

EXECUTIVE FUNCTIONS

Brain Development and Executive Functioning

Katie Knapp, MSc, J. Bruce Morton, PhD

Western University, Canada

January 2013

Introduction

Executive functions are processes that support many everyday activities, including planning, flexible thinking, focused attention and behavioural inhibition, and show continued development into early adulthood.^{1,2} One important backdrop to the development of these psychological abilities is the structural and functional development of the brain.^{3,4,5,6} Among the slowest developing brain regions is the prefrontal cortex, a large expanse of cortex located in the front half of the brain. Remarkably, this region of the brain continues to develop into the third decade of life.^{7,8} Brain imaging research^{9,10} and studies of patients with brain damage^{11,12,13} suggest that the prefrontal cortex is vital for controlling attention, thinking and behaviour, in part because it bridges perceptual, emotional and motor control centres located elsewhere in brain. The fact that prefrontal cortex is both slow to develop^{14,15} and important for executive control has led to the suggestion that the development of executive functioning is closely related to the maturation of the prefrontal cortex.^{16,17,18} One implication is that basic everyday challenges, such as not playing with a forbidden toy, will be difficult even for normally-developing children.

Subject

Understanding that the prefrontal cortex is important for behavioural self-regulation and develops gradually may provide insight into why, for example, children have difficulty: (a) stopping one activity and switching to a new one; (b) planning ahead; (c) doing more than one thing at a time; (d) concentrating for long periods of time; and (e) foregoing immediate rewards. Findings from developmental cognitive neuroscience research suggests these behaviours are a normal part of growing up and are rooted to some degree in how the brain works at this stage in life.

Problems

Understanding precisely how the development of the prefrontal cortex contributes to advances in executive functioning is extremely challenging. First, executive functions are difficult to precisely define and measure, in part because core concepts such as inhibition and cognitive flexibility actually do more to describe than explain behaviour. Second, it is unclear whether processes involved in regulating one kind of behaviour, such as language, are the same as those involved in regulating other kinds of behaviour, such as the emotions. Third, tasks that are appropriate for testing executive functioning at one age will not typically be suitable for testing executive functioning in older children. This makes it difficult to compare executive functioning in children of different ages. Ultimately though, developmental cognitive neuroscientists are interested in linking age-related changes in executive functioning with developmental changes in brain function. To achieve this, it is necessary to not only adequately define and measure executive functioning, but to simultaneously collect a direct measure of brain function. One approach is functional magnetic resonance imaging (or fMRI), a safe and relatively non-invasive means of probing changes in brain activity that occur as people perform certain tasks. While viable and safe for use even with newborn infants,^{19,20} fMRI requires that participants remain very still for at least 5 to 10 minutes while the images are acquired. Abrupt movements 5 to 10 mm can render images noisy and virtually uninterpretable. Complicating matters further, if young children perform the prescribed tasks differently than older children, it becomes impossible to know whether age-related differences in patterns of brain activity relate solely to differences in the age of the participants or additionally to differences in the way younger and older children performed the tasks. Put simply, instructing 7-year-olds to perform a task in the way 4-year-olds do could, in principle, cause patterns of brain activity in 7-year-olds to look indistinguishable from those observed in 4-year-olds. To mitigate these problems, researchers are developing new imaging protocols that can be administered quickly and do not require children to perform a task. In these so-called resting-state scans, children simply lay still for as little as five minutes with their eyes

open.²¹ Resulting images are used to probe for age-related changes in “intrinsic” patterns of cortical connectivity, which then can be associated with measures of executive functioning collected outside the MRI scanner.

Research Context

Findings from fMRI studies of executive functioning development paint a fascinating but complex picture. Some studies, for example, report that younger children show less prefrontal cortex (PFC) activity in the context of executive function tasks than do older participants, findings that are consistent with the intuition that as a brain region functionally develops, it shows more robust activity and executive functioning improves.^{22,23} Other findings suggest a slightly more complicated story, insofar as some regions of PFC exhibit increasing activity with increasing age, while others show decreasing activity with increasing age.^{24,25,26} One interpretation of this pattern is that early in life, executive functioning is associated with weak but diffuse PFC activity, whereas later in development, executive functioning is associated with robust but focal PFC activity.²⁶ Thus, at the centre of a developing region, activity increases with age, whereas in the surround, activity decreases with increasing age. Another interpretation is that certain regions within PFC become more efficient with increasing age. Thus, early in development, these regions need to work very hard to support a certain level of executive functioning performance. However, later in development when these regions function more efficiently, they can support a comparable level of executive functioning performance with less energy expenditure. Clearly, more research is required to clarify this complex picture.

One consistent finding from developmental fMRI investigations of executive functioning performance is that there are many additional regions outside of the PFC linked to the development of executive functioning performance, including anterior cingulate, anterior insula, parietal and motor cortices.^{27,28} One interpretation of this evidence is that executive functioning performance tasks are very complex and involve many different subprocesses such as holding instructions in mind,^{27,29,30} attending to some stimuli and ignoring others,²² planning and executing motor responses,²⁶ and evaluating performance feedback. It is possible then that executive functioning tasks are associated with activity in many brain regions because the tasks themselves involve many different subprocesses, each of which is associated with activity in a different brain region. If this is true, then the challenge moving forward is to identify which subprocesses are subject to age-related change, and to link these changes with changes in the function of specific brain regions. A second interpretation is that PFC does not function independently, but forms part

of a broader, functionally homogenous, network. On this view, regardless of whether a participant is holding instructions in mind, planning a response, or evaluating feedback, robust activity will be observed throughout the entire network. If this is true, then the challenge moving forward is to identify how the organization of the larger network changes over development. Possibilities include changes in the regions comprising the larger network as well as changes in the number and strength of connections between constituent regions.

Key Research Questions

1. What are the constituent processes underlying executive functioning task performance?
2. Are different executive functioning's uniquely linked to different brain regions?
3. How do changes in brain function contribute to changes in executive functioning?

Recent Research Results

Recently, researchers have begun examining developmental changes in brain networks thought to be important for executive functioning, by examining changes in connections between PFC and other regions commonly associated with executive functioning such as the parietal, cingulate and insular cortices.²⁸ As these networks can be observed and measured even while participants are at rest, many recent studies have used so-called resting-state fMRI to probe the organization of cognitive control networks at different ages.^{31,32} Initial findings suggested widespread network reorganization of over development, with new long-range connections forming and pre-existing short-range connections being taken away as children grow older.³³ More recent evidence has called these initial findings into question, and suggests the re-organization of executive functioning networks over development may be less pronounced than originally thought.³⁴ However, despite these initial missteps, the study of network organization over development continues to attract attention as researchers increasingly recognize that brain regions work together to realize high-level thoughts and actions.

Research Gaps

Perhaps the most significant research gap in fMRI research on the development of executive functioning is evidence from longitudinal studies. Unlike cross-sectional studies, in which one group of younger children is compared with a different group of older children, longitudinal studies compare the same group of children at different ages. Needless to say, longitudinal studies are

very expensive, take a long time to conduct, and can be very risky, which is the reason why so little longitudinal evidence currently exists. Still, longitudinal designs afford a number of important advantages over cross-sectional designs. First, whenever two groups of children of different ages are compared, there are many factors that could potentially differ between the groups beyond age, including differences in intelligence, temperament/personality, and socio-economic status, to name only a few. Given that each of these factors is related to executive functioning, inferences concerning the importance of age for explaining group differences in patterns of brain activation become tenuous. Second, an important goal of developmental cognitive neuroscience is to identify early patterns of psychological and neural organization that predict future states, both positive (e.g., intellectual and social well-being) and negative (e.g., psychopathology). Identifying these patterns is best achieved when the same group of children is followed repeatedly over time until the outcome of interest (e.g., giftedness, addiction, risky sexual behaviour, etc.) is observed in some children. Only then can one go back and see which brain or behavioural measure collected earlier in time successfully predict future outcomes.

Conclusions

The brain takes the first two decades of life to develop to adult levels. During this time, different regions of the brain develop at different rates. Alongside these regional changes, the connections between brain regions also develop gradually over the course of childhood and adolescence. In conjunction with these developments in brain structure and function are advances in the ability to perform executive functioning tasks. Children show gradual improvements in their ability to plan ahead, to switch between tasks and to inhibit a response when instructed to do so. The study of brain networks and their development may offer a useful avenue for quantifying the relationship between brain development and the maturation of executive functioning. The frontal and parietal cortices need to communicate in order to effectively perform executive functioning tasks. Effective communication between these regions is not fully developed until late adolescence, and this may explain why executive functioning abilities do not mature until late in the second decade of life.

Implications for Parents, Services and Policy

We need to remember that children's brains are a work in progress. Whether we measure, grey matter thickness, white matter volume, synaptic density, or any other anatomical feature of the brain, continued change will be observed well into early adulthood. These changes will obviously

impact a child's cognitive functioning, and this will be particularly true of executive functioning, given the complexity of the processes involved. Given the importance of executive functioning for academic achievement and social well-being, identifying problems in cognitive and behavioural self-regulation early-on is clearly important. At the same time, all young children will struggle to plan ahead, resist temptations, regulate their emotions and stay on task: it's just the way the brain works at this age.

References

1. Best JR, Miller PH, Jones LL. Executive functions after age 5: Changes and correlates. *Dev Rev.* 2009;29(3):180-200.
2. Luna B, Garver KR, Urban TA, Lazar, NA, Sweeney JA. Maturation of cognitive processes from late childhood to adulthood. *Child Dev.* 2004;75(5):1357-1372.
3. Shaw P, Kabani, NJ, Lerch JP, et al. Neurodevelopmental trajectories of the human cerebral cortex. *J Neurosci.* 2008;28(14):3586-3594.
4. Huttenlocher PR, de Courten C, Garey LJ, Van der Loos H. Synaptogenesis in human visual cortex – evidence for synapse elimination during normal development. *Neurosci Lett.* 1982;33(3):247-252.
5. Giedd JN, Blumenthal J, Jeffries NO, et al. Brain development during childhood and adolescence: A longitudinal MRI study. *Nat Neurosci.* 1999;2(10):861-863.
6. Sowell ER, Peterson BS, Thompson PM, Welcome SE, Henkenius AL, Toga AW. Mapping cortical change across the human life span. *Nat Neurosci.* 2003;6(3):309-315.
7. Gogtay N, Giedd JN, Lusk L, et al. Dynamic mapping of human cortical development during childhood through early adulthood. *P Natl Acad Sci USA.* 2004;101(21):8174-8179.
8. Huttenlocher PR. Dendritic and synaptic development in human cerebral cortex: Time course and critical periods. *Dev Neuropsychol.* 1999;16(3):347-349.
9. Lie C, Specht K, Marshall JC, Fink GR. Using fMRI to decompose the neural processes underlying the Wisconsin Card Sorting Test. *Neuroimage.* 2006;30(3):1038-1049.
10. Aarts E, Roelofs A, van Turenout M. Attentional control of task and response in lateral and medial frontal cortex: Brain activity and reaction time distributions. *Neuropsychologia.* 2009;47(10):2089-2099.
11. Perrett E. The left frontal lobe of man and the suppression of habitual responses in verbal categorical behaviour. *Neuropsychologia.* 1974;12(3):323-330.
12. Aron AR, Fletcher PC, Bullmore ET, Sahakian BJ, Robbins TW. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nat Neurosci.* 2003;6(2):115-116.
13. Milner B. Effects of different brain lesions on card sorting: The role of the frontal lobes. *Arch Neurol.* 1963;9(1):90-100.
14. Huttenlocher PR. Synaptic density in human frontal cortex – developmental changes and effects of aging. *Brain Res.* 1979;163(2):195-205.
15. Sowell ER, Thompson PM, Tessner KD, Toga AW. Mapping continued brain growth and gray matter density reduction in dorsal frontal cortex: Inverse relationships during postadolescent brain maturation. *J Neurosci.* 2001;21(22):8819-8829.
16. Bunge SA, Zelazo PD. A brain-based account of the development of rule use in childhood. *Curr Dir Psychol Sci.* 2006;15(3):118-121.

17. Dempster FN. The rise and fall of the inhibitory mechanism: Toward a unified theory of cognitive development and aging. *Dev Rev.* 1992;12(2):45-75.
18. Diamond A. Normal development of prefrontal cortex from birth to young adulthood: Cognitive functions, anatomy, and biochemistry. In: Stuss DT, Knight RT, eds. *Principles of Frontal Lobe Function*. Oxford: Oxford University Press; 1992:466-503.
19. Smyser CD, Inder TE, Shimony JS, et al. Longitudinal analysis of neural network development in preterm infants. *Cereb Cortex.* 2010;20(12):2852-2862.
20. Davidson MC, Thomas KM, Casey BJ. Imaging the developing brain with fMRI. *Ment Retard Dev D R.* 2003;9(3):161-167.
21. Kelly AMC, Di Martino A, Uddin LQ, et al. Development of anterior cingulate functional connectivity from late childhood to early adulthood. *Cereb Cortex.* 2009;19(3):640-657.
22. Adleman NE, Menon V, Blasey CM, et al. A developmental fMRI study of the Stroop color-word task. *Neuroimage.* 2002;16(1):61-75.
23. Luna B, Thulborn KR, Munoz DP, et al. Maturation of widely distributed brain function subserves cognitive development. *Neuroimage.* 2001;13(5):786-793.
24. Morton JB, Bosma R, Ansari D. Age-related changes in brain activation associated with dimensional shifts of attention: An fMRI study. *Neuroimage.* 2009;46(1):249-256.
25. Bunge SA, Dudukovic NM, Thomason ME, Vaidya CJ, Gabrieli JDE. Immature frontal lobe contributions to cognitive control in children: Evidence from fMRI. *Neuron.* 2002;33(2):301-311.
26. Casey BJ, Trainor RJ, Orendi JL, et al. A developmental functional MRI study of prefrontal activation during performance of a go-no-go task. *J Cognitive Neurosci.* 1997;9(6):835-847.
27. Braver TS, Cohen JD, Nystrom LE, Jonides J, Smith EE, Noll DC. A parametric study of prefrontal cortex involvement in human working memory. *Neuroimage.* 1997;5(1):49-62.
28. Cole MW, Schneider W. The cognitive control network: Integrated cortical regions with dissociable functions. *Neuroimage.* 2007;37(1):343-360.
29. Bunge SA, Wright SB. Neurodevelopmental changes in working memory and cognitive control. *Curr Opin Neurobiol.* 2007;17(2):243-250.
30. Kwon H, Reiss AL, Menon V. Neural basis of protracted developmental changes in visuo-spatial working memory. *P Natl Acad Sci USA.* 2002;99(20):13336-13341.
31. Biswal B, Yetkin FZ, Haughton VM, Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med.* 1995;34(4):537-541.
32. Vogel AC, Power JD, Petersen SE, Schlagger BL. Development of the brain's functional network architecture. *Neuropsychol Rev.* 2010;20(4):362-375.
33. Fair DA, Dosenbach NUF, Church JA, et al. Development of distinct control networks through segregation and integration. *P Natl Acad Sci USA.* 2007;104(33):13507-13512.
34. Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage.* 2012;59(3):2142-2154.