Pediatric Neurology 52 (2015) 383–388

Contents lists available at ScienceDirect

Pediatric Neurology

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

Topical Review

Brain Imaging and Electrophysiology Biomarkers: Is There a Role in Poverty and Education Outcome Research?

Alexandra E. Pavlakis MSc [a,1], Kimberly Noble MD, PhD [b,1], Steven G. Pavlakis MD [c,*,1], Noorjahan Ali MD [d], Yitzchak Frank MD [e]

[a] *Educational Leadership & Policy Analysis, University of Wisconsin-Madison, Madison, Wisconsin*
[b] *Pediatrics, Columbia University, New York, New York*
[c] *Center for Brain and Behavior, Maimonides Medical Center, Brooklyn, New York*
[d] *Pediatrics, Maimonides Medical Center, Brooklyn, New York*
[e] *Psychiatry, Pediatrics, and Neurology, Mount Sinai Medical Center, New York, New York*

ABSTRACT

BACKGROUND: Prekindergarten educational interventions represent a popular approach to improving educational outcomes, especially in children from poor households. Children from lower socioeconomic groups are at increased risk for delays in cognitive development that are important for school success. These delays, which may stem from stress associated with poverty, often develop before kindergarten. Early interventions have been proposed, but there is a need for more information on effectiveness. By assessing socioeconomic differences in brain structure and function, we may better be able to track the neurobiologic basis underlying children's cognitive improvement. **METHODS:** We conducted a review of the neuroimaging and electrophysiology literature to evaluate what is known about differences in brain structure and function as assessed by magnetic resonance imaging and electrophysiology and evoked response potentials among children from poor and nonpoor households. **RESULTS:** Differences in lower socioeconomic groups were found in functional magnetic resonance imaging, diffusion tensor imaging, and volumetric magnetic resonance imaging as well as electroencephalography and evoked response potentials compared with higher socioeconomic groups. **CONCLUSIONS:** The findings suggest a number of neurobiologic correlates for cognitive delays in children who are poor. Given this, we speculate that magnetic resonance imaging and electrophysiology parameters might be useful as biomarkers, after more research, for establishing the effectiveness of specific prekindergarten educational interventions. At the very least, we suggest that to level the playing field in educational outcomes, it may be helpful to foster communication and collaboration among all professionals involved in the care and education of children.

Keywords: brain imaging, electrophysiology, biomarkers, poverty, education

Pediatr Neurol 2015; 52: 383-388
© 2015 Elsevier Inc. All rights reserved.

Introduction

In the United States, there has been great interest in prekindergarten and early childhood education to level the educational and developmental playing field across all socioeconomic status (SES) strata. Increasingly, many cities and states are prioritizing early childhood programs and interventions.[1]

The evidence concerning developmental disparities among socioeconomically disadvantaged children has evolved over the past decade, and it is now clear that children who are poor are more likely to score lower on tests of language, memory, and executive function, as well as to exhibit increased aggressive behavior, relative to higher SES children.[2,3] These disparities develop early in childhood—possibly as early as infancy.[4] In one study of kindergarten children, children who were poor tested a full standard deviation below middle class children on certain

Article History:
Received June 17, 2014; Accepted in final form November 9, 2014
* Communications should be addressed to: Dr. Pavlakis; Center for Brain and Behavior; Maimonides Medical Center; 977 48th Street; Brooklyn, New York 11219.
E-mail address: SPavlakis@maimonidesmed.org
[1] Equally responsible for the work described in this paper.

0887-8994/$ - see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.pediatrneurol.2014.11.005

cognitive measures.[5,6] Good language skills and executive functions are integral to successful educational performance,[6-8] and delays in these cognitive parameters may lead to academic underachievement in general.

The mechanisms by which SES impacts early brain development are unclear but, in part, may be secondary to increased stress produced by poverty seen in early childhood.[9] Other factors could include prenatal conditions, parent-child interactions, and fewer cognitively stimulating materials in the home, such as books or educational toys.[2,9] A rodent model suggested that mice that are stressed in childhood might perform less well on cognitive tasks as adults.[10] There was an associated hippocampus atrophy in adult mice that were stressed in childhood.[10] Research in both animals and humans suggests that stressful experiences may be associated with reductions in hippocampus size.[11] Evidence suggests that these hippocampal abnormalities are likely related to activation of corticotropin hormone receptors by increasing hormone production and leading to a dysregulation of stress physiology.[11] In the rodent model, blocking the corticotropin activation ameliorates the hippocampal changes.[10]

Here we review the literature on SES disparities in brain development to evaluate what is known about differences in brain structure and function as assessed by magnetic resonance imaging (MRI) and electrophysiology and evoked response potentials (ERPs) among children from poor and nonpoor households. With the premise of a neurobiologic component to SES disparities, we focus on the potential use of MRI and electroencephalography (EEG) and/or ERPs as biomarkers for educational studies and suggest the need for increased collaboration between the medical and educational communities. This is the first review with this focus.

Materials and methods

We explored the relationship between SES (defined as parental income and/or education and/or occupation) and brain MRI and EEG and/or ERPs in the context of schooling. We conducted a literature search for English-language articles using PubMed, EBSCO, Cochrane Library, and Google Scholar. A Boolean search used the following terms: “SES,” “socioeconomic,” “ERP,” “EEG,” “school,” “education,” “kindergarten,” “MRI,” “imaging,” “brain,” and “neuroanatomy.” We extracted papers that had these keywords in full text and included any cognitive and behavioral correlates to neuroimaging, ERPs, and SES. We included studies limited mostly to children, adolescents, or adults who in childhood were from lower SES. Articles that did not use parental SES but instead used the individuals’ own educational attainment or other markers of individual SES were excluded. References within the articles were also scanned for relevant sources and articles.

Results

We found 17 papers that mentioned imaging techniques, cognition, and SES and had primary imaging data performed in childhood or in adults who had low SES as children (Table 1).[7,12-27] An additional six papers studied EEG and/or ERPs and correlations with SES (Table 2).[4,28-32]

SES differences were found in routine MRI measuring volumes of brain structures as well as diffusion tensor imaging (DTI), functional magnetic resonance imaging (fMRI) using blood oxygen level dependent (BOLD), and EEG and/or ERPs.

Functional MRI

Three studies have used neuroimaging to examine SES disparities in reading ability. In one fMRI study conducted in children at risk for reading impairment, the correlation between phonological awareness and BOLD activation during a reading task varied as a function of SES in children with the same phonological skills.[7] Specifically, among children who struggled with reading in the context of a lower SES environment, phonological awareness was a positive predictor of left fusiform activation during reading (i.e., a typical brain-behavior relationship). In contrast, among children who struggled with reading despite the resources of a higher SES environment, phonological awareness did not predict left fusiform activation during reading (i.e., an atypical brain-behavior relationship in this group). In an fMRI study of 70 adult subjects from diverse SES in childhood who had been struggling readers and who either became better readers as adults or remained struggling readers, low SES struggling readers were again showing typical brain-behavior relationships.[12] Higher SES individuals showed evidence of neural compensation (other areas were activated during reading, more than in lower SES struggling readers who improved).[12] Raizada et al.[13] showed that higher SES was associated with greater recruitment of the left inferior frontal gyrus in young children during a rhyming task, relative to right-sided inferior frontal gyrus recruitment.

Four studies have used neuroimaging to investigate other neural systems, including the limbic and prefrontal cortices. In one study of 33 adults, there was greater amygdala reactivity to threatening faces in adults who lived in low SES families as children.[14] Similarly, Kim et al.[15] studied adults who had low income-to-needs ratios at age 9 years; these adults had lower prefrontal activation and also had an inability to suppress amygdala activation with a stressor. Sheridan et al.[16,17] reported that prefrontal activation was decreased in children from lower SES families during a stimulus-response mapping task in one paper and, in another, found that hippocampal activation was decreased during a declarative memory task in children from lower SES families.

MRI (structural)

Five structural MRI studies have shown some association between hippocampal structure and SES. In a study of 23 children that assessed volumetric differences in regional brain volumes, lower SES was associated with smaller gray matter volumes in the hippocampus, as well as middle temporal gyrus, fusiform gyrus, and right inferior occipitotemporal gyrus; SES was not associated with white matter volumes.[18] SES differences in the volume of both the hippocampus and amygdala were found in another study with 60 children.[19] An investigation with 317 children showed decreases in a measure of hippocampal density with lower SES.[20] A study of 145 children showed family income-to-needs ratio correlated with total white and gray

TABLE 1.
Summary of Imaging Literature

Author	n	Modality	Finding
Noble et al.[7]	35 children	fMRI	The link between reading precursor skills and reading related fusiform activation is moderated by SES.
Shaywitz et al.[12]	70 adults	fMRI	Children who improved in reading later in life had activation of multiple brain regions including those on the right with a pattern different from those who did not improve; some association with SES.
Raizada et al.[13]	14 children	fMRI	SES is correlated with degree of hemispheric specialization in the left inferior frontal gyrus during a rhyming task. Higher SES predicts greater left hemispheric specialization.
Gianaros et al.[14]	33 adults	fMRI	Greater amygdala reactivity to threatening faces in adults who came from low SES in childhood.
Kim et al.[15]	49 adults	fMRI	Decreased prefrontal activation and failure to suppress amygdala activation with stress in lower SES groups (income to needs at age 9 years).
Sheridan et al.[16]	18 children	fMRI	Prefrontal activation decreased in children with lower SES at age 9 years.
Sheridan et al.[17]	40 right-handed children	fMRI	Maternal social status related to hippocampal function.
Jednorog et al.[18]	23 children	MRI	Lower SES associated with smaller volumes of gray matter including hippocampus.
Noble et al.[19]	60 children	MRI	Hippocampus and amygdala volume correlate with SES.
Hanson et al.[20]	317 children	MRI	Hippocampal volume correlates with SES.
Luby et al.[21]	145 children	MRI	Family income to needs correlated with total white and gray matter as well as amygdala and hippocampus volume.
Staff et al.[22]	249 adults	MRI	Smaller hippocampus in adults with low SES in childhood, even when controlling for adult SES.
Lawson et al.[23]	283 children	MRI	Parental education correlates with right cingulate and left superior frontal gyrus cortical thickness.
Hanson et al.[24]	77 children	MRI	Lower rate of volume growth in frontal and parietal gray matter.
Lange et al.[25]	285 children	MRI	Parental education levels not correlated with brain volumes (volumes were sum of gray and white matter).
Eckert et al.[26]	39 children	MRI	SES and planar asymmetry independently predicted phonological awareness.
Chiang et al.[27]	705 twin pairs age 12-29 years	DTI	SES interacts with genetic affects in white matter integrity.

Abbreviations:
DTI = Diffusion tensor imaging
fMRI = Functional magnetic resonance imaging
MRI = Magnetic resonance imaging
SES = Socioeconomic status

matter volume including amygdala and hippocampus volume.[21] Likewise, a study of 242 adults who were in different SES groups as children found that the hippocampus volume was lower into adulthood in the subjects who came from the lower SES strata, even when controlling for SES in adulthood.[22]

In a study of 283 children, parental education was correlated with cortical thickness in the right cingulate and left superior gyrus.[23] In another study, 77 children between 5 months and 4 years of age underwent repeated MRIs. Children from lower SES had a lower rate of brain growth and specifically lower gray matter volumes in both frontal and parietal lobes.[24] In contrast, a study with 285 children showed no association between SES and the sum of white and gray matter volume, although it did report a correlation between child's IQ and parental education.[25] Finally, Eckert et al.[26] showed that planar asymmetry predicted phonological awareness independently of SES.

Diffusion tensor imaging

One study found correlations between DTI and parental SES measures. Examining 705 twin pairs (both fraternal and identical) between the ages of 12 to 24 years, the authors found that SES significantly interacted with genetic effects of fiber integrity.[27]

Electrophysiology

Six papers using EEG and ERPs assessed correlates between SES and electrophysiologic function.[4,28-32] Tomalski et al.[4] studied infants and found that lower SES infants had

TABLE 2.
EEG/ERP

Author	n	Modality	Findings
Tomalski et al.[4]	45 infants	EEG	Lower SES infants had lower frontal gamma power.
Kishiyama et al.[28]	28 children	ERP	Lower prefrontal activation in lower SES children.
D'Anghuilli et al.[29]	14 children	ERP and EEG	ERP: higher SES children showed higher differential activation between a relevant and nonrelevant stimulus. EEG: lower SES children showed higher theta power when ignoring the activation than when attending to the task.
Stevens et al.[30]	32 children	ERP	Activation to irrelevant stimuli was greater in lower SES children.
Skoe et al.[31]	66 children	ERP	Auditory responses to speech were noisier, weaker, and more variable in low SES.
Neville et al.[32]	143 children	ERP	Family-based therapies resulted in changes in activation for an attention task.

Abbreviations:
EEG = Electroencephalography
ERP = Evoked response potentials
SES = Socioeconomic status

lower frontal gamma power on EEG at baseline compared with infants with higher SES status. Three studies have looked at SES disparities in electrophysiologic function during various tasks of attention. Using ERPs and a sample of 28 children, Kishiyama et al.[28] found SES disparities in the prefrontal activation during an attention task. Similarly, D'Anguilli et al. used EEG and ERPs in 14 adolescents during a task of attention and found that higher SES children showed a greater differentiation between relevant and irrelevant stimuli (auditory tones). Lower SES children also showed higher theta power when ignoring the activation task than when they were attending to the task.[29] In a study of 32 children, SES disparities in prefrontal ERP patterns were related to children from the lower SES group being less able to suppress irrelevant task-related information.[30] Skoe et al. found in a study of auditory event-related potentials (ERPs) that adolescents who had mothers with lower maternal education had noisier neural activity as reflected by greater activity in the absence of auditory stimulation. Additionally, these adolescents had a more erratic neural response to speech.[31]

Finally, Neville et al.[32] examined 143 lower SES children and showed that family-based interventions not only improved cognitive skills in children but also resulted in changes in ERPs during an attention task. Although all the children were enrolled in a Head Start program, those who were randomly assigned to a family-based intervention exhibited cognitive improvements compared with those who either attended Head Start alone or who were assigned to an active control that was child focused, rather than both child and family focused.

Discussion

Socioeconomic disparities in brain structure and function are complex but, in part, may stem from stress associated with poverty. SES is associated with disparities in language, memory, executive function, and behavior even as early as 1 year of age. Three primary cognitive disparities include language (left hemisphere), cognitive control (prefrontal cortex), and memory (hippocampus).[3] These three domains are crucial to school success.[3] Structural and fMRI studies show SES disparities in a number of regions that support these skills. Evidence suggests that, compared with their lower SES counterparts, higher SES individuals may show greater task-related activation of the prefrontal cortex and hippocampus and reduced activation of the amygdala. Further, early development of the neural system that supports reading may fundamentally interact with family SES. These studies are small and have not been replicated, however. Volumetric MRI studies as a group suggest that low SES is associated with smaller gray matter volume, especially in the hippocampus. Electrophysiologic studies reveal prefrontal differences in lower SES infants and children, potentially related to neural differences in the attention process. One study using ERPs in children has shown neural differences after parental interventions.

How to improve cognitive disparities is a process unfolding. Intervening early may lead to higher returns than responding to problems later in life,[33] although coupling early interventions with later investments adds greater benefit.[34] Research suggests that "high-quality" early education programs have the potential to improve educational and life outcomes[35]; for instance, the Perry Preschool Project led to positive outcomes in educational attainment and a range of broader improvements in income and family environment.[35,36] However, although there is strong support for early education, there are scholarly tensions over what constitutes "quality"—particularly around play-based versus more scripted curricula. Although a considerable body of research supports the value of certain types of play and teacher-child interactions, in response to accountability and school readiness pressures, direct instruction models—which tend to exclude play—are often implemented.[37] Furthermore, early interventions in the home or with a strong parent or family component may be required as well.[32] Early intervention may be especially important; if one waits to see abnormalities in development or neural structure and function, it might be too late to intervene successfully[38] (although it is also possible that such changes may be reversible with effective intervention). In the midst of city and statewide rollouts of early education programs, more information on the efficacy of individual programs and approaches could expand the conversation and help inform effective curricular and policy responses.

Volumetric studies are feasible in children at a kindergarten level. It is thus possible to imagine an experiment in which subcortical structural volumes could be used in future educational research. The extent to which the associations between SES and gray matter reflect an underlying causal relationship is not understood. Nor is it known how hippocampal volume changes in childhood as a function of changes in SES, changes in other life circumstances, or exposure to educational interventions.

DTI may also play a role in assessing a subset of children after intervention. DTI, however, is relatively less studied, and so its utility in this research requires further investigation.

fMRI using BOLD might also be useful to test different educational interventions to determine effects on brain function. Children from different SES backgrounds with different prekindergarten interventions could undergo fMRI with cognitive testing. It is possible that changes as a result of educational interventions could be detected using fMRI before changes using standardized cognitive assessments. fMRI, however, is limited to children often older than age 6 years, is cumbersome, expensive, and has poor control data.

Resting EEG is cheap, relatively reproducible, and could have utility as a biomarker. EEG has great intersubject variability but could be used serially after intervention. A confound is the maturational effects of EEG over time, but this could be calculated and controlled. ERP is difficult to standardize across multiple sites and, like fMRI, requires an activation paradigm. However, this is the one modality that has been successfully applied in the field as a biomarker in a group of low SES children, and as such, it has promise.

We conclude that SES disparities in neuroimaging and electrophysiology studies may underlie known socioeconomic disparities in cognitive development, although the etiology is likely a complex interaction of multiple factors. We have an opportunity for the neurological community to work with the policy makers and educators to help determine the best interventions that improve outcomes and reduce the achievement gap by SES. The potential use of imaging and electrophysiology could contribute to the assessment of various interventions that have been heretofore proposed without consensus between and among scholars, practitioners, child development experts, and policymakers. Because there are neurobiologic correlates of socioeconomic disparities that can be measured using MRI and EEG and/or ERPs, we can potentially apply neuroimaging and electrophysiologic methods to better understand educational programs and their efficacy in children. Following continued research, it may be possible for structural or functional neuroimaging and electrophysiology to be performed after implementation of a specific early intervention designed to reduce SES disparities. Many unanswered questions remain. Experiments on a small sample of children might ultimately help elucidate both mechanisms and interventions that improve outcome in children who are poor. Such efforts would require the collaboration of educators, neurologists, psychologists, pediatricians, and neuroimaging experts but may lead to neuroimaging and electrophysiology playing a role in the development of effective early interventions for children. At the very least, we suggest that to level the playing field in educational outcomes, it may be helpful to foster communication and collaboration among all professionals involved in the care and education of children.

References

1. Perez-Pena R, Rich M. *Preschool push moving ahead in many states*. The New York Times; February 3, 2014.
2. Evans G, Kim P. Childhood poverty, chronic stress, self-regulation and coping. *Child Dev Perspectives*. 2013;7:43-48.
3. McEwen B, Gianaros P. Central role of the brain in stress and adaptation: links to socioeconomic status, health and disease. *Ann NY Acad Sci*. 2010;1186:190-222.
4. Tomalski P, Moore D, Ribeiro H, et al. Socioeconomic status and functional brain development-associations in early infancy. *Dev Sci*. 2013;16:676-687.
5. Noble KG, Norman MF, Farah MJ. Neurocognitive controls of socioeconomic status in kindergarten children. *Dev Sci*. 2005;8:74-87.
6. Noble KG, Tottenham N, Casey BJ. Neuroscience perspectives on disparities in school readiness and cognitive achievement. *Future Child*. 2005;15:71-89.
7. Noble KG, Wolmetz ME, Ochs LG, Farah MJ, McCandliss BD. Brain-behavior relationships in reading acquisition are modulated by socioeconomic factors. *Dev Sci*. 2006;9:642-654.
8. Noble KG, Farah MJ, McCandliss BD. Socioeconomic background modulates cognition-achievement relationships in reading. *Cogn Dev*. 2006;21:349-368.
9. Hackman D, Farah M, Meaney M. Socioeconomic status and the brain: mechanistic insights from human and animal research. *Nat Rev*. 2010;11:651-659.
10. Ivy A, Rex C, Chen Y, et al. Hippocampal dysfunction and cognitive impairments provoked by chronic early-life stress involve activation of CRH receptors. *J Neurosci*. 2010;30:13005-13015.
11. Tottenham N, Sheridan M. A review of adversity, the amygdala and the hippocampus: a consideration of developmental timing. *Frontiers in Hum Neurosci*. 2010;3:1-18.
12. Shaywitz SE, Shaywitz BA, Fulbright RK, et al. Neural systems for compensation and persistence: young adult outcome of childhood reading disability. *Biol Psychiatry*. 2003;54:25-33.
13. Raizada RDS, Richards TL, Meltzoff A, et al. Socioeconomic status predicts hemispheric specialization of the left inferior frontal gyrus in young children. *Neuroimage*. 2008;40:1392-1401.
14. Gianaros PJ, Horenstein JA, Hariri AR, et al. Potential neural embedding of parental social standing. *Soc Cogn Affect Neurosci*. 2008;3:91-96.
15. Kim P, Evans G, Angstadt M, et al. Effects of childhood poverty and chronic stress on emotion regulatory brain function in adulthood. *PNAS*. 2013;110:1-6.
16. Sheridan MA, Sarsour K, Jutte D, D'Esposito M, Boyce WT. The impact of social disparity on prefrontal function in childhood. *PLoS One*. 2012;7:e35744.
17. Sheridan M, How J, Araujo M, et al. What are the links between maternal social status, hippocampal function and HPA axis function in children? *Dev Sci*. 2013;16:665-675.
18. Jednorog K, Altarelli I, Monzalvo K, et al. The influence of socioeconomic status on children's brain structure. *PLoS One*. 2012;7:e42488.
19. Noble K, Houston S, Kan E, Sowell E. Neural correlates of socioeconomic status in the developing human brain. *Dev Sci*. 2012;15:516-527.
20. Hanson J, Chandra A, Wolfe B, Pollack S. Association between income and hippocampus. *PLOS One*. 2011;6:1-8.
21. Luby J, Belden A, Botteron K, et al. The effects of poverty on childhood brain development the mediating effect of caregiving and stressful life events. *JAMA Pediatr*. 2013;167:1135-1142.

22. Staff RT, Murray AD, Ahearn TS, et al. Childhood socioeconomic status and adult brain size: childhood socioeconomic status influences adult hippocampal size. *Ann Neurol*. 2012;71:653-660.
23. Lawson G, Duda J, Avants B, Wu J, Farah M. Association between children's socioeconomic status and prefrontal cortical thickness. *Dev Sci*. 2013;16:641-652.
24. Hanson J, Hair N, Shen D, Shi F Gilmore J, Wolfe B, Pollak S. Family poverty affects the rate of human infant brain growth. *PLoS One*. 2013;8:1-9.
25. Lange N, Froimowitz M, Bigler E, et al. Associations between IQ, total and regional brain volumes and demography in a large normative sample of healthy children and adolescents. *Dev Neuropsychol*. 2010;35:296-317.
26. Eckert MA, Lombardino LJ, Leonard CM. Planar asymmetry tips the phonological playground and environment raises the bar. *Child Dev*. 2001;72:988-1002.
27. Chiang M, McMahon K, deZubicaray G, et al. Genetics of white matter development: a DTI study of 705 twins and their siblings aged 12-29. *Neuroimage*. 2011;54:2308-2317.
28. Kishiyama MM, Boyce WT, Jimenez A, et al. Socioeconomic disparities affect prefrontal function in children. *J Cogn Neurosci*. 2009;21:1108-1125.
29. D'Anguilli A, Weinberg J, Oberlander T, et al. Frontal EEG/ERP correlated of attentional process, cortisol and motivational states in adolescents from lower and higher socioeconomic status. *Frontiers of Hum Neurosci*. 2012;6:1-15.
30. Stevens C, Lauinger B, Neville H. Differences in neural mechanisms of selective attention in children from different socioeconomic backgrounds: an event related brain potential study. *Dev Sci*. 2009;12:634-646.
31. Skoe E, Krizman J, Kraus N. The impoverished brain: disparities in maternal education affect the neural response to sound. *J Neurosci*. 2013;33:17221-17231.
32. Neville H, Stevens C, Pakulak E, et al. Family based training program improved brain function, cognition, and behavior in lower socioeconomic status and preschoolers. *PNAS*. 2013;110:12138-12142.
33. Heckman JJ, et al. Skill formation and the economics of investing in disadvantaged children. *Science*. 2006;312:1900-1902.
34. Heckman JJ. The economics, technology, and neuroscience of human capability formation. *Proc Natl Acad Sci U.S.A*. 2007;104:13250-13255.
35. Weikart DP. Changing early childhood development through educational intervention. *Prev Med*. 1998;27:233-237.
36. Muennig P, Schweinhart L, Montie J, et al. Effects of a prekindergarten educational intervention on adult health: 37-year follow-up results of a randomized controlled trial. *Am J Public Health*. 2009;99:1431-1437. 28.
37. Nicolopoulou A. The alarming disappearance of play from early childhood education. *Hum Dev*. 2010;53:1-4.
38. Nelson CA, Sheridan MA. Lessons from neuroscience research for understanding causal links between family and neighborhood characteristics and educational outcomes. In: Duncan GJ, Murnane RJ, eds. *Whither Opportunity? Rising Inequality, Schools, and Children' s Life Chances*. New York, NY: Russell Sage Foundation; 2011. 2011.