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Interacting Experiencial and Genetic Effects on Human Neurocognitive Development

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Recent advances in brain imaging now allow for the investigation of the neural bases of cognitive processes important for academic achievement, and the effects of environmental and genetic factors on the development of these processes. Similar methods are used to characterize neuroplasticity, or the 'changeability' of brain processes following different kinds of experience. This research has shown that neuroplasticity confers the possibility for brain systems important for academic achievement to be both enhanceable when experiences are good and also vulnerable to deficit if experiences are not adequate. An understanding of the development of these systems, and in particular of the time periods during development when these effects of experience are maximal, can provide important evidence-based information for parents, educators, and policymakers, who can use evidence from this research to inform the development of evidence-based curricula. Here we describe basic research in our laboratory on the neuroplasticity of selective attention. Selective attention plays a critical role in all aspects of learning and memory. Also, as described below, systems important for selective attention are both vulnerable in children from lower socioeconomic status (SES) households (and thus at risk for school failure) and at the same time they display a high degree of enhanceability for example following sensory deprivation within one modality (Stevens and Neville, in press). Therefore we are testing the hypotheses that attention itself is trainable, and that attention acts as a 'force multiplier' that amplifies abilities across different domains of cognition/thinking/skills. If attention does act across domains of processing, then training attention should result in gains across a number of domains important for academic success. As discussed below, in this research we also examine the interacting roles of genetics and experience on the development of attention.

Socioeconomic status

A substantial and growing literature documents the consequences of growing up in different childhood environments on cognitive development and academic achievement (for recent review, see Raizada & Kishiyama,

2010) These environmental differences are typically quantified using measures of socio-economic status (SES), a variable usually quantified by measuring household differences in parental education level, occupational prestige, and income (Ensminger & Fothergill, 2003). While this is the most common method for measuring SES, many other, correlated, factors contribute to differences in household environments related to SES, including prenatal care, stress, physical health and nutrition, substance abuse, parenting attitudes, and school and neighborhood characteristics (Bornstein & Bradley, 2003).

While 'unpacking' SES through the assessment of the individual effects of these factors is at present underexplored, the aggregate effect of SES on academic achievement is substantial. Numerous studies, using assessments such as standardized test scores, grades, and graduation rates, have found that children from lower SES backgrounds are at risk for school failure or reduced academic achievement (e.g., Duncan, Brooks-Gunn, & Klebanov, 1994; McLoyd, 1998; Walker, Greenwood, Hart, & Carta, 1994). Research on academic achievement has shown that children from lower SES backgrounds are both under-identified and under-represented in advanced, rigorous coursework of any kind (for review, see Burney & Beilke, 2008). As discussed below, research in developmental cognitive neuroscience has shifted the focus to specific cognitive skills which are central to academic achievement. One such skill is attention.

Neuroplasticity of attention

While attention is a complex construct, most researchers agree on several distinct components of attention. Selective attention is the ability to orient to targeted stimuli and select particular signals for further processing, an ability that depends both on enhancing the signal of interest and suppressing unattended distractors. Alerting is the ability to maintain an alert and focused state, either transiently or in a sustained manner (Posner & Rothbart, 2007). Executive function includes cognitive flexibility, inhibitory control, and working memory (Diamond, 2006). Of these components, selective attention is of particular importance in enabling the neuroplasticity of different brain systems. For example, in monkeys, experience-dependent changes to brain regions important for hearing and touch have been documented; however, these changes do not occur with mere exposure, but rather only when attention is directed toward relevant stimuli (Recanzone, Schreiner, & Merzenich, 1993). Given this, and the central role of attention in learning more generally, the study of the development and neuroplasticity of selective attention is a key focus of research in our laboratory.

In this research a key method we employ is the recording of event-related brain potentials (ERPs), a non-invasive electrophysiological measure of neural processing. The ERP technique enables researchers to 'eavesdrop' on the electrical signals that neurons send when they are processing information. It is similar to the way using a stethoscope enables one to 'eavesdrop' on the functions of the heart. Silver 'buttons' are sewn into a hat worn by the child, and they pick up and amplify the electrical 'brain waves' associated with the task in which the children are asked to engage. Thus, ERPs provide an on-line, multidimensional index of cognitive processes with a temporal resolution of milliseconds in which no overt behavioral response is required, and thus are well suited for use with young children.

Using this methodology we have examined the effects of sustained, selective attention on neural processing using a child-friendly experimental paradigm adapted from well-tested paradigms developed in adults (Hillyard, *et al.*, 1973). In this approach attention is manipulated while keeping physical stimuli, arousal levels, and task demands constant (i.e., the 'Hillyard principle'). For example, competing streams of stimuli are presented (e.g., two different trains of auditory stimuli delivered to different ears), with participants alternating attention to one stream at a time in order to detect rare events in the attended stream. By comparing the brain response to the same physical stimuli (e.g., tones or flashes of light) when a participant is paying attention to these stimuli versus when the participant is attending the other stream, the effects of selective attention can be quantified. Studies of adults using such paradigms have found consistently that selective attention amplifies the neural response to attended stimuli: the electrical response is twice as large to the same physical stimuli when attended versus ignored, and this enhancement occurs by at least 100 milliseconds (Hillyard, Hink, Schwent, & Picton, 1973; Luck, Woodman, & Vogel, 2000; Mangun & Hillyard, 1990). This early attentional modulation is in part domain-general in that it is observed across multiple sensory modalities (e.g., auditory, visual, tactile) and in selection based on different attributes of stimuli, such as timing or location in space. In addition, ERPs can separately index processes of signal enhancement (larger response for attended stimuli) and distractor suppression (reduced response for unattended stimuli).

In several studies we have documented the neuroplasticity of this early attentional modulation in the form of enhancements that accompany profoundly different kinds of early experience. In adults born deaf we observe enhancements of this early attentional modulation of visual stimuli compared to hearing adults. Furthermore these effects are specific to the peripheral, but not central, visual field (Bavelier, *et al.*, 2001; Bavelier, *et al.*, 2000; Neville & Lawson, 1987). Similarly, in studies of auditory spatial attention among congenitally blind adults, we observe enhancements of the early attentional modulation compared to sighted adults and these are also specific to peripheral auditory space (Röder, *et al.*, 1999). In a recent study, we have observed that these enhancements of the early attentional modulation are not present in adults blinded later in life, suggesting that early neural mechanisms for selective attention may show the greatest neuroplasticity (i.e., be both enhanceable and vulnerable) earlier in development (Fieger, Röder, Teder-Sälejärvi, Hillyard, & Neville, 2006).

In line with this hypothesis, recent behavioral studies suggest that children at-risk for school failure, including those with poor language or reading abilities or from lower socioeconomic backgrounds, exhibit deficits in aspects of attention including filtering and noise exclusion (Atkinson, 1991; Cherry, 1981; Lipina, Martelli, Vuelta, & Colombo, 2005; Noble, Norman, & Farah, 2005; Sperling, Lu, Manis, & Seidenberg, 2005; Stevens, Sanders, Andersson, & Neville, 2006; Ziegler, Pech-Georgel, George, Alanio, & Lorenzi, 2005). These attentional deficits are found across linguistic and nonlinguistic domains within the auditory and visual modalities, suggesting that the deficits are domain general.

In order to further pursue this hypothesis, we have used ERPs to examine the neural mechanisms of selective attention in typically developing, young children and in groups of children at-risk for school failure. We developed a child-friendly paradigm based on those used with adults in which two different children's stories were presented concurrently, one each from speakers to the left and right of the participant while the participant was asked to attend to one story and ignore the other. Superimposed on the stories were auditory probes to which ERPs were recorded. Typically-developing adults tested with this paradigm showed the early attentional modulation described above (Coch, Sanders, & Neville, 2005). Children as young as three years of age also showed an early attentional modulation within the first 100 milliseconds of processing (Sanders, Stevens, Coch, & Neville, 2006), suggesting that with sufficient cues, children as young as three years of age are able to attend selectively to one of two auditory streams and that doing so doubles the amplitude of neural activity within the attended stream and reduces that of the unattended stream within 100 milliseconds of processing.

We have employed this paradigm to examine selective auditory attention in children with specific language impairment (SLI) aged six to eight years and typically developing control children matched for age, gender, nonverbal IQ, and SES (Stevens, Sanders, & Neville, 2006). As shown in Figure 1

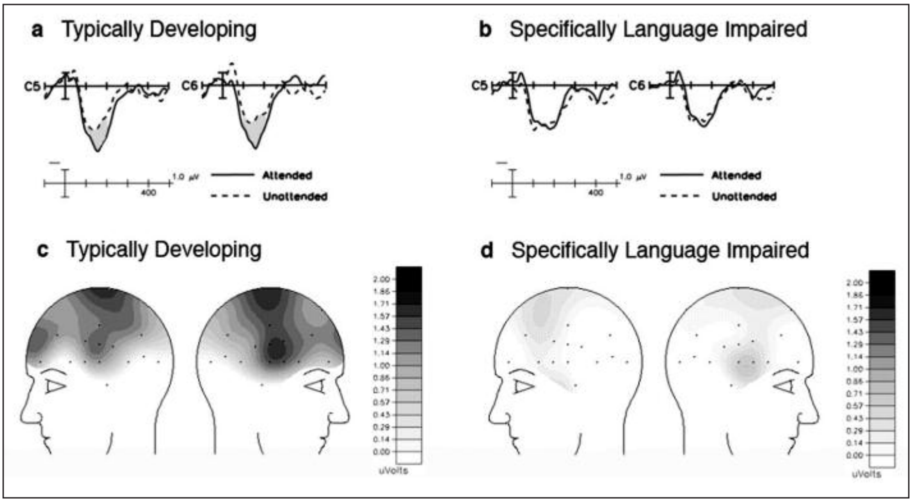

Figure 1. Data from the selective auditory attention ERP paradigm showing the early attentional modulation between 100-200 milliseconds. This modulation is the difference between attended and unattended stimuli, (a) in typically developing children (p = .001; shaded area) and (b) in children with specific language impairment ($p > 0.4$). Voltage maps of this early attentional modulation show where on the scalp this modulation (darker areas) is present: (c) in typically developing children a large, broadly distributed effect and (d) in children with specific language impairment no modulation with attention. Data from Stevens, *et al.* (2006). Permission pending from Brain Research.

a, c, by 100 milliseconds, typically developing children in this study showed an early attentional modulation as observed in our larger samples of typically developing children. In contrast, children with SLI showed no evidence of neural modulation with attention, despite behavioral performance indicating that they were performing the task as directed (Fig. 1, b, d). These results suggested that deficits in neural mechanisms for attention may in part underlie language difficulties in at least some children with SLI.

In a related line of research, we examined the neural mechanisms of selective attention in children from different SES backgrounds. Previous behavioral studies indicated that children from lower SES backgrounds experience difficulty with selective attention, and particularly in tasks of executive function and in those tasks that require filtering irrelevant information or suppressing automatic responses (Farah, *et al.*, 2006; Lupien, King, Meaney, & McEwen, 2001; Mezzacappa, 2004; Noble, McCandliss, & Farah, 2007; Noble, *et al.*, 2005). Using the same task described above, we observed that children from lower SES backgrounds showed reduced effects of selective attention on neural processing compared to children from higher SES backgrounds (Fig. 2) (Stevens, Lauinger, & Neville, 2009). These deficits arose from a reduced ability to filter irrelevant information. It has been hypothesized that early deficits in such foundational skills could have consequences for later development and learning (Mezzacappa, 2004; Noble, Norman, & Farah, 2005; Stevens, Lauinger, & Neville, 2009). Since attention acts as a force-multiplier with the possibility to enhance processing across multiple domains, these consequences would likely be reflected in low performance across multiple academic domains. This is consistent with the literature documenting the risk for reduced academic achievement in lower SES children.

Thus, together with the studies of deaf and blind adults described above, studies of children with SLI and of children from lower SES backgrounds point to two sides of the plasticity of early mechanisms of attention. That is, these mechanisms possess considerable neuroplasticity and show both enhancements and vulnerabilities in different populations. This raises the hypothesis that early environmental enrichment in the form of interventions can protect and enhance the plastic and thus potentially vulnerable neurocognitive systems in children with, or at risk for, developmental deficits.

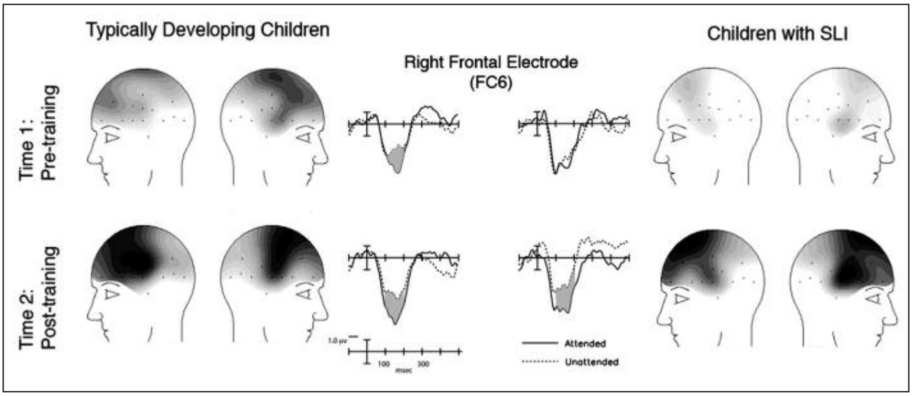

Figure 2. Data from the selective auditory attention ERP paradigm showing the early attentional modulation between 100-200 milliseconds in three- to eight-year-old children from different socioeconomic backgrounds. This modulation is the difference between attended and unattended stimuli (shaded) in children from higher socioeconomic backgrounds (upper panel) and lower socioeconomic backgrounds (lower panel). The early attentional modulation is significantly larger in children from higher socioeconomic backgrounds *(p* = .001). Data from Stevens, *et al.*, 2009. Permission pending from Developmental Science.

Effects of genetics

While the findings that foundational skills such as selective attention vary as a function of SES are compelling, because they are correlational they do not permit the inference that factors related to different SES environments *cause* these differences. Another reasonable hypothesis is that both environmental differences and the cognitive differences associated with lower SES status are the result of shared genetic information between parents and children. One way to investigate this is to directly examine effects of genetic variation on specific aspects of cognition such as selective attention.

A growing literature documents the impact of variation in genes important in the transport, reception, and metabolism of neurotransmitters which have diverse effects on cognitive function, all of which are implicated in attention (for review, see Savitz, Solms, & Ramesar, 2006). We have examined the effects of variability in types, or alleles, of genes important for the function of neurotransmitters such as dopamine and serotonin on behavioral measures of cognition and the ERP index of selective attention described above. These results showed that in 3- to 5-year-old children, performance on both behavioral measures of cognition and the effects of selective attention on neural processing vary as a function of the variants of certain genes (Bell, *et al.*, 2008; Bell, Voelker, Braasch, & Neville, under review). For example, children with a certain variant of a gene associated with the transport of the chemical dopamine had reduced early attentional modulation (as described above). This same genetic variant has been linked with increased rates of ADHD (Fan, Fossella, Sommer, Wu, & Posner, 2003; Parasuraman, Greenwood, Kumar, & Fosella, 2005; Rueda, Rothbart, McCandliss, Saccamanno, & Posner, 2005; Savitz, *et al.*, 2006). However, as discussed below, these genetic effects interact with characteristics of the environment. Moreover, to date we have not observed any distributional differences in alleles between higher and lower SES children.

Interventions

Another way to approach the question of the direction of the relation between environments and SES is to directly manipulate the environment. Given the research reviewed above showing that mechanisms of selective attention are both vulnerable and enhanceable early in development, we have been investigating the possibility that attention itself is trainable. Further, given the results that attention skills are predictive of academic achievement, this research is also testing the hypothesis that training attention will result in gains across cognitive domains important for academic success.

In one study we found that, after six weeks of high-intensity (100 min/day) training with a computerized intervention program designed to improve language skills, both children with SLI and typically developing children who received training showed both increases in standardized measures of receptive language as well as increases in the early attentional modulation following training (Stevens, Fanning, Coch, Sanders, & Neville, 2008) (Fig. 3). Similar gains were not observed in a group of typically developing children who did not receive the training, but were also tested and re-tested after six weeks (Stevens, *et al.*, 2008). In a second study, we examined the neural mechanisms of selective attention in kindergarten children who were either on-track in preliteracy skills or at-risk for reading failure. They were studied at the beginning and following the first semester of kindergarten, with the at-risk group receiving supplemental instruction with a reading intervention (Stevens, Currin, *et al.*, 2008; Stevens, *et al.*, in press). The at-risk group raised their performance on behavioral measures of preliteracy skills close to that of the on-track group by the end of the year and also showed larger increases in early attentional modulation. In both cases, increases in the early attentional modulation were accompanied

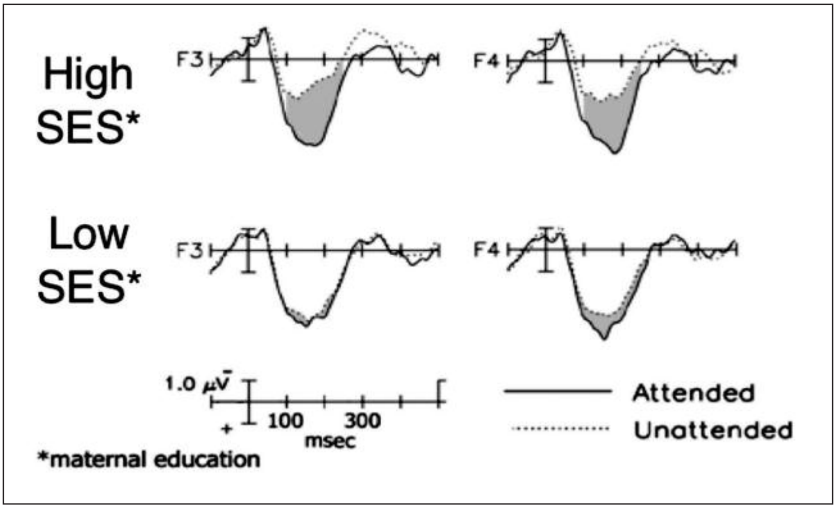

Figure 3. Data from the selective auditory attention ERP paradigm showing the early attentional modulation between 100-200 milliseconds in typically developing (TD) children and children with specific language impairment (SLI) before and after six weeks of daily, 100-minute computerized language training. Voltage maps of this early attentional modulation show where on the scalp this modulation (darker areas) is present. Following training, both children with SLI ($p < .05$) and typically developing children ($p < .1$) showed evidence of increased early attentional modulation which were larger than those made in a no-treatment control group ($p < .01$). This group showed no change in the early attentional modulation when retested after a comparable time period ($p = 0.96$). Data from Stevens, *et al.*, in press, *Journal of Learning Disabilities*. Permission pending.

by behavioral changes in other domains also targeted by the training programs, including language and preliteracy skills.

In our latest research, we have developed and implemented attention-training programs informed by basic research on the neuroplasticity of attention. We recently compared two models of an eight-week attention training program for preschool children in a randomized trial including children participating in half-day Head Start classrooms; the details of this study are discussed elsewhere (Stevens, *et al.,* 2010). The two programs, *Attention Boost for Children* (ABC) and *Parents and Children Making Connections – Highlighting Attention* (PCMC-A), both included a child-training component, as well as a family-based training component for parents, caregivers, and siblings (hereafter 'parents') of Head Start children.

For both the child and parent components, theory-informed and research-based activities and instructional methods were used to train attention and/or foster a less stressful and more cognitively stimulating home environment. The two programs differed in their relative emphasis (parent- versus child-training) and method of delivery (primarily outside of versus during the school day). The ABC model emphasized child-directed training in small groups (4-6 children: 2 adults). Child sessions lasted 40 minutes/day, four days per week, for eight weeks, and were held as pull-out sessions during the regular Head Start day. Across the eight-week program period, parents received three small group sessions lasting 90 minutes and four support phone calls, held in alternating weeks. The PCMC-A model emphasized parent training in eight weekly, two-hour classes that occurred in the evenings or on weekends, with seven phone calls from the instructor between meetings. The extended hours spent with parents in PCMC-A allowed for more in-depth instructional techniques. The child-directed portion of PCMC-A was an abbreviated version of the ABC child component (eight-session format versus 32-session). Child sessions were 50 minutes in duration and held concurrently with adult sessions.

The child component included a set of small group activities designed to increase self-awareness, self-monitoring, and self-regulation of attention and emotion states. In line with cognitive models of attention, the activities targeted aspects of attention including general alertness, selective attention (including the suppression of distractions), working memory, and switching between tasks. Activities also focused on the awareness of what it means and feels like to pay attention and strategies for emotion regulation, such as the use of full, deep breaths to calm down when feeling frustrated or upset.

The parent-directed component of both interventions included strategies delivered in small group format to address the goals of (a) family stress regulation with predictability, planning, and problem solving strategies, (b) consistent family structure with contingency-based discipline strategies, (c) cognitive instruction using visualization strategies (e.g., picture notes), (d) language enrichment strategies, and (e) knowledge of age-appropriate behavior and achievement across multiple domains, with a focus on attention. Parents also received information on the attention activities their children participate in, with suggestions for home-based implementation to provide further practice.

Prior to and following the eight-week program period, outcomes were assessed in both children and parents. Assessments of children included laboratory measures of cognition (nonverbal IQ, receptive language, preliteracy skills, and executive functioning) and parent and teacher ratings of children's social skills and problem behaviors. Assessments of parents included self-report measures of stress and parenting confidence/ability as well as direct observations of parents' language use and interaction behaviors with their children.

Across measures of both child and parent outcomes, strong support was found for the PCMC-A model relative to the ABC model. The more parent-focused program was associated with greater gains in nonverbal IQ and receptive language scores for children, as well as higher ratings of social skills and lower ratings of problem behaviors by parents. The more parent-focused program was also associated with higher levels of parents' perceived confidence and ability in parenting, as well as lower levels of parenting stress. Parents' functional language and interaction behaviors with their children additionally showed greater enhancements following the more parent-emphasized model of training. Taken together, these data support both the positive role of early childhood programs in supporting preschool children's attention and early school readiness skills, as well as the powerful role of parents and families in providing effective and comprehensive programs for children.

Gene-environment interactions

As discussed above, we have documented genetic effects on behavioral measures of cognition and an ERP measure of selective attention in preschool children from lower SES backgrounds. However, recent studies suggest that such genetic effects display plasticity that is dependent on and modified by environmental input including parenting quality, parental interventions, and small group interventions (e.g., Caspi, *et al.*, 2003; Caspi, *et al.*, 2002; Bakermans-Kranenburg & van Ijzendoorn, 2006; Bakermans-Kranenburg, van Ijzendoorn, Pijlman, Mesman, & Juffer, 2008; Sheese, Voelker, Rothbart & Posner, 2007). This is consistent with a vast and growing literature from studies of animals and humans documenting the processes by which environmental conditions in early life can up- and down-regulate gene expression and thus influence the phenotype over the lifetime of the individual (i.e., gene-environment interactions; for recent review, see Meaney, 2010).

A growing body of evidence suggests that environmental factors interact with, and actually modify, genetic effects on aspects of brain function and behavior. To investigate the degree to which the genetic effects we have reported may be modified by environmental input, we have recently begun to examine the effects of our interventions in preschoolers on behavioral measures of cognition and our ERP measure of selective attention as a function of genetic variability (Dennis, Bell, & Neville, in preparation; unpublished observations from our laboratory). We have observed interactions between groups of children who possess different variants of certain genes and their performance gains on behavioral measures of language, early literacy, and other cognitive measures, as well as the effects of selective attention on neural processing. Interestingly, in several cases the genetic variants associated with lower group pre-intervention scores were also associated with greater group gains as a function of the intervention, suggesting that these genetic variants confer a sensitivity to the environment such that environmental enrichment in the form of focused intervention may be particularly powerful. While further research is necessary, this raises the intriguing possibility that in the future genetic information could serve as a valuable tool in modifying learning environments and teaching strategies to better support children's cognitive and academic development. Indeed, a framework to guide future educational policy recently put forth recognizes the potential to leverage cutting-edge biodevelopmental research to inspire fresh thinking in educational policy (Shonkoff, 2010).

Conclusions

The importance of children's early school readiness skills has coincided with a burgeoning interest in training programs to support these skills in preschool aged children. While many programs emphasize child-only models of attention training, the present study supports more family-centered models of preschool intervention that incorporate parents and caregivers in more than a peripheral way. These findings also underscore the important role of parents and caregivers in providing a nurturing environment to support children's developing attention and school readiness skills, and their capacity to support meaningful change in the lives of their children.

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