

# **HHS Public Access**

Author manuscript *Child Dev Perspect*. Author manuscript; available in PMC 2017 June 01.

Published in final edited form as: *Child Dev Perspect.* 2016 June ; 10(2): 105–110. doi:10.1111/cdep.12170.

### **Executive Function in Previously Institutionalized Children**

Emily C. Merz, Columbia University

Katia M. Harlé, University of California, San Diego

**Kimberly G. Noble**, and Columbia University

**Robert B. McCall** University of Pittsburgh

#### Abstract

In studies of children adopted from institutions, being raised in an institution has been associated consistently with an increased risk of persistent cognitive, academic, and social-emotional problems. These findings raise questions about the neurocognitive mechanisms that contribute to these negative outcomes. Theory and models based on studies of animals indicate that development of the prefrontal cortex (PFC) and executive function (EF) may be particularly susceptible to environmental influences during early childhood. In this article, we review recent studies of postinstitutionalized children that examined EF components such as inhibitory control, working memory, shifting, and planning. We then describe emerging research on the structure and function of the PFC. Converging evidence suggests both EF difficulties and alterations in development of the PFC following early institutionalization. We conclude by discussing possible explanations for these findings and implications for prevention and intervention, and by offering suggestions for ongoing research.

#### Keywords

early deprivation; executive function; inhibitory control; working memory

Around the world, many orphaned or abandoned children spend their early lives in orphanages. These institutions tend to be profoundly depriving environments characterized by deficiencies that include high child-to-caregiver ratios, frequent changes in caregivers, infrequent social and cognitive stimulation, and in some cases, inadequate physical resources (1). Children adopted from institutions (postinstitutionalized children) present a unique opportunity to investigate the effects of a circumscribed period of early deprivation followed by placement into supportive, middle-class families (2). More than a half century of research, including more recent, well-controlled studies, has established that although

Correspondence concerning this article should be addressed to Emily C. Merz, Mailman School of Public Health, Columbia University, 722 West 168th St., Room 720F, New York, NY 10032; emilymerz@gmail.com.

postinstitutionalized children recover following adoption, they are at greater risk of persistent cognitive deficits, academic difficulties, and emotional and behavioral disorders (3, 4). The risk of these problems increases with age at adoption and the duration of early institutionalization (5). These findings have generated interest in identifying the underlying neurocognitive mechanisms that link early institutionalization with increased risk of negative longer-term outcomes. Understanding these mechanisms can inform the design of effective targeted interventions that promote positive outcomes among postinstitutionalized children.

In this article, we focus on recent research examining the development of executive function (EF, also called cognitive control) and the prefrontal cortex (PFC) in postinstitutionalized children. EF refers to cognitive skills that support flexible, goal-directed behavior and depend on areas of the PFC (6). Core EF processes include the ability to suppress automatic or dominant responses (inhibitory control), store and update information over short periods (working memory), shift flexibly among attentional or behavioral responses (shifting), and identify and organize sequential steps to a goal (planning; 7). Extensive evidence suggests that EF robustly predicts academic achievement and social-emotional functioning (6). In our review of research on postinstitutionalized children, we describe studies of EF and of the structure and function of the PFC. We then discuss mechanisms by which early institutionalization might influence the PFC, and thus the development of EF, as well as prevention and intervention programs targeting EF. We conclude with recommendations for ongoing research.

#### Theoretical Perspectives and Animal Models of Early Deprivation

Experience-expectant models of development propose that expected environmental input (e.g., care that is typical for children, such as the presence of an attachment figure, adequate nutrition, social and linguistic stimulation) must be provided at certain times or sensitive periods for typical neural development to proceed (8). EF and the PFC develop postnatally over a protracted period, with rapid development during early childhood (7, 9), and thus may be particularly vulnerable to environmental influences during early childhood. Early exposure to institutional environments, which deviate markedly from the care that is typical for children, may lead to lasting alterations in PFC and thus the development of EF. In animal models, which experimentally control exposure to deprivation, early maternal deprivation leads to persistent abnormalities in PFC development and less optimal performance on EF tasks in rodents (10, 11) and nonhuman primates (12-14). These findings provide a strong foundation for examining similar effects in humans.

#### Executive Function in Postinstitutionalized Children

In this section, we review studies of postinstitutionalized children that used performancebased measures of four core components of EF: inhibitory control, working memory, shifting, and planning (see supplementary Table S1 online for descriptions of tasks). Although researchers have also used parent and teacher rating scales to examine EF in postinstitutionalized children (15), we limited our review to direct assessments of specific EF components. Comparison groups were 1) nonadopted children raised in their birth families and 2) children adopted from noninstitutional settings, such as foster care, who are

similar to postinstitutionalized children in terms of potentially confounding risk factors (e.g., genetic background, poor prenatal care and birth circumstances, transitions in caregivers) but likely experienced a higher-quality early environment. For postinstitutionalized children, we also covered associations between EF and age at adoption, which is a proxy for the timing or duration of institutional rearing (5). Supplementary Table S2, available online, provides detailed information about the studies included in this review.

#### **Inhibitory Control**

Postinstitutionalized children tend to perform less optimally on inhibitory control tasks, including the go/no go (16), delay of gratification (17), knock and tap (18), Stroop (19), and flanker tasks (20, 21), than nonadopted children raised in their biological families and children adopted from noninstitutional settings. For example, 11-year-old postinstitutionalized children had more Stroop task errors than children adopted from noninstitutional setting for verbal ability (19). However, in two studies, there were no group differences on go/no go task accuracy to no go cues (20, 22).

In terms of age at adoption, postinstitutionalized children adopted after 14 months performed less optimally on the stop-signal task than those adopted before 9 months (23). Performance on the knock and tap task was significantly negatively associated with age at adoption from 12 to 78 months (18). Also, postinstitutionalized children adopted after 6 months performed at lower levels on the Stroop task than those adopted before 6 months (19). However, some studies reported only marginally significant associations with age at adoption (16, 20), and performance on go/no go tasks was not significantly associated with age at adoption in two studies (20, 22). Thus, despite some inconsistencies, postinstitutionalized children had lower inhibitory control relative to both comparison groups, and older age at adoption was associated with lower inhibitory control.

#### Working Memory

Postinstitutionalized children also performed less optimally on tasks of spatial working memory than nonadopted children raised in their biological families and children adopted from noninstitutional settings (17, 18, 24-26, 27). For example, 8-year-old Romanian children with a history of institutionalization made more errors on a self-ordered search task than nonadopted Romanian children raised in their biological families (25). Postinstitutionalized children adopted after 6 months also differed marginally on the backward digit span task when compared with the combined comparison group of children adopted from institutional or noninstitutional settings before 6 months of age (28).

In terms of age at adoption, performance on a self-ordered search task did not differ between postinstitutionalized children adopted after 14 months and those adopted before 9 months (23), and was not associated significantly with age at adoption in postinstitutionalized children adopted after 9-12 months (18, 25). Thus, postinstitutionalized children consistently had difficulties with working memory relative to both comparison groups, but the risk of having difficulties with working memory did not increase with age at adoption.

#### Shifting

In three studies, postinstitutionalized children performed less optimally on shifting tasks than nonadopted children raised in their birth families (17, 24, 26). For example, 9- to 11-year-old postinstitutionalized children had significantly more errors on a version of the Wisconsin Card Sort Task than nonadopted children raised in their biological families (24). However, in one study, postinstitutionalized children did not differ on this task from nonadopted children or children adopted from noninstitutional settings, and task performance was not associated with age at adoption from 12 to 78 months (18). Therefore, in studies of shifting, postinstitutionalized children performed less optimally than nonadopted children but not children adopted from noninstitutional settings, and there was no evidence of an age-at-adoption effect.

#### Planning

Across three studies, postinstitutionalized children performed less optimally on planning tasks than nonadopted children raised in their biological families (24, 26) and children adopted from noninstitutional settings (28). For example, 11-year-old postinstitutionalized children adopted after 6 months had significantly fewer correct solutions on the Tower of London task than the pooled comparison group of children adopted from institutional or noninstitutionalized children did not differ significantly on a version of the Tower of London task from nonadopted children (25) or children adopted from noninstitutional settings (18). Performance on planning tasks was not associated with age at adoption in postinstitutionalized children adopted after 9-12 months (18, 25). Thus, findings are inconsistent for planning, both in terms of group comparisons and associations with age at adoption. In summary, findings across studies indicate EF difficulties in postinstitutionalized children, with evidence especially strong for inhibitory control and working memory.

### Structure and Function of the Prefrontal Cortex in Postinstitutionalized Children

Given that EF relies on areas of the PFC, early institutionalization may disrupt the development of PFC circuitry. In convergence with research on animals, neuroimaging research has revealed structural and functional changes in the PFC of postinstitutionalized children. Specifically, prefrontal cortical volume was smaller in 12- to 14-year-old postinstitutionalized children than in nonadopted children raised in their biological families (29). In addition, Romanian 8- to 10-year-olds who had been institutionalized had reduced prefrontal cortical thickness compared to nonadopted Romanian children raised in their biological families (30). Postinstitutionalized children (31-33), and this was associated with less optimal performance on planning tasks (26). PFC volume was not significantly associated with age at adoption or time in an institution (29, 30), but reductions in prefrontal white matter organization were greater in children exposed to longer early institutional care (33).

Functionally, in late childhood, at-rest metabolism in postindustrialized children is reduced in the ventromedial PFC and orbitofrontal cortex (34). In addition, postinstitutionalized children displayed an altered pattern of amygdala-medial PFC connectivity compared to nonadopted children (35). Electrophysiological studies have also pointed to differences between postinstitutionalized children and comparison groups while performing EF tasks. For example, postinstitutionalized children had smaller N2 and error-related negativity amplitudes (which reflect electrical brain activity associated with inhibitory control and response monitoring following an incorrect response) while performing EF tasks than nonadopted children and children adopted from noninstitutional settings (20). Thus, postinstitutionalized children may differ from comparison groups in the neural correlates of

## Summary

EF.

Collectively, the studies we have reviewed suggest that postinstitutionalized children are at greater risk of EF deficits, and differ in the structure and function of PFC systems that support EF. Researchers used rigorous methods to account for potentially confounding risk factors, and evidence that postinstitutionalized children had less optimal EF than children adopted from noninstitutional settings suggests that lower performance on EF tasks was due, at least in part, to early institutional rearing. Intervention studies also suggest that many of the developmental effects of institutionalization may be related to institutionalization itself rather than wholly attributable to genetic or prenatal factors (1). Thus, consistent with theory and findings from animal models, exposure to a depriving institutional environment in early childhood may have lasting effects on PFC and EF development.

Evidence of postinstitutionalized children's EF difficulties was stronger for inhibitory control and working memory than for planning and, to some extent, shifting. EF components may differ in their sensitive periods or potential for developmental recovery. Indeed, EF processes may vary in their developmental trajectories, with inhibitory control and working memory developing earlier and thus possibly particularly vulnerable to early deprivation (7, 36). However, in the studies examining planning and shifting, each EF component was measured using a single task, which may not have been consistently sensitive to the effects of early institutional rearing.

#### Why Early Institutionalization Might Influence PFC and EF Development

Institutions are depriving environments often characterized by deficiencies that may disrupt children's development of EF, such as a lack of opportunities to form attachments, low caregiver sensitivity and contingent responsiveness, and inadequate social and cognitive stimulation. The absence of an attachment figure and low levels of caregiver responsiveness may lead to dysregulated stress physiology, which in turn undermines the development of the PFC. Both animal models and studies of people suggest that being deprived of a caregiver early in life and experiencing low-quality care compromise the development and functioning of the hypothalamic-pituitary-adrenal (HPA) axis, often elevating levels of stress hormones (37). Chronic stress and elevated HPA axis reactivity can affect PFC structure and function in strong and enduring ways (38, 39).

Inadequate social and cognitive stimulation may also affect PFC and EF development. Caregivers in institutions often do not speak to children frequently and fail to provide them with cognitively enriching experiences; in addition, children's activities are often the same from day to day, they interact infrequently with adults, and they lack books and toys

from day to day, they interact infrequently with adults, and they lack books and toys matched to their interests and developmental ability. In animal models of cognitive enrichment, those deprived of environmental complexity have reduced cortical thickness due to decreases in synaptic density and dendritic branching (40). Finally, lack of adequate nutrition may contribute to EF and PFC abnormalities in postinstitutionalized children. For instance, children raised in institutions often have iron deficiency, which predicts lower EF in postinstitutionalized children (41).

The severity, timing, and duration of exposure to these institutional deficiencies may moderate PFC and EF outcomes. Across studies, older age at adoption tended to be associated with lower inhibitory control among postinstitutionalized children. However, age-at-adoption effects were more equivocal for the other EF components and for PFC structural outcomes, possibly because most postinstitutionalized studies included only children adopted after 9-12 months. Postinstitutionalized children adopted from severely depriving institutions after 6 months had lower inhibitory control, working memory (marginally significant), and planning than those adopted before 6 months, suggesting that exposure to severe deprivation beyond the first 6 months may increase the risk of EF problems (19, 28). These findings increase our understanding of the role of timing and also suggest that longer early deprivation may heighten the risk of inhibitory control problems among postinstitutionalized children. In addition, genetic background may moderate the effects of early deprivation, with genetically susceptible children particularly vulnerable to the effects of early institutional rearing on planning and PFC structure (42).

#### Implications for Prevention and Intervention

Disrupted PFC and EF development may be a neurodevelopmental mechanism that partially explains postinstitutionalized children's increased risk of academic difficulties and emotional and behavioral disorders. Indeed, lower EF may partially mediate the association between early institutionalization and emotional and behavioral difficulties (19, 23). Moreover, reduced prefrontal cortical thickness partially mediated the association of institutionalization with inattention and impulsivity, suggesting that atypical PFC structure may be partially responsible for the markedly elevated rates of attention-deficit hyperactivity disorder among postinstitutionalized children (30). As such, evaluating children's EF shortly after adoption and providing those in need with support for EF recovery may help prevent these negative outcomes.

Although we do not know yet which services will be effective with postinstitutionalized children, a variety of interventions targeting EF are effective with other groups. While early interventions capitalize on the considerable plasticity of EF early in life, interventions provided in later childhood and adolescence also enhance EF. Following adoption, postinstitutionalized children's home and school environments should be structured to support the development of EF. For example, preschool programs emphasizing pretend play and those promoting self-regulatory strategies and social-emotional problem solving have

Page 7

improved young children's EF (43). Additionally, both computer-based training programs (e.g., computer games that progressively increase demands on working memory) and mindfulness training (which includes meditation and sensory awareness activities) have enhanced EF development in older children (44).

#### **Conclusion and Looking Ahead**

Given these findings suggesting EF difficulties in postinstitutionalized children, research should specify precisely the PFC circuits and EF processes affected by early institutionalization, including further investigation into executive control in emotionally significant contexts and the corresponding neural circuitry. EF has a protracted developmental course and EF components may differ in the degree to which they retain plasticity later in life. Thus, researchers should also examine longitudinal change in EF processes in adoptive homes from early childhood through adolescence, and determine whether developmental trajectories vary by moderating factors such as the timing, duration, and severity of early deprivation, as well as genetic background. Early institutionalization may be linked with altered PFC and EF development via mechanisms including the lack of early attachment, reduced environmental complexity, and nutritional deficiencies. An ideal test of these mechanisms would involve intervention studies that use random assignment, target these aspects of institutional environments, and measure stress physiology along with EF and PFC outcomes. Finally, we must identify effective prevention and intervention strategies that improve postinstitutionalized children's development of EF and in turn support their potential for positive academic and social-emotional outcomes.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

#### Acknowledgments

Authors' Note: This article was made possible by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (HD39017 and HD050212 to Robert B. McCall and Christina J. Groark). In addition, a National Institute of Mental Health training grant supported Emily Merz (T32MH13043).

#### References

- 1. The St. Petersburg-USA Orphanage Research Team. The effects of early social-emotional and relationship experience on the development of young orphanage children. Monographs of the Society for Research in Child Development. 2008; 73:vii–295.
- Rutter M, Beckett C, Castle J, Colvert E, Kreppner J, Mehta M, Sonuga-Barke E. Effects of profound early institutional deprivation: An overview of findings from a UK longitudinal study of Romanian adoptees. European Journal of Developmental Psychology. 2007; 4:332–350. http:// dx.doi.org/10.1080/17405620701401846.
- 3. MacLean K. The impact of institutionalization on child development. Development and Psychopathology. 2003; 15:853–884. http://dx.doi.org/10.1017/S0954579403000415. [PubMed: 14984130]
- 4. Tottenham N. Risk and developmental heterogeneity in previously institutionalized children. Journal of Adolescent Health. 2012; 51:S29–S33. http://dx.doi.org/10.1016/j.jadohealth.2012.04.004. [PubMed: 22794530]

- Julian MM. Age at adoption from institutional care as a window into the lasting effects of early experiences. Clinical Child and Family Psychology Review. 2013; 16:101–145. http://dx.doi.org/ 10.1007/s10567-013-0130-6. [PubMed: 23576122]
- Hughes C. Changes and challenges in 20 years of research into the development of executive functions. Infant and Child Development. 2011; 20:251–271. http://dx.doi.org/10.1002/icd.736.
- Garon N, Bryson SE, Smith IM. Executive function in preschoolers: A review using an integrative framework. Psychological Bulletin. 2008; 134:31–60. http://dx.doi.org/ 10.1037/0033-2909.134.1.31. [PubMed: 18193994]
- 8. Marshall PJ, Kenney JW. Biological perspectives on the effects of early psychosocial experience. Developmental Review. 2009; 29:96–119. http://dx.doi.org/10.1016/j.dr.2009.05.001.
- 9. Grossmann, T. Mapping prefrontal cortex functions in human infancy; Infancy, 18. 2013. p. 303-324.http://dx.doi.org/10.1111/infa.12016
- Lovic V, Fleming AS. Artificially-reared female rats show reduced prepulse inhibition and deficits in the attentional set shifting task—reversal of effects with maternal-like licking stimulation. Behavioural Brain Research. 2004; 148:209–219. http://dx.doi.org/10.1016/ S0166-4328(03)00206-7. [PubMed: 14684261]
- Roceri M, Cirulli F, Pessina C, Peretto P, Racagni G, Riva MA. Postnatal repeated maternal deprivation produces age-dependent changes of brain-derived neurotrophic factor expression in selected rat brain regions. Biological Psychiatry. 2004; 55:708–714. http://dx.doi.org/10.1016/ j.biopsych.2003.12.011. [PubMed: 15038999]
- Lyons DM, Afarian H, Schatzberg AF, Sawyer-Glover A, Moseley ME. Experience-dependent asymmetric variation in primate prefrontal morphology. Behavioral Brain Research. 2002; 136:51– 59. http://dx.doi.org/10.1016/S0166-4328(02)00100-6.
- Sanchez M, Ladd CO, Plotsky PM. Early adverse experience as a developmental risk factor for later psychopathology: Evidence from rodent and primate models. Development and Psychopathology. 2001; 13:419–449. http://dx.doi.org/10.1017/S0954579401003029. [PubMed: 11523842]
- Spinelli S, Chefer S, Suomi SJ, Higley JD, Barr CS, Stein E. Early-life stress induces long-term morphologic changes in primate brain. Archives of General Psychiatry. 2009; 66:658–665. http:// dx.doi.org/10.1001/archgenpsychiatry.2009.52. [PubMed: 19487631]
- Merz EC, McCall RB, Groza V. Parent-reported executive functioning in postinstitutionalized children: A follow-up study. Journal of Clinical Child & Adolescent Psychology. 2013; 42:726– 733. http://dx.doi.org/10.1080/15374416.2013.764826. [PubMed: 23413815]
- 16. Eigsti IM, Weitzman C, Schuh J, de Marchena A, Casey BJ. Language and cognitive outcomes in internationally adopted children. Development and Psychopathology. 2011; 23:629–646. http:// dx.doi.org/10.1017/S0954579411000204. [PubMed: 23786701]
- Hostinar CE, Stellern SA, Schaefer C, Carlson SM, Gunnar MR. Associations between early life adversity and executive function in children adopted internationally from orphanages. Proceedings of the National Academy of Sciences. 2012; 109:17208–17212. http://dx.doi.org/10.1073/pnas. 1121246109.
- Pollak SD, Nelson CA, Schlaak MF, Roeber BJ, Wewerka SS, Wiik KL, Frenn KA, Loman MM, Gunnar MR. Neurodevelopmental effects of early deprivation in postinstitutionalized children. Child Development. 2010; 81:224–236. http://dx.doi.org/10.1111/j.1467-8624.2009.01391.x. [PubMed: 20331664]
- Colvert E, Rutter M, Kreppner J, Beckett C, Castle J, Groothues C, Hawkins A, Stevens S, Sonuga-Barke EJ. Do theory of mind and executive function deficits underlie the adverse outcomes associated with profound early deprivation?: Findings from the English and Romanian Adoptees Study. Journal of Abnormal Child Psychology. 2008; 36:1057–1068. http://dx.doi.org/10.1007/ s10802-008-9232-x. [PubMed: 18427975]
- Loman MM, Johnson AE, Westerlund A, Pollak SD, Nelson CA, Gunnar MR. The effect of early deprivation on executive attention in middle childhood. Journal of Child Psychology and Psychiatry. 2013; 54:37–45. http://dx.doi.org/10.1111/j.1469-7610.2012.02602.x. [PubMed: 22924462]

- McDermott JM, Troller-Renfree S, Vanderwert R, Nelson CA, Zeanah CH, Fox NA. Psychosocial deprivation, executive functions, and the emergence of socio-emotional behavior problems. Frontiers in Human Neuroscience. 2013; 7:167. http://dx.doi.org/10.3389/fnhum.2013.00167. [PubMed: 23675333]
- 22. McDermott JM, Westerlund A, Zeanah CH, Nelson CA, Fox NA. Early adversity and neural correlates of executive function: Implications for academic adjustment. Developmental Cognitive Neuroscience. 2012; 2:S59–S66. http://dx.doi.org/10.1016/j.dcn.2011.09.008. [PubMed: 22682911]
- Merz EC, McCall RB, Wright AJ, Luna B. Inhibitory control and working memory in postinstitutionalized children. Journal of Abnormal Child Psychology. 2013; 41:879–890. http:// dx.doi.org/10.1007/s10802-013-9737-9. [PubMed: 23519375]
- Bauer PM, Hanson JL, Pierson RK, Davidson RJ, Pollak SD. Cerebellar volume and cognitive functioning in children who experienced early deprivation. Biological Psychiatry. 2009; 66:1100– 1106. http://dx.doi.org/10.1016/j.biopsych.2009.06.014. [PubMed: 19660739]
- Bos KJ, Fox N, Zeanah CH, Nelson CA III. Effects of early psychosocial deprivation on the development of memory and executive function. Frontiers in Behavioral Neuroscience 3. 2009; 16 http://dx.doi.org/10.3389/neuro.08.016.2009.
- 26. Hanson JL, Adluru N, Chung MK, Alexander AL, Davidson RJ, Pollak SD. Early neglect is associated with alterations in white matter integrity and cognitive functioning. Child Development. 2013; 84:1566–1578. http://dx.doi.org/10.1111/cdev.12069. [PubMed: 23480812]
- 27. Peñarrubia M, Palacios J, Román M, Moreno C, Leon E. Executive function in postinstitutionalized children. 2015 Unpublished manuscript.
- Beckett C, Castle J, Rutter M, Sonuga-Barke EJ. VI. Institutional deprivation, specific cognitive functions, and scholastic achievement: English and Romanian adoptee (ERA) study findings. Monographs of the Society for Research in Child Development. 2010; 75:125–142. http:// dx.doi.org/10.1111/j.1540-5834.2010.00553.x. [PubMed: 20500636]
- Hodel AS, Hunt RH, Cowell RA, Van Den Heuvel SE, Gunnar MR, Thomas KM. Duration of early adversity and structural brain development in post-institutionalized adolescents. NeuroImage. 2015; 105:112–119. http://dx.doi.org/10.1016/j.neuroimage.2014.10.020. [PubMed: 25451478]
- McLaughlin KA, Sheridan MA, Winter W, Fox NA, Zeanah CH, Nelson CA. Widespread reductions in cortical thickness following severe early-life deprivation: A neurodevelopmental pathway to attention-deficit/hyperactivity disorder. Biological Psychiatry. 2014; 76:629–638. http://dx.doi.org/10.1016/j.biopsych.2013.08.016. [PubMed: 24090797]
- Behen ME, Muzik O, Saporta AS, Wilson BJ, Pai D, Hua J, Chugani HT. Abnormal fronto-striatal connectivity in children with histories of early deprivation: A diffusion tensor imaging study. Brain Imaging and Behavior. 2009; 3:292–297. http://dx.doi.org/10.1007/s11682-009-9071-6. [PubMed: 19727404]
- Eluvathingal TJ, Chugani HT, Behen ME, Juhász C, Muzik O, Maqbool M, Makki M. Abnormal brain connectivity in children after early severe socioemotional deprivation: A diffusion tensor imaging study. Pediatrics. 2006; 117:2093–2100. http://dx.doi.org/10.1542/peds.2005-1727. [PubMed: 16740852]
- Govindan RM, Behen ME, Helder E, Makki MI, Chugani HT. Altered water diffusivity in cortical association tracts in children with early deprivation identified with tract-based spatial statistics (TBSS). Cerebral Cortex. 2010; 20:561–569. http://dx.doi.org/10.1093/cercor/bhp122. [PubMed: 19546156]
- Chugani HT, Behen ME, Muzik O, Juhász C, Nagy F, Chugani DC. Local brain functional activity following early deprivation: A study of postinstitutionalized Romanian orphans. Neuroimage. 2001; 14:1290–1301. http://dx.doi.org/10.1006/nimg.2001.0917. [PubMed: 11707085]
- Gee DG, Gabard-Durnam LJ, Flannery J, Goff B, Humphreys KL, Telzer EH, Tottenham N. Early developmental emergence of human amygdala–prefrontal connectivity after maternal deprivation. Proceedings of the National Academy of Sciences. 2013; 110:15638–15643. http://dx.doi.org/ 10.1073/pnas.1307893110.
- Jurado MB, Rosselli M. The elusive nature of executive functions: A review of our current understanding. Neuropsychology Review. 2007; 17:213–233. http://dx.doi.org/10.1007/ s11065-007-9040-z. [PubMed: 17786559]

- Hostinar CE, Sullivan RM, Gunnar MR. Psychobiological mechanisms underlying the social buffering of the hypothalamic-pituitary-adrenocortical axis: A review of animal models and human studies across development. Psychological Bulletin. 2014; 140:256–282. http://dx.doi.org/10.1037/ a0032671. [PubMed: 23607429]
- Arnsten AF. Stress signalling pathways that impair prefrontal cortex structure and function. Nature Reviews Neuroscience. 2009; 10:410–422. http://dx.doi.org/10.1038/nrn2648. [PubMed: 19455173]
- McEwen BS, Morrison JH. The brain on stress: Vulnerability and plasticity of the prefrontal cortex over the life course. Neuron. 2013; 79:16–29. http://dx.doi.org/10.1016/j.neuron.2013.06.028. [PubMed: 23849196]
- Sheridan MA, McLaughlin KA. Dimensions of early experience and neural development: Deprivation and threat. Trends in Cognitive Sciences. 2014; 18:580–585. http://dx.doi.org/ 10.1016/j.tics.2014.09.001. [PubMed: 25305194]
- 41. Doom JR, Gunnar MR, Georgieff MK, Kroupina MG, Frenn K, Fuglestad AJ, Carlson SM. Beyond stimulus deprivation: Iron deficiency and cognitive deficits in postinstitutionalized children. Child Development. 2014; 85:1805–1812. http://dx.doi.org/10.1111/cdev.12231. [PubMed: 24597672]
- Brett ZH, Sheridan M, Humphreys K, Smyke A, Gleason MM, Fox N, Drury S. A neurogenetics approach to defining differential susceptibility to institutional care. International Journal of Behavioral Development. 2015; 39:150–160. http://dx.doi.org/10.1177/0165025414538557. [PubMed: 25663728]
- Diamond A, Lee K. Interventions shown to aid executive function development in children 4 to 12 years old. Science. 2011; 333:959–964. http://dx.doi.org/10.1126/science.1204529. [PubMed: 21852486]
- 44. Zelazo PD, Carlson SM. Hot and cool executive function in childhood and adolescence: Development and plasticity. Child Development Perspectives. 2012; 6:354–360. http://dx.doi.org/ 10.1111/j.1750-8606.2012.00246.x.