor region. A method was developed to compose a movie sequence for all the myelination process using volumetric data. *Results:* A plot of age against relative volume of myelinated white matter graphically detailed the myelination progress in the lateral brain. The changes started in sensorimotor white matter and the Heschl gyrus and ultimately extended to the language-related areas. Both comprehension and production regions showed a very similar myelination course, suggesting simultaneous maturation of the temporofrontal language network. The movie sequence of white matter images dynamically displayed the anatomic details of myelin deposition in this part of the brain. The analysis of language performance showed acceleration in children's vocabulary after 18 months, once a rapid myelination phase was attained in the language brain. *Conclusions:* This volumetric study may contribute to further characterize the early stages of brain maturation by showing the fine progression of myelin deposition in the language domains and illustrating its relationship to children's vocabulary acquisition.

NEUROLOGY 2006;66:339–343

Language is a complex cognitive ability that develops with extraordinary speed during early childhood.[1] Maturation of the developing brain is also accelerated in the early years and involves many changes in all neuronal elements, including the progressive myelination of white matter.[2,3] Myelin is present at birth in the pyramidal tract and primary sensory pathways. During the following months, myelin deposition progressively spreads to neocortical domains devoted to higher cognitive processes.[4,5] Most of the histologic and imaging studies assessing myelination during the first years of life are based on the estimation of the age at which representative cerebral structures achieve myelination maturity.[6-14] Nevertheless, there are no studies specifically assessing the course of myelination in language-related areas.

In this study, we quantitated myelination in the lateral aspect of the left hemisphere in the living human brain from birth to 3 years using volumetric MRI. Children with no imaging evidence of brain damage were assessed to describe the course of myelination in temporal and frontal language-related areas and in the reference sensorimotor region. The MRI exams from a subgroup of neurologically intact children were used to create a movie sequence that dynamically showed the anatomic details of myelin deposition in this part of the brain. Word production was also evaluated in the normal children as a representative measurement of language performance to illustrate the relationship between vocabulary growth and rapid myelination occurring in the studied age period.

Additional material related to this article can be found on the *Neurology* Web site. Go to www.neurology.org and scroll down the Table of Contents to the February 14 issue to find the title link for this article.

Methods. *Subjects.* We studied 100 children showing normal MRI. Forty of these subjects were neurologically intact children, referred for noncranial MRI examination and showing no active systemic disease, whose parents agreed to the acquisition of the additional three-dimensional brain sequence. A family report of normal development was required, and each subject in this neurologically normal group received specific language assessment. The

Editorial, see page 304

From the Institut d'Alta Tecnologia (J.P., C.S.-M., H.O., J.D.), Parc de Recerca Biomèdica de Barcelona, Department of Basic Psychology (N.S.-G.), University of Barcelona, Departments of Psychobiology and Methodology (J.M.L.) and Clinical and Health Psychology (J.D.), Autonomous University of Barcelona, Spain.

Supported in part by the James S. McDonnell Research Grant, Bridging Brain Mind and Behavior Program (2000), and the Direcció General de Recerca de la Generalitat de Catalunya (grants 2000XT-43, 2003XT-97, and 2002SGR-108).

Disclosure: The authors report no conflicts of interest.

Received July 12, 2005. Accepted in final form December 12, 2005.

Address correspondence and reprint requests to Dr. J. Pujol, Institut d'Alta Tecnologia, Parc de Recerca Biomèdica de Barcelona, Passeig Marítim 25-29, Barcelona 08003, Spain; e-mail: jpujol@crccorp.es

Brain and Cognition 72 (2010) 134–145

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Review Article

Social brain development and the affective consequences of ostracism in adolescence

Catherine Sebastian [a,*], Essi Viding [b], Kipling D. Williams [c], Sarah-Jayne Blakemore [a]

[a] Institute of Cognitive Neuroscience, UCL, UK
[b] Research Department of Clinical, Educational and Health Psychology, Division of Psychology and Language Sciences, UCL, UK
[c] Department of Psychological Sciences, Purdue University, UK

ARTICLE INFO

Article history:
Available online 22 July 2009

Keywords:
Adolescence
Ostracism
Social exclusion
Self
Social cognition
Social brain emotion regulation
Puberty
fMRI
Prefrontal cortex

ABSTRACT

Recent structural and functional imaging studies have provided evidence for continued development of brain regions involved in social cognition during adolescence. In this paper, we review this rapidly expanding area of neuroscience and describe models of neurocognitive development that have emerged recently. One implication of these models is that neural development underlies commonly observed adolescent phenomena such as susceptibility to peer influence and sensitivity to peer rejection. Experimental behavioural evidence of rejection sensitivity in adolescence is currently sparse. Here, we describe a study that directly compared the affective consequences of an experimental ostracism manipulation (Cyberball) in female adolescents and adults. The ostracism condition led to significantly greater affective consequences in the adolescents compared with adults. This suggests that the ability to regulate distress resulting from ostracism continues to develop between adolescence and adulthood. The results are discussed in the context of models of neurocognitive development.

1. Introduction

Human adolescence is a period of physical, psychological and social transition between childhood and adulthood (Spear, 2000). In recent years it has been established that substantial neural development also occurs during this period of life (see Paus, 2005 for a review; Gogtay & Thompson, 2010; Paus, this issue; Giedd & Lenroot, 2010; Schmithorst, 2010). There are significant changes in grey matter and white matter volumes in brain regions responsible for complex human behaviours, notably the prefrontal cortex and temporo-parietal regions (Giedd et al., 1999; Gogtay et al., 2004; Shaw et al., 2008; Sowell et al., 1999). These regions are involved in a variety of cognitive functions, including social cognition, mentalising (the attribution of mental states to oneself and to other people) and self-related processing. In this paper, we review developmental functional imaging studies of social cognition, mentalising and self-processing, and discuss recent models of adolescent neurocognitive development. We then describe a behavioural study that investigated affective reactions to an instance of experimentally induced ostracism in adolescents, compared with adults. Finally, we evaluate how the results of our study can inform models of adolescent development.

* Corresponding author. Address: UCL Institute of Cognitive Neuroscience, 17 Queen Square, London, WC1N 3AR, UK. Fax: +44 20 7813 2835.
E-mail address: c.sebastian@ucl.ac.uk (C. Sebastian).

0278-2626/$ - see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.bandc.2009.06.008

2. Developmental functional imaging studies of the social brain

2.1. The social brain

The social brain is defined as the network of brain regions subserving social cognition, i.e. those enabling us to recognise others, and to evaluate our own and others' mental states (intentions, desires and beliefs), feelings, enduring dispositions and actions (Brothers, 1990; Frith & Frith, 2007). Many different brain regions are involved in social cognition, including medial prefrontal cortex (mPFC), anterior cingulate cortex (ACC), inferior frontal gyrus, posterior superior temporal sulcus (pSTS), temporo-parietal junction (TPJ), the amygdala and anterior insula (see Fig. 1). Some of these brain regions are activated during the attribution of mental states to oneself and to others. This ability, known as mentalising or theory of mind, enables us to understand other people's behaviour and actions in terms of underlying mental states such as intentions, desires and beliefs (Frith & Frith, 2007). Social cognitive processes underlying mentalising range from basic perceptual processes such as biological motion and face perception (Frith, 2007; Pelphrey & Carter, 2008) to those enabling us to perceive and understand emotional responses in ourselves and others (Olsson & Ochsner, 2008), to more abstract meta-representational abilities enabling us to hold an 'intentional stance', i.e. the idea that others' act on the basis of their mental states (Dennett, 1987).

Using functional imaging and a wide range of stimuli, several studies have shown remarkable consistency in identifying the

NeuroImage 57 (2011) 686–694

Contents lists available at ScienceDirect

NeuroImage
39
journal homepage: www.elsevier.com/locate/ynimg

Developmental influences on the neural bases of responses to social rejection: Implications of social neuroscience for education

Catherine L. Sebastian [a,b,*], Geoffrey C.Y. Tan [c], Jonathan P. Roiser [a], Essi Viding [b], Iroise Dumontheil [a], Sarah-Jayne Blakemore [a]

[a] Institute of Cognitive Neuroscience, University College London, 17 Queen Square, London, WC1N 3AR, UK
[b] Clinical, Educational and Health Psychology, University College London, 26 Bedford Way, London, WC1H 0AP, UK
[c] Wellcome Trust Centre for Neuroimaging, University College London, 12 Queen Square, London, WC1N 3BG, UK

ARTICLE INFO

Article history:
Received 3 June 2010
Revised 20 September 2010
Accepted 24 September 2010
Available online 12 October 2010

Keywords:
Social rejection
Adolescence
fMRI
Prefrontal cortex
Peer relationships
Education
Social neuroscience

ABSTRACT

Relational aggression such as social rejection is common within school peer groups. Converging evidence suggests that adolescent females are particularly sensitive to social rejection. We used a novel fMRI adaptation of the Cyberball social rejection paradigm to investigate the neural response to social rejection in 19 mid-adolescent (aged 14–16) and 16 adult female participants. Across all participants, social exclusion (relative to inclusion) elicited a response in bilateral medial prefrontal cortex (mPFC) extending into ventral and subgenual anterior cingulate cortex and medial orbitofrontal cortex; and the left ventrolateral PFC (vlPFC); regions that have been associated in previous studies with social evaluation, negative affective processing, and affect regulation respectively. However, the exclusion-related response in right vlPFC, a region associated in previous studies with the regulation of rejection-related distress, was attenuated in adolescents. Within mPFC, greater activation during exclusion vs. inclusion was associated with greater self-reported susceptibility to peer influence in adolescents but not in adults. This suggests that the brain's response to experimentally-induced social rejection relates to adolescent behaviour in real-world social interactions. We speculate about the potential implications of these findings for educational settings. In particular, functional development of affective circuitry during adolescence may influence social interaction within the school peer group.

Introduction

In exploring the contributions that neuroscience can make to educational practice, it is important to consider the pastoral role that schools must fill, particularly at secondary level. Adolescence is a time of opportunity for learning new skills and forging an adult identity. However, it is also a time of vulnerability, as adolescents begin to face adult challenges while still developing physically, socially and cognitively (Steinberg, 2005). Understanding the brain basis of social development and functioning during adolescence is crucial for the fostering of social competence and psychological wellbeing inside and outside the classroom (Blakemore, 2010).

Managing social relationships is a significant challenge for adolescents. Relational or social forms of bullying are common within school peer groups, particularly among adolescent girls. One recent study (Wang et al., 2009) found that 27.4% of adolescent girls (mean age 14.3 years) reported being excluded or ignored by a group of peers while at school. Being bullied (including relational aggression) is associated with decreased school achievement and psychological wellbeing (Hawker and Boulton, 2000; Boulton et al., 2008); thus, a greater understanding of adolescent responses to phenomena such as social rejection may contribute to greater understanding of the factors contributing to schooling success and failure (Blakemore, 2010). Recently, several influential fMRI studies have investigated the neural bases of responses to social rejection. However, responses in adolescents and adults have not been directly compared. Given evidence showing continuing structural and functional development in social brain regions during adolescence (Blakemore, 2008) the current study investigated whether adolescents differ from adults in the neural processing of social rejection.

One of the difficulties in investigating social rejection with fMRI is the choice of an appropriate rejection paradigm. This must aim to preserve some of the ecological validity of social rejection, while maintaining sufficient experimental control. The paradigm most commonly used with fMRI is the Cyberball game (Williams et al., 2000). Participants believe they are playing a game of 'catch' over an internet connection with two other players, whereas the actions of these players are actually pre-programmed to include or exclude the

* Corresponding author. Clinical, Educational and Health Psychology, University College London, 26 Bedford Way, London, WC1H 0AP, UK. Fax: +44 20 7436 4276.
E-mail addresses: c.sebastian@ucl.ac.uk (C.L. Sebastian), g.tan@ucl.ac.uk (G.C.Y. Tan), j.roiser@ucl.ac.uk (J.P. Roiser), e.viding@ucl.ac.uk (E. Viding), i.dumontheil@ucl.ac.uk (I. Dumontheil), s.blakemore@ucl.ac.uk (S.-J. Blakemore).

1053-8119/$ - see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2010.09.063

Brain Imaging and Behavior (2018) 12:1197–1210
DOI 10.1007/s11682-017-9761-4

40

REVIEW ARTICLE

Developmental trajectory of the prefrontal cortex: a systematic review of diffusion tensor imaging studies

Sónia S. Sousa[1] · Edson Amaro Jr[2] · Alberto Crego[1] · Óscar F. Gonçalves[1,3,4] · Adriana Sampaio[1]

Published online: 15 September 2017

Abstract Fluctuations in gray and white matter volumes in addition to the fibers' reorganization and refinement of synaptic connectivity apparently happen in a particular temporo-spatial sequence during the dynamic and prolonged process of cerebral maturation. These developmental events are associated with regional modifications of brain tissues and neural circuits, contributing to networks' specialization and enhanced cognitive processing. According to several studies, improvements in cognitive processes are possibly myelin-dependent and associated to white matter maturation. Of particular interest is the developmental pattern of the prefrontal cortex (PFC), more specifically the PFC white matter, due to its role in high-level executive processes such as attention, working memory and inhibitory control. A systematic review of the literature was conducted using the Web of Science, PubMed and Embase databases to analyze the development of PFC white matter using Diffusion Tensor Imaging (DTI), a widely used non-invasive technique to assess white matter maturation. Both the research and reporting of results were based on Cochrane's recommendations and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. Information extracted from 27 published studies revealed an increased myelination, organization and integrity of frontal white matter with age, as revealed by DTI indexes (fractional anisotropy [FA], mean diffusivity [MD], radial diffusivity [RD] and axial diffusivity [AD]). These patterns highlight the extended developmental course of the frontal structural connectivity, which parallels the improvements in higher-level cognitive functions observed between adolescence and early adulthood.

Keywords Prefrontal cortex · White matter · Myelination · Diffusion tensor imaging · Development

✉ Sónia S. Sousa
soniamachado@psi.uminho.pt

[1] Neuropsychophysiology Lab, CIPsi, School of Psychology, University of Minho, Campus Gualtar, 4710-057 Braga, Portugal

[2] Department of Radiology, School of Medicine, University of Sao Paulo, São Paulo, Brazil

[3] Spaulding Neuromodulation Center, Department of Physical Medicine & Rehabilitation, Spaulding Rehabilitation Hospital and Massachusetts General Hospital, Harvard Medical School, Charlestown campus: 79/96 13th Street, Charlestown, MA 02129, USA

[4] Department of Applied Psychology, Bouvé College of Health Sciences, Northeastern University, 404 International Village, Boston, MA 02115, USA

Introduction

Several studies assessed white matter maturation through non-invasive imaging techniques such as DTI. This technique has become popular considering its sensitivity in evaluating axons' features, using the random motion of water molecules known as thermal Brownian motion (Hagmann et al. 2006; Le Bihan 2003; Thomason and Thompson 2011). This random motion of water molecules is essential to the accuracy of DTI and therefore deserves a detailed explanation of its underlying mechanism. The random displacement observed in biological tissues, seems to be driven by its anatomical architecture, and dependent on the histological properties of tissues such as cell membranes, myelin sheaths and molecules (Hagmann et al. 2006; Mori and Zhang 2006). In this sense, water diffusion within a specific milieu might be classified as isotropic—water molecules travel randomly in all directions,

Less Guilty by Reason of Adolescence

Developmental Immaturity, Diminished Responsibility, and the Juvenile Death Penalty

Laurence Steinberg — *Temple University*
Elizabeth S. Scott — *University of Virginia School of Law*

The authors use a developmental perspective to examine questions about the criminal culpability of juveniles and the juvenile death penalty. Under principles of criminal law, culpability is mitigated when the actor's decision-making capacity is diminished, when the criminal act was coerced, or when the act was out of character. The authors argue that juveniles should not be held to the same standards of criminal responsibility as adults, because adolescents' decision-making capacity is diminished, they are less able to resist coercive influence, and their character is still undergoing change. The uniqueness of immaturity as a mitigating condition argues for a commitment to a legal environment under which most youths are dealt with in a separate justice system and none are eligible for capital punishment.

Since 1990, only a handful of countries in the world—Congo, Iran, Yemen, Saudi Arabia, Pakistan, Nigeria, and the United States—have executed individuals whose crimes were committed when they were juveniles (Bradley, 2002; de la Vega, 2002). Twenty-one states in the United States allow the execution of individuals under the age of 18, and in most of these states, adolescent offenders as young as 16 can be sentenced to death (Streib, 2002). The United States Supreme Court has held that the death penalty is unconstitutional for youths who are under 16 at the time of their offense (*Thompson v. Oklahoma*, 1998) but has declined to categorically prohibit capital punishment for 16- and 17-year-olds (*Stanford v. Kentucky*, 1989).

Several events have occurred recently that, considered together, suggest that it is time to reexamine the constitutionality of the juvenile death penalty. First, in *Atkins v. Virginia* (2002), the Supreme Court ruled that the execution of mentally retarded offenders violates the U.S. Constitution; some of the reasons offered by the Court for the ban may also apply to the capital punishment of juveniles. Second, following the *Atkins* decision, three Supreme Court justices took the unusual step of urging reconsideration of the constitutional status of the juvenile death penalty, suggesting considerable dissatisfaction at the highest level with current doctrine (Lane, 2002). Finally, after the apprehension of the Washington-area serial snipers, one of whom, Lee Malvo, was 17 years old, prosecutors vied for the right to try the case in their jurisdiction. It was widely speculated that Attorney General Ashcroft selected Virginia as the venue, in large part, because that jurisdiction permits the execution of juveniles, whereas Maryland, where the majority of the killings took place, does not (Lichtblau, 2002). Thus, this highly publicized case has focused national attention on the debate over the juvenile death penalty.

The juvenile death penalty is a critically important issue in juvenile crime policy, but it is not our sole focus in this article. We are interested in the broader question of whether juveniles should be punished to the same extent as adults who have committed comparable crimes. Capital punishment is the extreme case, but in practical effect, it is not the most important one in an era in which youth crime policy has become increasingly punitive. The question of whether juveniles should be punished like adults is important to discussions about sentencing guidelines, the transfer of juvenile offenders into the adult criminal justice system, and the incarceration of juveniles in adult facilities (Fagan & Zimring, 2000). High-profile murder cases, like those involving Lee Malvo or Lionel Tate, the Florida 14-year-old who was sentenced to life in prison for killing a playmate during a wrestling match, generate public attention to these matters (e.g., Browning, 2001), but questions about the appropriate punishment of juvenile offenders arise in many less visible cases, including those involving nonviolent crimes such as drug selling (Clary, 2001).

In this article, we draw on research and theory about adolescent development to examine questions about the criminal culpability of juveniles. Recent shifts in juvenile justice policy and practice toward the harsher treatment of youthful offenders are grounded in concerns about public protection and the belief that there is no good reason to exercise leniency with young offenders. This view rejects

Laurence Steinberg, Department of Psychology, Temple University; Elizabeth S. Scott, University of Virginia School of Law.

Work on this article was supported by the John D. and Catherine T. MacArthur Foundation Research Network on Adolescent Development and Juvenile Justice, of which the authors are members.

Correspondence concerning this article should be addressed to Laurence Steinberg, Department of Psychology, Temple University, Philadelphia, PA 19122. E-mail: lds@temple.edu

Developmental Psychology
2007, Vol. 43, No. 6, 1531–1543

42

0012-1649/07/$12.00 DOI: 10.1037/0012-1649.43.6.1531

Age Differences in Resistance to Peer Influence

Laurence Steinberg and Kathryn C. Monahan
Temple University

Prior research describes the development of susceptibility to peer pressure in adolescence as following an inverted U-shaped curve, increasing during early adolescence, peaking around age 14, and declining thereafter. This pattern, however, is derived mainly from studies that specifically examined peer pressure to engage in antisocial behavior. In the present study, age differences and developmental change in resistance to peer influence were assessed using a new self-report instrument that separates susceptibility to peer pressure from willingness to engage in antisocial activity. Data from four ethnically and socioeconomically diverse samples comprising more than 3,600 males and females between the ages of 10 and 30 were pooled from one longitudinal and two cross-sectional studies. Results show that across all demographic groups, resistance to peer influences increases linearly between ages 14 and 18. In contrast, there is little evidence for growth in this capacity between ages 10 and 14 or between 18 and 30. Middle adolescence is an especially significant period for the development of the capacity to stand up for what one believes and resist the pressures of one's peers to do otherwise.

Keywords: adolescence, peer pressure, peer influence

The heightened importance of peer influence is a hallmark of adolescent psychosocial functioning (Brown, 2004). Peer pressure is commonly invoked in discussions of adolescent misbehavior and is implicated in many accounts of adolescent risk taking, because most risky behavior in which adolescents engage, such as delinquency, substance use, and reckless driving, takes place in the company of peers (Chassin et al., 2004; Simons-Morton, Lerner, & Singer, 2005). Although studies of homophily (the tendency for individuals to affiliate with like-minded friends) during adolescence have yielded different estimates of the relative importance of selection versus socialization as contributors to behavioral and attitudinal similarity between adolescents and their friends (Brown, 2004), there is little doubt that peers actually influence each other and that the effects of peer influence are stronger during adolescence than in adulthood. Indeed, one recent experimental study found that exposure to peers during a risk-taking task doubled the amount of risky behavior among middle adolescents, increased it by 50% among college undergraduates, and had no impact at all among adults (Gardner & Steinberg, 2005).

Two mutually compatible explanations for the increased significance of peer influence during adolescence have been offered (Brown, Clasen, & Eicher, 1986). One, which stresses changes in the salience of peers as a reference group, points to the increasingly important role that peer crowds play in defining the social landscape of early and middle adolescence. As individuals begin to sort themselves into crowds, both perceived and actual pressure to adopt the styles, values, and interests of one's friends may intensify as adolescents use social influence to regulate each other's behavior in an attempt to foster solidarity and uniformity within their group and to develop and maintain a group identity that distinguishes them from other students. This process of *normative regulation* may be an especially powerful force during middle adolescence, when upwards of 85% of American youth report membership in at least one peer crowd (Brown, 2004).

The second account focuses more on the individual than the social context. According to this view, the heightened significance of peer influence in adolescence is due mainly to changes in individuals' susceptibility to peer pressure. The increased importance of peers leads adolescents to want to alter their behavior in order to fit in; because they care more about what their friends think of them, they are more likely to go along with the crowd to avoid being rejected (Brown et al., 1986). It is possible that this heightened conformity to peer pressure during early adolescence is a sign of a sort of emotional "way station" between becoming emotionally autonomous from parents and becoming a genuinely autonomous person (Steinberg & Silverberg, 1986). In other words, the adolescent may become emotionally autonomous from parents before he or she is emotionally ready for this degree of independence and may turn to peers to fill this void. There is also some emerging evidence, albeit preliminary, that brain systems that are important in the processing of social information may

Laurence Steinberg and Kathryn C. Monahan, Department of Psychology, Temple University.

Data for this study come from three sources: The MacArthur Juvenile Capacity Study, which has been funded by the John D. and Catherine T. MacArthur Foundation; the MacArthur Juvenile Competence Study, which was funded by the MacArthur Foundation and the Open Society Institute; and Research on Pathways to Desistance, an ongoing investigation supported by grants from the Office of Juvenile Justice and Delinquency Prevention, the Centers for Disease Control and Prevention, the National Institute of Drug Abuse, the National Institute of Justice, the John D. and Catherine T. MacArthur Foundation, the William T. Grant Foundation, the Robert Wood Johnson Foundation, the William Penn Foundation, the Pennsylvania Council on Crime and Delinquency, and the Arizona Juvenile Justice Commission. We are grateful to our collaborators on each of these investigations for permitting us to use the data sets for purposes of the analyses reported here.

Correspondence concerning this article should be addressed to Laurence Steinberg, Department of Psychology, Temple University, Philadelphia, PA 19122. E-mail: lds@temple.edu

Available online at www.sciencedirect.com
ScienceDirect
Developmental Review 28 (2008) 78–106
DEVELOPMENTAL REVIEW
www.elsevier.com/locate/dr

A social neuroscience perspective on adolescent risk-taking

Laurence Steinberg *

Department of Psychology, Temple University, Philadelphia, PA 19122, United States

Received 9 May 2007
Available online 28 January 2008

Abstract

This article proposes a framework for theory and research on risk-taking that is informed by developmental neuroscience. Two fundamental questions motivate this review. First, why does risk-taking increase between childhood and adolescence? Second, why does risk-taking decline between adolescence and adulthood? Risk-taking increases between childhood and adolescence as a result of changes around the time of puberty in the brain's socio-emotional system leading to increased reward-seeking, especially in the presence of peers, fueled mainly by a dramatic remodeling of the brain's dopaminergic system. Risk-taking declines between adolescence and adulthood because of changes in the brain's cognitive control system—changes which improve individuals' capacity for self-regulation. These changes occur across adolescence and young adulthood and are seen in structural and functional changes within the prefrontal cortex and its connections to other brain regions. The differing timetables of these changes make mid-adolescence a time of heightened vulnerability to risky and reckless behavior.

Keywords: Adolescents; Risk-taking; Social neuroscience; Reward-seeking; Self-regulation; Prefrontal cortex; Peer influence; Decision making; Dopamine; Oxytocin; Brain development

* Fax: +1 215 204 1286.
E-mail address: lds@temple.edu.

0273-2297/$ - see front matter © 2007 Elsevier Inc. All rights reserved.
doi:10.1016/j.dr.2007.08.002

Reconciling the Complexity of Human Development With the Reality of Legal Policy

Reply to Fischer, Stein, and Heikkinen (2009)

Laurence Steinberg — *Temple University*
Elizabeth Cauffman — *University of California, Irvine*
Jennifer Woolard — *Georgetown University*
Sandra Graham — *University of California, Los Angeles*
Marie Banich — *University of Colorado*

The authors respond to both the general and specific concerns raised in Fischer, Stein, and Heikkinen's (2009) commentary on their article (Steinberg, Cauffman, Woolard, Graham, & Banich, 2009), in which they drew on studies of adolescent development to justify the American Psychological Association's positions in two Supreme Court cases involving the construction of legal age boundaries. In response to Fischer et al.'s general concern that the construction of bright-line age boundaries is inconsistent with the fact that development is multifaceted, variable across individuals, and contextually conditioned, the authors argue that the only logical alternative suggested by that perspective is impractical and unhelpful in a legal context. In response to Fischer et al.'s specific concerns that their conclusion about the differential timetables of cognitive and psychosocial maturity is merely an artifact of the variables, measures, and methods they used, the authors argue that, unlike the alternatives suggested by Fischer et al., their choices are aligned with the specific capacities under consideration in the two cases. The authors reaffirm their position that there is considerable empirical evidence that adolescents demonstrate adult levels of cognitive capability several years before they evince adult levels of psychosocial maturity.

Keywords: policy, science, adolescent development, chronological age

In our article (Steinberg, Cauffman, Woolard, Graham, & Banich, 2009, this issue), we asked whether there was scientific justification for the different positions taken by the American Psychological Association (APA) in two related Supreme Court cases—*Hodgson v. Minnesota* (1990; a case concerning minors' competence to make independent decisions about abortion, in which APA argued that adolescents were just as mature as adults) and *Roper v. Simmons* (2005; a case about the constitutionality of the juvenile death penalty, in which APA argued that adolescents were not as mature as adults). On the basis of our reading of the extant literature in developmental psychology, as well as findings from a recent study of our own, we concluded that the capabilities relevant to judging individuals' competence to make autonomous decisions about abortion reach adult levels of maturity earlier than do capabilities relevant to assessments of criminal culpability, and that it was therefore reasonable to draw different age boundaries between adolescents and adults in each instance.

In their commentary on our article, Fischer, Stein, and Heikkinen (2009, this issue) raised both general and specific objections to our conclusions. The general issue concerns how developmental evidence may or may not inform the construction and analysis of legal age boundaries. The specific issues involve the conclusions we drew from our analysis of data on age differences in cognitive capabilities and psychosocial maturity. We appreciate the opportunity to reply to both of these concerns.

When psychologists agree to provide guidance on matters of law, they must be able and willing to simultaneously plant their feet in two worlds—that of social science and that of legal policy and practice. These worlds operate on different principles and with different expectations. Social scientists are accustomed to providing complicated answers to seemingly simple questions, whereas legal professionals typically want simple answers to complicated ones. Social scientists avoid casting things in black and white, whereas legal professionals are often forced to do so.

The question at hand is whether developmental scientists can provide meaningful guidance that can help legal

Editor's note. June P. Tangney served as the action editor for this article.

Authors' note. Laurence Steinberg, Department of Psychology, Temple University; Elizabeth Cauffman, Department of Psychology and Social Behavior, University of California, Irvine; Jennifer Woolard, Department of Psychology, Georgetown University; Sandra Graham, Psychological Studies in Education, University of California, Los Angeles; Marie Banich, Departments of Psychology and Psychiatry, University of Colorado.

Correspondence concerning this article should be addressed to Laurence Steinberg, Department of Psychology, Temple University, Philadelphia, PA 19122. E-mail: lds@temple.edu

 0003-066X/09/$12.00
Vol. 64, No. 7, 601–604 DOI: 10.1037/a0017246

Selected Bibliography

Collins, W. A., Maccoby, E., Steinberg, L., Hetherington, E. M., & Bornstein, M. (2000). Contemporary research on parenting: The case for nature and nurture. *American Psychologist, 55,* 218–232.

Darling, N., & Steinberg, L. (1993). Parenting style as context: An integrative model. *Psychological Bulletin, 113,* 487–496.

Greenberger, E., & Steinberg, L. (1986). *When teenagers work: The psychological and social costs of adolescent employment.* New York: Basic Books.

Scott, E., & Steinberg, L. (2008). *Rethinking juvenile justice.* Cambridge, MA: Harvard University Press.

Steinberg, L. (1988). Reciprocal relation between parent–child distance and pubertal maturation. *Developmental Psychology, 24,* 122–128.

Steinberg, L. (2001). We know some things: Adolescent–parent relationships in retrospect and prospect. *Journal of Research on Adolescence, 11,* 1–20.

Steinberg, L. (2004). *The 10 basic principles of good parenting.* New York: Simon & Schuster.

Steinberg, L. (2008). *Adolescence* (8th ed.). New York: McGraw-Hill.

Steinberg, L. (2008). A social neuroscience perspective on adolescent risk-taking. *Developmental Review, 28,* 78–106.

Steinberg, L., & Cauffman, E. (1996). Maturity of judgment in adolescence: Psychosocial factors in adolescent decision making. *Law and Human Behavior, 20,* 249–272.

Steinberg, L., Cauffman, E., Woolard, J., Graham, S., & Banich, M. (2009). Are adolescents less mature than adults? Minors' access to abortion, the juvenile death penalty, and the alleged APA "flip-flop." *American Psychologist, 64,* 583–594.

Steinberg, L., Dahl, R., Keating, D., Kupfer, D., Masten, A., & Pine, D. (2006). Psychopathology in adolescence: Integrating affective neuroscience with the study of context. In D. Cicchetti & D. Cohen (Eds.), *Developmental psychopathology: Vol. 2. Developmental neuroscience* (pp. 710–741). New York: Wiley.

Steinberg, L., Dornbusch, S., & Brown, B. (1992). Ethnic differences in adolescent achievement: An ecological perspective. *American Psychologist, 47,* 723–729.

Steinberg, L., Dornbusch, S., & Brown, B. (1996). *Beyond the classroom.* New York: Simon & Schuster.

Steinberg, L., Elmen, J., & Mounts, N. (1989). Authoritative parenting, psychosocial maturity, and academic success among adolescents. *Child Development, 60,* 1424–1436.

Steinberg, L., Lamborn, S., Dornbusch, S., & Darling, N. (1992). Impact of parenting practices on adolescent achievement: Authoritative parenting, school involvement, and encouragement to succeed. *Child Development, 63,* 1266–1281.

Steinberg, L., & Levine A. (1997). *You and your adolescent: A parent's guide for ages 10–20.* New York: Harper-Perennial/HarperCollins.

Steinberg, L., & Scott, E. (2003). Less guilty by reason of adolescence: Developmental immaturity, diminished responsibility, and the juvenile death penalty. *American Psychologist, 58,* 1009–1018.

Steinberg, L., & Silverberg, S. (1986). The vicissitudes of autonomy in early adolescence. *Child Development, 57,* 841–851.

Steinberg, L., & Steinberg, W. (1994). *Crossing paths: How your child's adolescence triggers your own crisis.* New York: Simon & Schuster.

Should the Science of Adolescent Brain Development Inform Public Policy?

Laurence Steinberg
Temple University

One factor that has contributed to confusion in discussions of the use of adolescent neuroscience in the development of public policies affecting young people is a blurring of

Editor's Note
Laurence Steinberg received the Award for Distinguished Contributions to Research in Public Policy. Award winners are invited to deliver an award address at the APA's annual convention. A version of this award address was delivered at the 117th annual meeting, held August 6–9, 2009, in Toronto, Ontario, Canada. Articles based on award addresses are reviewed, but they differ from unsolicited articles in that they are expressions of the winners' reflections on their work and their views of the field.

three very different issues that need to be separated: (a) what science does and does not say about brain development in adolescence; (b) what neuroscience does and does not imply for the understanding of adolescent behavior; and (c) what these implications suggest for public policy. In this article, the author argues that a good deal is known about adolescent brain development, that this knowledge has in fact been useful in shaping our understanding of adolescent behavior, and that neuroscience, like behavioral science, can usefully inform policy discussions. He cautions, however, that nonexperts may be unduly swayed by neuroscience evidence and thus that such evidence should be presented with special care.

Keywords: adolescence, neuroscience, public policy

The oddest question I have ever been asked during the 35 years that I have been studying adolescent development is this: "Do you believe that someone would need to be capable of formal operational thinking in order to build an IED?" For readers unfamiliar with the study of adolescent development, formal operational thinking is, according to Piaget's theory, the highest level of cognitive development, which is not attained until early adolescence, and even then, not consistently displayed by everyone (Kuhn, 2009). And for those who might not immediately recognize the acronym, an IED is an improvised explosive device, a homemade bomb often planted along a roadside in an effort to attack an enemy.

This unusual question was posed to me during a pretrial investigation held at Guantánamo Bay, where I was serving as an expert witness in a case involving a detainee who had been accused of building and setting IEDs in eastern Afghanistan, as an assistant to al-Qaeda and Taliban operatives, and throwing a hand grenade that killed an American soldier. Omar Khadr, the detainee, was 15 at the time he was captured by American soldiers (Glaberson, 2007). Khadr's defense team, which had retained me, was planning to argue in court that a 15-year-old, by virtue of his developmental immaturity, warranted special consideration under the law, consideration that Khadr had not been afforded by the interrogators who questioned him after his capture and that he would not likely be afforded by those prosecuting him for his alleged actions.

My purpose in this article is to examine the relation between developmental science, and neuroscience in particular, and public policy involving adolescents. I begin with the Khadr case to illustrate just how far-reaching the application of developmental science has become. For if one can find developmental science in as unlikely a place as Guantánamo Bay, one can probably find it just about everywhere.

Discussions of adolescent brain research in the popular media and in debates about public policy are frequently hyperbolic and misinformed. Many who advocate on behalf of young people take issue with those who suggest that new knowledge about brain development should influence our view of adolescence. While it is undoubtedly true that the neuroscience evidence has sometimes been embraced too uncritically, explained too glibly, or extended too broadly, it is also true that the very same evidence frequently has been dismissed too readily, described as less conclusive than it actually is, and banished from the discussion prematurely, almost on principle. As I argue, we know a good deal about brain development during adolescence that usefully informs policy discussions, even if the image of young people that sometimes emerges from developmental neuroscience clashes with the "strength-based" vision of youth promoted by youth advocates and adherents of the Positive Youth Development movement, an ideological partiality that has dominated youth policy discussions for the past two decades (e.g., Damon, 2004).

One factor that has contributed to the hyperbole noted above is a blurring of three very different issues that really need to be kept distinct: (a) what science does and does not say about brain development in adolescence; (b) what neuroscience does and does not imply for the understanding of adolescent behavior; and (c) what these implications do or do not suggest for public policy. In this article, I explore each of these questions.

The article is divided into four parts. I begin with a discussion of the Omar Khadr case, illustrating how and in what ways developmental science might inform how this Guantánamo Bay detainee should be treated. Next, I discuss the current state of knowledge about adolescent brain development. In the third section, I examine whether and in what ways this knowledge contributes to an understanding of adolescent behavior and development. I conclude by asking how brain and behavioral evidence should, and should not, inform policy discussions.

The U.S. Versus Omar Khadr

The person questioning me at Guantánamo Bay about formal operations and IEDs was Marine Major Jeff Groharing, the attorney prosecuting the case against Khadr for the U.S. government. Major Groharing was looking for evidence that Khadr, by virtue of his bomb-building ability, demonstrated adult-like cognitive maturity, which argued in favor of treating him as an adult and viewing his responses during the interrogation as no different from those an adult would have provided. He was hoping I would say that in order to do what he did, Khadr would have had to be functioning at an adult level of logical ability.

As far as I know, Piaget never created any tasks designed to test the hypothesis that abstract reasoning was required for bomb-making, so my answer to the prosecu-

Journal of Medicine and Philosophy, 38: 256–267, 2013
doi:10.1093/jmp/jht017
Advance Access publication April 21, 2013

Does Recent Research on Adolescent Brain Development Inform the Mature Minor Doctrine?

LAURENCE STEINBERG*
Temple University, Philadelphia, USA

*Address correspondence to: Laurence Steinberg, PhD, Department of Psychology, Temple University, Weiss Hall, 1701 North 13th Street, Philadelphia, PA 19122-6085, USA.
E-mail: lds@temple.edu

US Supreme Court rulings concerning sanctions for juvenile offenders have drawn on the science of brain development and concluded that adolescents are inherently less mature than adults in ways that render them less culpable. This conclusion departs from arguments made in cases involving the mature minor doctrine, in which teenagers have been portrayed as comparable to adults in their capacity to make medical decisions. I attempt to reconcile these apparently incompatible views of adolescents' decision-making competence. Adolescents are indeed less mature than adults when making decisions under conditions that are characterized by emotional arousal and peer pressure, but adolescents aged 15 and older are just as mature as adults when emotional arousal is minimized and when they are not under the influence of peers, conditions that typically characterize medical decision-making. The mature minor doctrine, as applied to individuals 15 and older, is thus consistent with recent research on adolescent development.

Keywords: *adolescence, decision-making, maturity, Supreme Court*

In its landmark 2005 decision abolishing the juvenile death penalty, *Roper v. Simmons*, the US Supreme Court held that the inherent immaturity of adolescents relative to adults mitigated teenagers' criminal responsibility to the extent that it barred the imposition of capital punishment for crimes committed under the age of 18, regardless of their heinousness.[1] Five years later, in *Graham v. Florida*, the Court applied much of the logic behind its ruling in *Roper* and banned the sentence of life without parole for juveniles convicted of nonhomicides.[2]

Cerebral Cortex March 2010;20:534–548
doi:10.1093/cercor/bhp118
Advance Access publication June 11, 2009

48

Brain Maturation in Adolescence and Young Adulthood: Regional Age-Related Changes in Cortical Thickness and White Matter Volume and Microstructure

Christian K. Tamnes[1], Ylva Østby[1], Anders M. Fjell[1,2], Lars T. Westlye[1], Paulina Due-Tønnessen[3] and Kristine B. Walhovd[1,2]

[1]Center for the Study of Human Cognition, Department of Psychology, University of Oslo, 0317 Oslo, Norway, [2]Department of Neuropsychology, Ullevaal University Hospital, 0407 Oslo, Norway and [3]Department of Radiology, Rikshospitalet University Hospital, 0027 Oslo, Norway

The development of cortical gray matter, white matter (WM) volume, and WM microstructure in adolescence is beginning to be fairly well characterized by structural magnetic resonance imaging (sMRI) and diffusion tensor imaging (DTI) studies. However, these aspects of brain development have rarely been investigated concurrently in the same sample and hence the relations between them are not understood. We delineated the age-related changes in cortical thickness, regional WM volume, and diffusion characteristics and investigated the relationships between these properties of brain development. One hundred and sixty-eight healthy participants aged 8–30 years underwent sMRI and DTI. The results showed regional age-related cortical thinning, WM volume increases, and changes in diffusion parameters. Cortical thickness was the most strongly age-related parameter. All classes of measures showed unique associations with age. The results indicate that cortical thinning in adolescence cannot be explained by WM maturation in underlying regions as measured by volumetry or DTI. Moderate associations between cortical thickness and both volume and diffusion parameters in underlying WM regions were also found, although the relationships were not strong. It is concluded that none of the measures are redundant and that the integration of the 3 will yield a more complete understanding of brain maturation.

Keywords: cerebral cortex, cortical thinning, development, diffusion, MRI

Introduction

Total brain volume increases throughout the first years of life and then stays relatively stable. By the age of 6 years, the total size of the brain is approximately 90% of its adult size (Reiss et al. 1996; Giedd 2004). Regional maturational changes in the brain do continue throughout adolescence and into adulthood. Gray matter (GM) volume reductions appear counterweighted by white matter (WM) increases to produce a relatively stable total volume (Rivkin 2000). Although a complex interplay between cortical and WM development is assumed, it has rarely been investigated in a detailed manner, and very little is known about this relationship. The adolescent phase of cortical thinning may reflect pruning in the form of use-dependent selective synapse elimination (Bourgeois and Rakic 1993; Huttenlocher and Dabholkar 1997; Shaw et al. 2008). This could play a key role in shaping neural circuits and thus be a biological basis for ongoing development of cognitive abilities and behavior (Hensch 2004; Knudsen 2004). Alternatively, events occurring at the interface between cortical GM and WM might at least partly explain the apparent cortical thinning during adolescence. Proliferation of myelin into the periphery of the cortical neuropil is one possible such biological event (Yakovlev and Lecours 1967; Sowell et al. 2004; Shaw et al. 2008). This could change the MR signal in such a way that tissue in the lower cortical layers classified as GM in younger subjects would be classified as WM in older subjects. In this cross-sectional study, we report regional age-related differences in cortical thickness, WM volume, and WM diffusion parameters in a large sample of adolescents and young adults. The principal objectives of the present study were to map cortical and WM development in the same group of subjects and to investigate the relationships between cortical thickness and properties of the underlying WM in the developing brain. To reach this aim, we have used a novel approach to compare cortical thickness and WM properties in anatomically adjacent areas, minimizing inaccuracies and measurement biases due to intermodal and intersubject registration (Fjell et al. 2008).

Cortical thickness and volume have been shown to follow an inverted U-shaped developmental course with a period of initial childhood increase and a subsequent adolescent decline (Jernigan et al. 1991; Pfefferbaum et al. 1994; Reiss et al. 1996; Giedd et al. 1999; Courchesne et al. 2000; Kennedy et al. 2002; Giedd 2004; Gogtay et al. 2004; Shaw et al. 2008). The adolescent decline in thickness and volume is presumably followed by a period with slower decline and the more stable cortical dimensions of adulthood (Sowell et al. 2003; Shaw et al. 2008. Studies have also shown regional-specific patterns of cortical maturation, with different areas developing at different rates and at different times (Giedd et al. 1999; Giedd 2004; Gogtay et al. 2004; Shaw et al. 2008; Sowell et al. 2004). Cortical regions with simple laminar architecture, 3-layered allocortex, tend to show simpler developmental trajectories (linear), whereas regions with complex architecture, 6-layered isocortex, typically have more complex trajectories (cubic). Transition cortex tends to have relatively simple developmental trajectories (mix of linear and quadratic) (Shaw et al. 2008). Within isocortex, peak cortical thickness is generally attained in the primary sensory and motor areas before adjacent secondary areas and association areas. In general, maturation progresses in a posterior-to-anterior and peripheral-to-central fashion (Shaw et al. 2008).

In contrast to the mostly nonlinear and regionally specific development of the cerebral cortex, WM volume has been shown to increase in a generally linear manner throughout late childhood and adolescence, with only minor slope differences in the different lobes (Giedd et al. 1999; Paus et al. 2001; Sowell et al. 2002; Giedd 2004; Lebel et al. 2008;). This volume increase seems to peak in the fourth or fifth decade of life and then steadily declines (Bartzokis et al. 2001; Sowell et al. 2003; Walhovd et al. 2005). WM consists largely of myelinated

49

Behavioral/Systems/Cognitive

Becoming Consistent: Developmental Reductions in Intraindividual Variability in Reaction Time Are Related to White Matter Integrity

Christian K. Tamnes, Anders M. Fjell, Lars T. Westlye, Ylva Østby, and Kristine B. Walhovd
Center for the Study of Human Cognition, Department of Psychology, University of Oslo, 0317 Oslo, Norway

Cognitive development is known to involve improvements in accuracy, capacity, and processing speed. Less is known about the role of performance consistency, and there has been virtually no empirical examination of the neural underpinnings of within-person variability in development. In a sample of 92 healthy children and adolescents aged 8–19 years, we aimed to characterize age-related changes in trial-to-trial intraindividual variability (IIV) of reaction time (RT) and to test whether IIV is related to white matter (WM) integrity as indexed by diffusion tensor imaging. IIV was quantified as the SD of correct RTs in a speeded arrow flanker task, and Tract-Based Spatial Statistics was used to test relationships with diffusion characteristics. Large age-related reductions in IIV in both simple congruent trials and more complex incongruent trials were found. Independently of sex, age, and median RT (mRT), lower IIV was associated with higher fractional anisotropy and lower overall diffusivity. Effects were seen for IIV in one or both trial types in the corticospinal tract, the left superior longitudinal fasciculus, the uncinate fasciculus, the forceps minor, and in the genu and splenium of the corpus callosum. There were no significant associations between mRT and any of the diffusion indices. The findings support the proposition that developmental reductions in IIV reflect maturation of WM connectivity and highlight the importance of considering within-person variability in theories of cognitive development and its neurobiological foundation.

Introduction

Investigations of the neural mechanisms underlying behavioral change are fundamental to the understanding of cognitive development in childhood and adolescence. Cognitive development is typically described in terms of improvements in accuracy, capacity, or processing speed and is operationalized as mean level of performance across multiple measurements (e.g., Waber et al., 2007). Less is known about the role of within-person variability in development. Within persons, variability has been operationalized in two ways: across tasks, referred to as intraindividual differences or dispersion, and across trials or sessions of the same task, referred to as intraindividual variability (IIV) or inconsistency (Hultsch et al., 2002; Li et al., 2004a; MacDonald et al., 2009).

The preponderance of data on within-person variability concerns IIV of reaction time (RT) in older adults, with studies showing age-related increases in performance variability and concomitant impairments in various cognitive functions (Lindenberger and von Oertzen, 2006; MacDonald et al., 2009). IIV across the life span is characterized by a U-shaped function, such that childhood and senescence are associated with stronger inconsistency (Li et al., 2009, 2004b; Williams et al., 2005, 2007). Whereas differences in processing speed have been theorized to underlie many of the cognitive differences between children and adults (Fry and Hale, 1996), studies focused on developmental IIV changes are lacking.

A growing number of studies link IIV to structural brain characteristics in adults, and a key role of white matter (WM) alterations in increased IIV in aging is suggested (Anstey et al., 2007; Bunce et al., 2007; Walhovd and Fjell, 2007; Ullen et al., 2008). Importantly, two recent diffusion tensor imaging (DTI) studies (Fjell et al., 2011; Moy et al., 2011) found relationships between performance variability and the quality of WM and that the strength of these associations increased in older adults. DTI is a neuroimaging technique that is sensitive to the self-diffusion of water molecules and provides quantitative measures of WM microstructural integrity and connectivity (Basser and Jones, 2002; Beaulieu, 2002; Le Bihan, 2003). Various indices can be derived from the estimated diffusion tensor, including fractional anisotropy (FA), which indexes degree of net directionality in diffusion, and mean diffusivity (MD), reflecting average magnitude of diffusion. Additionally, diffusion along [axial diffusivity (AD)] and across [radial diffusivity (RD)] the main axis of the diffusion tensor can be estimated. Developmental changes in diffusion indices have consistently been reported in the form of FA increases and overall diffusivity decrease, with prolonged maturation of association tracts compared with projection and commissural tracts (Tamnes et al., 2010a; Westlye et al., 2010; Lebel and Beau-

Received Sept. 19, 2011; revised Nov. 16, 2011; accepted Nov. 29, 2011.

Author contributions: C.K.T., A.M.F., and K.B.W. designed research; C.K.T. and Y. Ø. performed research; C.K.T., A.M.F., and L.T.W. analyzed data; C.K.T., A.M.F., L.T.W., Y. Ø., and K.B.W. wrote the paper.

This work was supported by grants from the Norwegian Research Council (177404/W50, 186092/V50 to K.B.W., and 204966 to L.T.W.), the University of Oslo (K.B.W.), and the Department of Psychology, University of Oslo (A.M.F. and C.K.T.).

The authors declare no competing financial interests.

Correspondence should be addressed to Christian K. Tamnes, Department of Psychology, University of Oslo, P.O. Box 1094 Blindern, 0317 Oslo, Norway. E-mail: c.k.tamnes@psykologi.uio.no.

DOI:10.1523/JNEUROSCI.4779-11.2012

 0270-6474/12/320972-11$15.00/0

Development/Plasticity/Repair

Development of the Cerebral Cortex across Adolescence: A Multisample Study of Inter-Related Longitudinal Changes in Cortical Volume, Surface Area, and Thickness

Christian K. Tamnes,[1] Megan M. Herting,[2] Anne-Lise Goddings,[3] Rosa Meuwese,[5,6] Sarah-Jayne Blakemore,[4] Ronald E. Dahl,[7] Berna Güroğlu,[5,6] Armin Raznahan,[8] Elizabeth R. Sowell,[9] Eveline A. Crone,[5,6] and Kathryn L. Mills[10]

[1]Department of Psychology, University of Oslo, 0317 Oslo, Norway, [2]Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California 90032, [3]Institute of Child Health and [4]Institute of Cognitive Neuroscience, University College London, London WC1N 1EH United Kingdom, [5]Brain and Development Research Center, Institute of Psychology, and [6]Leiden Institute for Brain and Cognition, Leiden University, 2300 RA Leiden, The Netherlands, [7]Institute of Human Development, University of California Berkeley, Berkeley, California 94720, [8]Child Psychiatry Branch, National Institute of Mental Health, Bethesda, Maryland 20814, [9]Children's Hospital of Los Angeles, Los Angeles, California 90027, and [10]Department of Psychology, University of Oregon, Eugene, Oregon 97403

Before we can assess and interpret how developmental changes in human brain structure relate to cognition, affect, and motivation, and how these processes are perturbed in clinical or at-risk populations, we must first precisely understand typical brain development and how changes in different structural components relate to each other. We conducted a multisample magnetic resonance imaging study to investigate the development of cortical volume, surface area, and thickness, as well as their inter-relationships, from late childhood to early adulthood (7–29 years) using four separate longitudinal samples including 388 participants and 854 total scans. These independent datasets were processed and quality-controlled using the same methods, but analyzed separately to study the replicability of the results across sample and image-acquisition characteristics. The results consistently showed widespread and regionally variable nonlinear decreases in cortical volume and thickness and comparably smaller steady decreases in surface area. Further, the dominant contributor to cortical volume reductions during adolescence was thinning. Finally, complex regional and topological patterns of associations between changes in surface area and thickness were observed. Positive relationships were seen in sulcal regions in prefrontal and temporal cortices, while negative relationships were seen mainly in gyral regions in more posterior cortices. Collectively, these results help resolve previous inconsistencies regarding the structural development of the cerebral cortex from childhood to adulthood, and provide novel insight into how changes in the different dimensions of the cortex in this period of life are inter-related.

Key words: brain development; gray matter; morphometry; MRI; replication

Significance Statement

Different measures of brain anatomy develop differently across adolescence. Their precise trajectories and how they relate to each other throughout development are important to know if we are to fully understand both typical development and disorders involving aberrant brain development. However, our understanding of such trajectories and relationships is still incomplete. To provide accurate characterizations of how different measures of cortical structure develop, we performed an MRI investigation across four independent datasets. The most profound anatomical change in the cortex during adolescence was thinning, with the largest decreases observed in the parietal lobe. There were complex regional patterns of associations between changes in surface area and thickness, with positive relationships seen in sulcal regions in prefrontal and temporal cortices, and negative relationships seen mainly in gyral regions in more posterior cortices.

51

Neurobiological Consequences of Early Stress and Childhood Maltreatment: Are Results from Human and Animal Studies Comparable?

MARTIN H. TEICHER, AKEMI TOMODA, AND SUSAN L. ANDERSEN

Department of Psychiatry, Harvard Medical School and Developmental Biopsychiatry Research Program, McLean Hospital, Belmont, Massachusetts 02478, USA

ABSTRACT: **Recent studies have reported an association between exposure to childhood abuse or neglect and alterations in brain structure or function. One limitation of these studies is that they are correlational and do not provide evidence of a cause–effect relationship. Preclinical studies on the effects of exposure to early life stress can demonstrate causality, and can enrich our understanding of the clinical research if we hypothesize that the consequences of early abuse are predominantly mediated through the induction of stress responses. Exposure to early abuse and early stress has each been associated with the emergence of epileptiform electroencephalogram (EEG) abnormalities, alterations in corpous callosum area, and reduced volume or synaptic density of the hippocampus. Further, there is evidence that different brain regions have unique periods when they are maximally sensitive to the effects of early stress. To date, preclinical studies have guided clinical investigations and will continue to provide important insight into studies on molecular mechanisms and gene–environment interactions.**

KEYWORDS: **adolescence; maltreatment; hippocampus; corpus callosum; translational research; sensitive periods; stress; abuse or neglect**

INTRODUCTION

Childhood exposure to traumatic stress, in the form of abuse or neglect, is common throughout the world and is a major risk factor for later psychopathology.[1] Recent reports have shown that childhood abuse or neglect is

Address for correspondence: Martin H. Teicher, Developmental Biopsychiatry Research Program, McLean Hospital, 115 Mill Street Belmont, MA 02478. Voice: 617-855-2971; fax: 617-855-3712.
e-mail: martin_teicher@hms.harvard.edu

**Ann. N.Y. Acad. Sci. 1071: 313–323 (2006). © 2006 New York Academy of Sciences.
doi: 10.1196/annals.1364.024**

Mechanisms of Psychiatric Illness

Childhood Maltreatment and Psychopathology: A Case for Ecophenotypic Variants as Clinically and Neurobiologically Distinct Subtypes

Martin H. Teicher, M.D., Ph.D.

Jacqueline A. Samson, Ph.D.

Objective: Childhood maltreatment increases risk for psychopathology. For some highly prevalent disorders (major depression, substance abuse, anxiety disorders, and posttraumatic stress disorder) a substantial subset of individuals have a history of maltreatment and a substantial subset do not. The authors examined the evidence to assess whether those with a history of maltreatment represent a clinically and biologically distinct subtype.

Method: The authors reviewed the literature on maltreatment as a risk factor for these disorders and on the clinical differences between individuals with and without a history of maltreatment who share the same diagnoses. Neurobiological findings in maltreated individuals were reviewed and compared with findings reported for these disorders.

Results: Maltreated individuals with depressive, anxiety, and substance use disorders have an earlier age at onset, greater symptom severity, more comorbidity, a greater risk for suicide, and poorer treatment response than nonmaltreated individuals with the same diagnoses. Imaging findings associated with these disorders, such as reduced hippocampal volume and amygdala hyperreactivity, are more consistently observed in maltreated individuals and may represent a maltreatment-related risk factor. Maltreated individuals also differ from others as a result of epigenetic modifications and genetic polymorphisms that interact with experience to increase risk for psychopathology.

Conclusions: Phenotypic expression of psychopathology may be strongly influenced by exposure to maltreatment, leading to a constellation of ecophenotypes. While these ecophenotypes fit within conventional diagnostic boundaries, they likely represent distinct subtypes. Recognition of this distinction may be essential in determining the biological bases of these disorders. Treatment guidelines and algorithms may be enhanced if maltreated and nonmaltreated individuals with the same diagnostic labels are differentiated.

(Am J Psychiatry 2013; 170:1114–1133)

Maltreated children are more likely to suffer psychiatric disorders over the course of their lifetime. In particular, they are more likely to develop major depression (1–5), bipolar disorder (6), anxiety disorders (2, 3, 7), posttraumatic stress disorder (PTSD) (2, 3), substance abuse (2, 8, 9), personality disorders (10, 11), and psychoses (12). Furthermore, it appears that survivors of early maltreatment differ in critical ways from other individuals with the same psychiatric diagnoses. Disorders emerge earlier in maltreated individuals, with greater severity, more comorbidity, and a less favorable response to treatment (13–15). Maltreated individuals may also have discernible brain abnormalities that are not present in their nonmaltreated counterparts (16, 17). Childhood maltreatment is also linked to a wide array of medical disorders, shortened life expectancy, and reduced telomere length (18, 19). Hence, an understanding of maltreatment as an etiological risk factor is crucial to the development of a science of preventive psychiatry, to the design of effective therapeutic regimens, and to the delineation of an accurate nosology.

Our goal in this review is to advance the thesis (17, 20–23) that affected individuals with childhood maltreatment constitute a critically distinct subtype across depressive, anxiety, and substance use disorders. We also propose that the maltreated subtype may be thought of as a phenotypic specialization (phenocopy) resulting from environmental experience—or more precisely, an ecophenotype.

Why focus on maltreatment? It is maltreatment rather than exposure to other stressors, such as natural disasters, that consistently presents as the antecedent to psychopathology (24, 25). This makes sense. Children are dependent on the adults around them for their survival, and they can endure great hardship if they feel protected and cared for. But when the hardship is the product of their caretakers, and when it is the caretaker who must be protected against, it creates a stressor with far-reaching ramifications.

JOURNAL of CHILD PSYCHOLOGY and PSYCHIATRY
THE ASSOCIATION FOR CHILD AND ADOLESCENT MENTAL HEALTH
Journal of Child Psychology and Psychiatry 57:3 (2016), pp 241–266 doi:10.1111/jcpp.12507

53

Annual Research Review: Enduring neurobiological effects of childhood abuse and neglect

Martin H. Teicher[1,2] and Jacqueline A. Samson[1,2]
[1]Department of Psychiatry, Harvard Medical School, Boston, MA; [2]Developmental Biopsychiatry Research Program, McLean Hospital, Belmont, MA, USA

Background: Childhood maltreatment is the most important preventable cause of psychopathology accounting for about 45% of the population attributable risk for childhood onset psychiatric disorders. A key breakthrough has been the discovery that maltreatment alters trajectories of brain development. **Methods:** This review aims to synthesize neuroimaging findings in children who experienced caregiver neglect as well as from studies in children, adolescents and adults who experienced physical, sexual and emotional abuse. In doing so, we provide preliminary answers to questions regarding the importance of type and timing of exposure, gender differences, reversibility and the relationship between brain changes and psychopathology. We also discuss whether these changes represent adaptive modifications or stress-induced damage. **Results:** Parental verbal abuse, witnessing domestic violence and sexual abuse appear to specifically target brain regions (auditory, visual and somatosensory cortex) and pathways that process and convey the aversive experience. Maltreatment is associated with reliable morphological alterations in anterior cingulate, dorsal lateral prefrontal and orbitofrontal cortex, corpus callosum and adult hippocampus, and with enhanced amygdala response to emotional faces and diminished striatal response to anticipated rewards. Evidence is emerging that these regions and interconnecting pathways have sensitive exposure periods when they are most vulnerable. **Conclusions:** Early deprivation and later abuse may have opposite effects on amygdala volume. Structural and functional abnormalities initially attributed to psychiatric illness may be a more direct consequence of abuse. Childhood maltreatment exerts a prepotent influence on brain development and has been an unrecognized confound in almost all psychiatric neuroimaging studies. These brain changes may be best understood as adaptive responses to facilitate survival and reproduction in the face of adversity. Their relationship to psychopathology is complex as they are discernible in both susceptible and resilient individuals with maltreatment histories. Mechanisms fostering resilience will need to be a primary focus of future studies. **Keywords:** Child abuse; neglect; neuroimaging; resilience; stress.

Introduction

The deleterious effects of childhood maltreatment and early deprivation are widely reported and acknowledged. Both retrospective and prospective studies document associations between exposure to early maltreatment and poorer psychological and physical functioning in adulthood. Survivors of childhood maltreatment show higher prevalence of depression, anxiety, substance abuse, eating disorders, suicidal symptomatology, psychosis and personality disorder [see (Ball & Links, 2009; Bendall, Jackson, Hulbert, & McGorry, 2008; Norman et al., 2012; Teicher & Samson, 2013) for recent reviews] as well as diminished cognitive functioning (de Bellis, Hooper, Spratt, & Woolley, 2009; Gould et al., 2012) and poorer treatment response (Nanni, Uher, & Danese, 2012; Teicher & Samson, 2013). Green et al. (2010) estimated that maltreatment accounted for 45% of the population attributable risk for childhood onset psychiatric disorders. In addition, survivors of childhood maltreatment show higher adult rates of inflammation (Danese, Pariante, Caspi, Taylor, & Poulton, 2007), metabolic syndrome (Danese et al., 2009), arthritis (Spitzer et al., 2013), ischaemic heart disease (Dong et al., 2004), cancer (Brown et al., 2010) and shortened telomeres (Price, Kao, Burgers, Carpenter, & Tyrka, 2013) associated with reduced life expectancy (Brown et al., 2009). The exact pathways leading to these diverse negative outcomes remain to be revealed.

In this review, we examine the rapidly expanding body of research on the potential neurobiological consequences of childhood abuse and neglect, and summarize the most salient overarching discoveries. For this purpose, we included all studies we could identify that were published in English and presented a statistical analysis on the association between maltreatment (broadly defined) and brain measures of structure, function or connectivity as assessed using magnetic resonance imaging (MRI) or positron emission tomography (PET).

At the present time, a reasonably clear picture is emerging on the relationship between maltreatment and alterations in structure and function of stress-susceptible brain regions. New studies are also revealing substantial alterations in connectivity and network architecture. What is much less clear is the link between these discernible differences and psychopathology, which may require a revision in our understanding of the neurobiological basis of psychiatric disorders and a reconceptualization of resilience. Throughout the review, we will emphasize the importance of type and timing of exposure,

Conflict of interests statement: No conflicts declared.

Variations in the Catechol O-methyltransferase Polymorphism and Prefrontally Guided Behaviors in Adolescents

Dustin Wahlstrom, Tonya White, Catalina J. Hooper, Suzanne Vrshek-Schallhorn, William S. Oetting, Marcia J. Brott, and Monica Luciana

Background: The catechol-O-methyltransferase (COMT) gene codes for an enzyme that degrades prefrontal cortex (PFC) synaptic dopamine. Of two identified alleles (Met and Val), the Met allele results in COMT activity that is up to 4 times less pronounced than that conferred by the Val allele, resulting in greater PFC dopamine concentrations. Met-Met homozygotes perform better than individuals who possess the Val allele on PFC-mediated cognitive tasks. These genotypic variations and their associations with executive functions have been described in adults and prepubescent children, but there is a paucity of research assessing these relations in adolescent samples.

Methods: In this study, 70 children aged 9–17 were genotyped for COMT and completed measures of working memory, attention, fine motor coordination, and motor speed.

Results: COMT genotype modulated all but the motor speed measures. The Val-Met genotype was optimal for performance in this adolescent sample.

Conclusions: Results are discussed within the context of developmental changes in the dopaminergic system during adolescence.

Key Words: Adolescence, cognition, dopamine, genetics, prefrontal cortex, neuropsychology

The catechol *O*-methyltransferase (COMT) enzyme degrades synaptic catecholamines in the prefrontal cortex (PFC; Napolitano et al 1995; Weinshilboum et al 1999). The COMT gene resides on the q11 region of chromosome 22 (Grossman et al 1992), where a functional missense mutation causes a single G-to-A base-pair substitution, resulting in a single nucleotide polymorphism (SNP) in exon 4. This polymorphism results in the substitution of Methionine (Met) for Valine (Val) at codons 108/158 (Lachman et al 1996). Individuals can be homozygous for the Met or Val alleles, or they can possess one of each allele. The Met allele results in a fourfold decrease in enzymatic activity relative to the Val allele, resulting in functionally significant increases in PFC catecholamine activity (Lachmann et al 1996; Lotta et al 1995). The alleles are codominant. Heterozygotes exhibit intermediate levels of enzymatic activity relative to that of Val-Val and Met-Met individuals (Weinshilboum et al 1977). The $Val^{108/158}Met$ polymorphism's modulation of catecholamine levels is intriguing, because catecholamines modulate attention and working memory. Specifically, COMT's impact on dopamine activity has been of interest to investigators due to dopamine's modulation of PFC spatial working memory functions (Luciana et al 1997; Williams et al 1995). COMT genotype may partially underlie individual differences in the development of these functions.

COMT may play a specific role in the catabolism of PFC dopamine because of the relative lack of dopamine transporters in PFC (Moron et al 2002; Sesak et al 1998). COMT knockout mice demonstrate increased PFC dopamine, but striatal levels are unchanged (Gogos et al 1998; Huotari et al 2002). Psychopharmacologic challenges in mice suggest that COMT's influence on set-shifting performance is mediated specifically by dopaminergic systems, rather than generalized changes in other catacholamines (Tunbridge et al 2004).

Consistent with this proposed specificity, studies of healthy adults and those with psychopathology have linked variations in COMT genotype to performance on prefrontally dependent tasks such as the Wisconsin Card Sorting Test (WCST; Malhotra et al 2002; Rosa et al 2004) and the *N*-Back test (Goldberg et al 2003; Mattay et al 2003). Both tasks recruit lateral PFC regions. Successful performance relies on sufficient availability of prefrontal dopamine (Abi-Dargham et al 2002; Monchi et al 2004; Volkow et al 1998). Met-Met homozygosity predicts better task performance on both measures.

Additionally, COMT directly modulates task-related prefrontal activity (Egan et al 2001; Mattay et al 2003). Mattay et al (2003) demonstrated an interaction between COMT genotype, amphetamine response, and dorsolateral prefrontal activation during completion of the *N*-back task. Val-Val individuals generated more efficient prefrontal function (i.e., smaller BOLD responses) on amphetamine versus placebo despite no trade-off in performance. Conversely, Met-Met individuals demonstrated less efficient responses and impaired performance on the most difficult condition of the task in the amphetamine condition. The investigators suggested that COMT activity affects baseline levels of prefrontal dopamine. There appears to be an inverted U-shaped dose-response curve by which both deficient and excessive amounts of dopamine activity predict poor performance on cognitive tasks (Goldman-Rakic 1998; Granon et al 2000; Williams et al 1995). According to this model, individuals homozygous for the Met allele rest near the apex of this curve under basal conditions; heterozygous (Val-Met) and homozygous Val individuals lay toward

From the Department of Psychology (DW, CJH, SV-S, ML), Center for Neurobehavioral Development (DW, TW, CJH, ML), Department of Psychiatry (TW), Department of Medicine—Genetics (WSO, MJB), and Institute of Human Genetics (WSO, MJB), University of Minnesota—Twin Cities, Minneapolis, Minnesota.

Address reprint requests to Dustin Wahlstrom, B.A., Department of Psychology, 75 East River Rd., University of Minnesota, Minneapolis, MN 55455; E-mail: wahl0028@umn.edu.

Received October 10, 2005; revised April 26, 2006; accepted May 23, 2006.

0006-3223/07/$32.00
doi:10.1016/j.biopsych.2006.05.045

Brain and Cognition 72 (2010) 146–159

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Review Article

Developmental changes in dopamine neurotransmission in adolescence: Behavioral implications and issues in assessment

Dustin Wahlstrom [a,c], Paul Collins [a,c], Tonya White [b,c], Monica Luciana [a,c,*]

[a] Department of Psychology, University of Minnesota, Minneapolis MN, USA
[b] Department of Psychiatry, University of Minnesota, Minneapolis MN, USA
[c] Center for Neurobehavioral Development, University of Minnesota, Minneapolis MN, USA

ARTICLE INFO

Article history:
Accepted 22 October 2009
Available online 26 November 2009

Keywords:
Dopamine
Adolescence
Development
Prefrontal cortex

ABSTRACT

Adolescence is characterized by increased risk-taking, novelty-seeking, and locomotor activity, all of which suggest a heightened appetitive drive. The neurotransmitter dopamine is typically associated with behavioral activation and heightened forms of appetitive behavior in mammalian species, and this pattern of activation has been described in terms of a neurobehavioral system that underlies incentive-motivated behavior. Adolescence may be a time of elevated activity within this system. This review provides a summary of changes within cortical and subcortical dopaminergic systems that may account for changes in cognition and affect that characterize adolescent behavior. Because there is a dearth of information regarding neurochemical changes in human adolescents, models for assessing links between neurochemical activity and behavior in human adolescents will be described using molecular genetic techniques. Furthermore, we will suggest how these techniques can be combined with other methods such as pharmacology to measure the impact of dopamine activity on behavior and how this relation changes through the lifespan.

1. Introduction

As reviewed by other papers within this issue and in the literature as a whole, adolescence is characterized by widespread neurobiological changes such as shifts in brain matter composition (see papers by Paus, Gogtay, Thompson, and Schmithorst (this issue)), modifications of neural synchrony (Uhlhaas et al., 2009), increased hormonal release (Styne, 1994), and neurochemical alterations (Doremus-Fitzwater et al., this issue; Spear, 2000). Much of this work has focused on changes in brain structure as well as attempts to define adolescent-unique patterns of functional brain activity in the context of cognitive and emotional behaviors (see papers by Luna et al. (this issue) and Somerville et al. (this issue)). This latter set of findings has identified brain regions where activation patterns are distinct in adolescents versus children and adults as they perform cognitive and emotional tasks, leading to renewed conceptualizations of brain systems that operate in a distinctive manner during this period of the lifespan (Bjork et al., 2004; Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Ernst et al., 2005; Galvan et al., 2006; Luna, Garver, Urban, Lazar, & Sweeney, 2004; May et al., 2004). Moreover, it is clear that adolescents differ from adults on behavioral measures of decision-making, planning, working memory, and inhibitory control (Asato, Sweeney, & Luna, 2006; Crone & van der Molen, 2004; Hooper, Luciana, Conklin, & Yarger, 2004; Luciana, Collins, Olson, & Schissel, 2009; Luciana, Conklin, Hooper, & Yarger, 2005; Luna et al., 2004). That said, it has been a challenge to definitively associate the changes in neuroarchitecture that have been described across adolescence with changing patterns of behavior during this period of the lifespan, particularly with respect to risk-taking and aspects of behavioral regulation. Age-related sources of variation in structure–function relations are relatively small in magnitude (Olson et al., 2009; Schmithorst et al., 2005; Shaw et al., 2006), and some structure-function relations are not easily attributable to maturational processes (Olesen, Nagy, Westerberg, & Klingberg, 2003). Given that adolescence is a period in the lifespan characterized by alarming increases in risk-taking behaviors and that these behavioral patterns are relatively impervious to educational interventions (Steinberg, 2008), it has become commonplace to assert that they have a basis in brain development. Synaptic structure is becoming refined during adolescence, and the prefrontal cortex (PFC) may be among the last regions to attain a maturational plateau. Recent formulations have emphasized that adolescent patterns of frontal–limbic integration are different from what has been observed in adults and children (Fareri, Martin, & Delgado, 2008; Galvan et al., 2006). However, none of these brain substrates definitively underlies adolescents' tendencies to select risky alternatives when faced with options that are probabilistically risky versus safe or their

* Corresponding author. Address: Department of Psychology, 75 East River Road, University of Minnesota, Minneapolis MN 55455, USA.
E-mail address: lucia003@umn.edu (M. Luciana).

0278-2626/$ - see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.bandc.2009.10.013

Neuroscience and Biobehavioral Reviews 34 (2010) 631–648

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review

Neurobehavioral evidence for changes in dopamine system activity during adolescence

Dustin Wahlstrom [a,c], Tonya White [b,c], Monica Luciana [a,c,*]

[a] Department of Psychology, University of Minnesota, Minneapolis, MN 55455, USA
[b] Department of Psychiatry, University of Minnesota, Minneapolis, MN 55455, USA
[c] Center for Neurobehavioral Development, University of Minnesota, Minneapolis, MN 55455, USA

ARTICLE INFO

Keywords:
Dopamine
COMT
Brain development
Adolescence
Working memory

ABSTRACT

Human adolescence has been characterized by increases in risk-taking, emotional lability, and deficient patterns of behavioral regulation. These behaviors have often been attributed to changes in brain structure that occur during this developmental period, notably alterations in gray and white matter that impact synaptic architecture in frontal, limbic, and striatal regions. In this review, we provide a rationale for considering that these behaviors may be due to changes in dopamine system activity, particularly overactivity, during adolescence relative to either childhood or adulthood. This rationale relies on animal data due to limitations in assessing neurochemical activity more directly in juveniles. Accordingly, we also present a strategy that incorporates molecular genetic techniques to infer the status of the underlying tone of the dopamine system across developmental groups. Implications for the understanding of adolescent behavioral development are discussed.

Contents

* Corresponding author at: Department of Psychology, 75 East River Road, University of Minnesota, Minneapolis, MN 55455, USA. Tel.: +1 612 626 0757; fax: +1 612 626 2079.
E-mail address: lucia003@umn.edu (M. Luciana).

0149-7634/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neubiorev.2009.12.007

Childhood Maltreatment and Psychopathology Affect Brain Development During Adolescence

Sarah Whittle, Ph.D., Meg Dennison, Ph.D., Nandita Vijayakumar, B.Sc., Julian G. Simmons, Ph.D., Murat Yücel, Ph.D., Dan I. Lubman, M.B.Ch.B., Ph.D., F.R.A.N.Z.C.P., Christos Pantelis, M.D., M.R.C.Psych., F.R.A.N.Z.C.P., Nicholas B. Allen, Ph.D.

Objective: The hippocampus and amygdala have received much attention with regard to the deleterious effects of childhood maltreatment. However, it is not known if and when these effects emerge during adolescence and whether comorbid psychopathology is more likely to explain these effects. This study investigated whether childhood maltreatment was associated with hippocampal and amygdala development from early to midadolescence and whether the experience of psychopathology during this period mediated the relation. **Method:** One hundred seventeen (60 male) adolescents, recruited as part of a broader adolescent development study, participated in magnetic resonance imaging assessments during early and midadolescence (mean age at baseline 12.62 years, SD 0.44 years; mean follow-up period 3.78 years, SD 0.20 years), and completed self-report measurements of childhood maltreatment and diagnostic interviews assessing *DSM-IV* mental disorders. **Results:** Childhood maltreatment was associated with larger baseline left hippocampal volumes and retarded growth of the left amygdala over time and was indirectly associated, through the experience of psychopathology, with retarded growth of the left hippocampus and accelerated growth of the left amygdala over time. Exploratory cortical analysis showed that maltreatment influenced thickening of the superior parietal region through the experience of psychopathology. **Conclusions:** Childhood maltreatment was associated with altered brain development during adolescence. The experience of Axis I psychopathology during adolescence may be one mechanism by which childhood maltreatment has continuing effects on brain development during the adolescent years. These findings highlight the importance of early intervention for individuals who have experienced childhood maltreatment. J. Am. Acad. Child Adolesc. Psychiatry, 2013; 52(9):940–952. **Key Words:** adolescence, amygdala, brain development, hippocampus, maltreatment

It is well recognized that childhood maltreatment represents an important risk factor contributing to the development of psychopathology later in life.[1,2] The high prevalence of childhood maltreatment in the general community (up to 40%)[3] highlights the importance of understanding the mechanisms that influence its relation with poor mental health outcomes. There is growing evidence to suggest that maltreatment may alter the functioning of neurobiological stress systems, and that this may be one mechanism by which maltreatment contributes to the development of psychopathology.[4,5]

Supplemental material cited in this article is available online.

The hippocampus and amygdala play critical roles in stress reactivity,[6,7] and as such these brain regions have received much attention with regard to the deleterious effects of stress, trauma, and maltreatment.[4,8] Regarding the hippocampus, studies of adult humans have consistently found decreased volumes in those with a history of childhood maltreatment (see McCrory *et al.*,[4] Tottenham and Sherdan,[8] Dannlowski *et al.*,[9] and Teicher *et al.*[10]). Interestingly, similar studies of children and adolescents who have experienced maltreatment have produced mixed results, with some studies finding smaller volume (e.g., Edmiston *et al.*[11]) and many studies reporting no effects on hippocampal volume[12,13] or increased volume.[14] This discrepancy between studies of adults versus children and adolescents suggests that the

Developmental Cognitive Neuroscience 8 (2014) 7–17

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn

Positive parenting predicts the development of adolescent brain structure: A longitudinal study☆

Sarah Whittle[a,b], Julian G. Simmons[b,c], Meg Dennison[c], Nandita Vijayakumar[c], Orli Schwartz[c], Marie B.H. Yap[b,d], Lisa Sheeber[e], Nicholas B. Allen[b,c,*]

[a] Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne and Melbourne Health, Victoria, Australia
[b] Orygen Youth Health Research Centre, Centre for Youth Mental Health, The University of Melbourne, Victoria, Australia
[c] Melbourne School of Psychological Sciences, The University of Melbourne, Victoria, Australia
[d] Melbourne School of Population and Global Health, The University of Melbourne, Victoria, Australia
[e] Oregon Research Institute, Eugene, OR, USA

ARTICLE INFO

Article history:
Received 18 April 2013
Received in revised form 14 October 2013
Accepted 27 October 2013

Keywords:
Adolescence
Brain development
Environment
Parenting
Resilience
Positive

ABSTRACT

Little work has been conducted that examines the effects of positive environmental experiences on brain development to date. The aim of this study was to prospectively investigate the effects of positive (warm and supportive) maternal behavior on structural brain development during adolescence, using longitudinal structural MRI. Participants were 188 (92 female) adolescents, who were part of a longitudinal adolescent development study that involved mother–adolescent interactions and MRI scans at approximately 12 years old, and follow-up MRI scans approximately 4 years later. FreeSurfer software was used to estimate the volume of limbic-striatal regions (amygdala, hippocampus, caudate, putamen, pallidum, and nucleus accumbens) and the thickness of prefrontal regions (anterior cingulate and orbitofrontal cortices) across both time points. Higher frequency of positive maternal behavior during the interactions predicted attenuated volumetric growth in the right amygdala, and accelerated cortical thinning in the right anterior cingulate (males only) and left and right orbitofrontal cortices, between baseline and follow up. These results have implications for understanding the biological mediators of risk and protective factors for mental disorders that have onset during adolescence.

1. Introduction

Adverse childhood environments represent an important risk factor for the development of psychopathology later in life (Heim and Nemeroff, 2001; Moran et al., 2004), and there is accumulating evidence that neurobiological changes (particularly with regard to brain structure) may mediate this relationship (Tupler and De Bellis, 2006). Indeed, there has been a recent surge of interest in the effects of adverse childhood environments on structural brain development, with a number of recent reviews highlighting the deleterious effects of adverse early environments on brain structure (Andersen and Teicher, 2008; Hart and Rubia, 2012; Lupien et al., 2009; McCrory et al., 2010).

Although a focus on the effects of adverse childhood environments on structural brain development is important and has implications for the development of targeted interventions for at-risk individuals, the influence of *positive* childhood environments on brain development is equally important to consider, given their importance

* Corresponding author at: Melbourne School of Psychological Sciences, The University of Melbourne, Victoria 3010, Australia.
Tel.: +61 03 8344 6325.
E-mail address: nba@unimelb.edu.au (N.B. Allen).

1878-9293/$ – see front matter © 2013 The Authors. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.dcn.2013.10.006

59

JAMA Psychiatry | Original Investigation

Role of Positive Parenting in the Association Between Neighborhood Social Disadvantage and Brain Development Across Adolescence

Sarah Whittle, PhD; Nandita Vijayakumar, PhD; Julian G. Simmons, PhD; Meg Dennison, PhD; Orli Schwartz, PhD; Christos Pantelis, MD, Hon MD, FRANZCP; Lisa Sheeber, PhD; Michelle L. Byrne, PhD; Nicholas B. Allen, PhD

Supplemental content

IMPORTANCE The negative effects of socioeconomic disadvantage on lifelong functioning are pronounced, with some evidence suggesting that these effects are mediated by changes in brain development. To our knowledge, no research has investigated whether parenting might buffer these negative effects.

OBJECTIVE To establish whether positive parenting behaviors moderate the effects of socioeconomic disadvantage on brain development and adaptive functioning in adolescents.

DESIGN, SETTING, AND PARTICIPANTS In this longitudinal study of adolescents from schools in Melbourne, Australia, data were collected at 3 assessments between 2004 and 2012. Data were analyzed between August 2016 and April 2017.

EXPOSURES Both family (parental income-to-needs, occupation, and education level) and neighborhood measures of socioeconomic disadvantage were assessed. Positive maternal parenting behaviors were observed during interactions in early adolescence.

MAIN OUTCOMES AND MEASURES Structural magnetic resonance imaging scans at 3 times (early, middle, and late adolescence) from ages 11 to 20 years. Global and academic functioning was assessed during late adolescence. We used linear mixed models to examine the effect of family and neighborhood socioeconomic disadvantage as well as the moderating effect of positive parenting on adolescent brain development. We used mediation models to examine whether brain developmental trajectories predicted functional outcomes during late adolescence.

RESULTS Of the included 166 adolescents, 86 (51.8%) were male. We found that neighborhood, but not family, socioeconomic disadvantage was associated with altered brain development from early (mean [SD] age, 12.79 [0.425] years) to late (mean [SD] age, 19.08 [0.460] years) adolescence, predominantly in the temporal lobes (temporal cortex: random field theory corrected; left amygdala: B, −0.237; $P < .001$; right amygdala: B, −0.209; $P = .008$). Additionally, positive parenting moderated the effects of neighborhood disadvantage on the development of dorsal frontal and lateral orbitofrontal cortices as well as the effects of family disadvantage on the development of the amygdala (occupation: B, 0.382; $P = .004$; income-to-needs: B, 27.741; $P = .004$), with some male-specific findings. The pattern of dorsal frontal cortical development in males from disadvantaged neighborhoods exposed to low maternal positivity predicted increased rates of school noncompletion (indirect effect, −0.018; SE, 0.01; 95% CI, −0.053 to −0.001).

CONCLUSIONS AND RELEVANCE Our findings highlight the importance of neighborhood disadvantage in influencing brain developmental trajectories. Further, to our knowledge, we present the first evidence that positive maternal parenting might ameliorate the negative effects of socioeconomic disadvantage on frontal lobe development (with implications for functioning) during adolescence. Results have relevance for designing interventions for children from socioeconomically disadvantaged backgrounds.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Sarah Whittle, PhD, Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne and Melbourne Health, 161 Barry St, Carlton, VIC 3053, Australia (swhittle@unimelb.edu.au).

JAMA Psychiatry. 2017;74(8):824-832. doi:10.1001/jamapsychiatry.2017.1558
Published online June 21, 2017.

Brain and Cognition 83 (2013) 315–323

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Examining the link between adolescent brain development and risk taking from a social-developmental perspective

Teena Willoughby [a,*], Marie Good [b], Paul J.C. Adachi [a,1], Chloe Hamza [a,1], Royette Tavernier [a,1]

[a] Department of Psychology, Brock University, St Catharines, Ontario, Canada
[b] Department of Psychology, University of Toronto, Toronto, Ontario, Canada

ARTICLE INFO

Article history:
Available online 13 October 2013

Keywords:
Adolescent risk taking
Brain development
Social context
Dual system
Lifespan

ABSTRACT

The adolescent age period is often characterized as a health paradox because it is a time of extensive increases in physical and mental capabilities, yet overall mortality/morbidity rates increase significantly from childhood to adolescence, often due to preventable causes such as risk taking. Asynchrony in developmental time courses between the affective/approach and cognitive control brain systems, as well as the ongoing maturation of neural connectivity are thought to lead to increased vulnerability for risk taking in adolescence. A critical analysis of the frequency of risk taking behaviors, as well as mortality and morbidity rates across the lifespan, however, challenges the hypothesis that the peak of risk taking occurs in middle adolescence when the asynchrony between the different developmental time courses of the affective/approach and cognitive control systems is the largest. In fact, the highest levels of risk taking behaviors, such as alcohol and drug use, often occur among emerging adults (e.g., university/college students), and highlight the role of the social context in predicting risk taking behavior. Moreover, risk taking is not always unregulated or impulsive. Future research should broaden the scope of risk taking to include risks that are relevant to older adults, such as risky financial investing, gambling, and marital infidelity. In addition, a lifespan perspective, with a focus on how associations between neural systems and behavior are moderated by context and trait-level characteristics, and which includes diverse samples (e.g., divorced individuals), will help to address some important limitations in the adolescent brain development and risk taking literature.

1. Introduction

The adolescent age period is often characterized as a health paradox because it is a time of extensive increases in physical and mental capabilities, yet overall mortality/morbidity rates increase significantly from childhood to adolescence (Casey & Caudle, 2013; Dahl, 2004). Moreover, the primary causes of death and disability among adolescents are not related to disease, but rather to preventable forms of injuries (e.g., unintentional injuries, suicide, and homicide), and are linked to involvement in health-risk behaviors such as substance use and delinquency (Dahl, 2004). While extensive research has been conducted examining how the social context (e.g., peer and family influence) and individual differences in personality factors (e.g., sensation-seeking, impulsivity) are linked to adolescent risk taking behaviors (e.g., Donohew et al., 2000; Romer, Betancourt, Brodsky, Giannetta, & Yang, 2011), more recently researchers have started to focus on how adolescent brain development might be implicated in these behaviors (e.g., Steinberg, 2008; Telzer, Fuligni, Lieberman, & Galván, 2013).

Models of adolescent brain development such as the Dual Systems Model (see Steinberg, 2008) suggest that adolescents may experience a temporal gap between a relatively early maturing affective/approach system and a slower maturing cognitive control system (e.g., Ernst, Pine, & Hardin, 2006; Geier & Luna, 2009). The early maturing affective/approach system is hypothesized to be a result of increases in dopaminergic activity and subcortical brain structures such as the ventral striatum, perhaps linked to puberty, leading to increases in reward seeking and need for novelty (see also the Triadic model for a further distinction between the approach/reward and avoidance/emotion systems; Ernst et al., 2006). In contrast, the slower maturing cognitive control network is hypothesized to be led by the prefrontal cortex, responsible for planning, judgment, and inhibition, and is thought to not be fully mature until the mid-20s (Ernst et al., 2006; Galvan et al., 2006). Neural connections among brain regions also continue to strengthen across adolescence into young adulthood (Dosenbach, Petersen, & Schlaggar, 2013; Eluvathingal, Hasan, Kramer, Fletcher, & Ewing-Cobbs, 2007; Paus, 2009). This asynchrony in developmental time courses between the affective/approach and cognitive control

* Corresponding author. Address: Department of Psychology, Brock University, St. Catharines, Ontario L2S 3A1, Canada.
E-mail address: twilloug@brocku.ca (T. Willoughby).
[1] Order of authorship is alphabetical for the last three authors.

0278-2626/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.bandc.2013.09.008

Early childhood poverty, immune-mediated disease processes, and adult productivity

Kathleen M. Ziol-Guest[a,1], Greg J. Duncan[b], Ariel Kalil[c], and W. Thomas Boyce[d]

[a]Department of Policy Analysis and Management, Cornell University, Ithaca, NY 14853; [b]School of Education University of California, Irvine, CA 92697-5500; [c]Harris School of Public Policy Studies, University of Chicago, Chicago, IL 60091; and [d]School of Population and Public Health, University of British Columbia, BC, Canada V6T 1Z3

Edited by Gene E. Robinson, University of Illinois at Urbana–Champaign, Urbana, IL, and approved August 31, 2012 (received for review February 22, 2012)

This study seeks to understand whether poverty very early in life is associated with early-onset adult conditions related to immune-mediated chronic diseases. It also tests the role that these immune-mediated chronic diseases may play in accounting for the associations between early poverty and adult productivity. Data (n = 1,070) come from the US Panel Study of Income Dynamics and include economic conditions in utero and throughout childhood and adolescence coupled with adult (age 30–41 y) self-reports of health and economic productivity. Results show that low income, particularly in very early childhood (between the prenatal and second year of life), is associated with increases in early-adult hypertension, arthritis, and limitations on activities of daily living. Moreover, these relationships and particularly arthritis partially account for the associations between early childhood poverty and adult productivity as measured by adult work hours and earnings. The results suggest that the associations between early childhood poverty and these adult disease states may be immune-mediated.

health disparities | socioeconomic status

Existing research links early childhood income to adult productivity as measured by adult work hours and earnings (1), with much of the association related to variation in individuals' ability to sustain full-time work in adulthood. Such sustained capacity for work may, in turn, be related to the presence or absence of chronic health conditions, which impair the physical and mental abilities required to achieve and maintain gainful employment. Commonalities among many of these prevalent, chronic conditions, such as hypertension and arthritis, include their propensities to disrupt activities of daily living (ADLs), their known linkages to socioeconomic status in both childhood and adult life (2, 3), and their plausible partial mediation by neuroimmunological processes (4–7). Whether immune-mediated chronic diseases play a role in associations between early socioeconomic conditions and adult productivity is, therefore, an important and understudied question (8). This study investigates both whether low income during very early childhood vs. other stages of childhood is associated with immune-mediated chronic health conditions in adulthood and the extent to which these adult health conditions might explain associations between very early childhood income and adult productivity. The reported analyses help to inform arguments not only for the role of early-life conditions and immune-mediated disease processes in adulthood but also implicating physical and mental health conditions in the intergenerational transmission of poverty (8).

Early childhood income and later disease processes, especially immune-related processes, may be plausibly connected through several potential pathways (9). First, the fetal origins hypothesis posits a biological programming process, where exposures and insults during the prenatal period have long-lasting implications for physiology and disease risk (10). Maternal diet and smoking, for example, have known effects on the neonatal development of the immune system, which could play a role in the pathogenesis of immune-mediated disease (11). Furthermore, low caloric intake during pregnancy is found to be associated with increases in chronic health conditions, such as coronary heart disease, hypertension, and obesity, among infants later in life (12). Low birth weight has also been associated with chronic low-grade inflammatory processes in later life (13).

Second, psychological stress has well-documented influences on cellular and humoral immune processes (14, 15), and chronic stress from growing up poor could also play a role in dysregulation across multiple physiological systems with effects that persist (or possibly compound) into adulthood (16). Childhood poverty may actually calibrate immune system responsivity, dysregulating inflammatory processes and resulting in a shift to proinflammatory states (17). Third, parental behaviors associated with low income could increase susceptibility to immune- or inflammation-mediated diseases (18, 19). Poverty-related adversity is known, for example, to impede parents' abilities to engage in warm and sensitive interactions with their children (20), and parental warmth may moderate the effects of low socioeconomic status (SES) on inflammatory processes in children (21, 22).

Fourth, low-income children attain less education as adults, and education is an important determinant of health, in part through knowledge of healthy diet and health-inducing behaviors (23), which may help attenuate chronic inflammatory processes. Fifth, macrolevel conditions, such as the state of the business cycle during time of birth, are found to adversely impact health outcomes. Specifically, the risk of cardiovascular mortality increases among those individuals born during economic downturns (24, 25). Finally, low income in early childhood has been linked to poor mental health in adulthood (9). Disorders of mental health, especially depression, are associated with inflammation, and mental disorders are causally antecedent to inflammatory changes (21, 26).

Given the credibility of these immune mediation pathways, the present study sought to relate high-quality measures of very early childhood income to incident adulthood disease states with demonstrable ties to immune-mediated pathogenic processes. In contrast to many epidemiological studies that rely on retrospective data of childhood SES, our data allow us to follow individuals from birth to adulthood and use concurrent reports of family income gathered annually between the prenatal year and age 15 y. We examine the relationship between income in different stages of childhood and adult health (arthritis, hypertension, and conditions that limit daily activities) and labor market productivity

This paper results from the Arthur M. Sackler Colloquium of the National Academy of Sciences, "Biological Embedding of Early Social Adversity: From Fruit Flies to Kindergartners," held December 9–10, 2011, at the Arnold and Mabel Beckman Center of the National Academies of Sciences and Engineering in Irvine, CA. The complete program and audio files of most presentations are available on the NAS Web site at www.nasonline.org/biological-embedding.

Author contributions: K.M.Z.-G., G.J.D., and A.K. designed research; K.M.Z.-G., G.J.D., and A.K. performed research; K.M.Z.-G. analyzed data; and K.M.Z.-G., G.J.D., A.K., and W.T.B. wrote the paper.

The authors declare no conflict of interest.

This article is a PNAS Direct Submission.

[1]To whom correspondence should be addressed. E-mail: kmz7@cornell.edu.

This article contains supporting information online at www.pnas.org/lookup/suppl/doi:10.1073/pnas.1203167109/-/DCSupplemental.