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Associations between cortical thickness and neurocognitive skills during childhood vary by family socioeconomic factors

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ABSTRACT

Studies have reported associations between cortical thickness (CT) and socioeconomic status (SES), as well as between CT and cognitive outcomes. However, findings have been mixed as to whether CT explains links between SES and cognitive performance. In the current study, we hypothesized that this inconsistency may have arisen from the fact that socioeconomic factors (family income and parental education) may moderate the relation between CT and neurocognitive skills. Results indicated that associations between CT and cognitive performance did vary by SES for both language and executive function (EF) abilities. Across all ages, there was a negative correlation between CT and cognitive skills, with thinner cortices associated with higher language and EF scores. Similarly, across all cognitive skills, children from higher-SES homes outperformed their age-matched peers from lower-SES homes. Moderation analyses indicated that the impact of SES was not constant across CT, with SES more strongly predictive of EF skills among children with thicker cortices and more strongly predictive of language skills among children with thinner cortices. This suggests that socioeconomic advantage may in some cases buffer against a neurobiological risk factor for poor performance. These findings suggest that links between brain structure and cognitive processes vary by family socioeconomic circumstance.

1. Introduction

Extensive research has demonstrated socioeconomic disparities in brain structure and function (Brito & Noble, 2014; Hackman & Farah, 2009; Hackman, Farah, & Meaney, 2010; Lawson, Duda, Avants, Wu, & Farah, 2013; Luby et al., 2013; Menary et al., 2013; Noble, Grieve, et al., 2012; Noble, Houston, Kan, & Sowell, 2012; Noble et al., 2015; Noble, Korgaonkar, Grieve, & Brickman, 2013). However, it remains largely unknown how socioeconomic status (SES) shapes the development of brain structures and consequently affects cognitive performance. As brain development follows a nonlinear path (Giedd et al., 1999; Gogtay et al., 2004; Shaw et al., 2006), and varies from one cortical region to the next (Sowell et al., 2003), the association between socioeconomic status (SES) and children's cognitive development may be more pronounced at different stages of neural development and may relate more strongly to some cognitive processes relative to others (Casey, Giedd, & Thomas, 2000; Hackman & Farah, 2009). Several lines of evidence point to this possibility.

First, reported links between socioeconomic disparities and brain structure vary depending upon the morphometric property being studied. The evidence for associations among socioeconomic factors and cortical volume are mixed and discrepant, depending in part on which brain regions are investigated (Brito & Noble, 2014). Some studies report no associations (Brain Development Cooperative Group, 2012; Gianaros et al., 2007; Lange, Froimowitz, Bigler, Lainhart, & Brain Development Cooperative Group, 2010) whereas others do observe relations (Butterworth, Cherbuin, Sachdev, & Anstey, 2012; Cavanagh et al., 2013; Hair, Hanson, Wolfe, & Pollak, 2015; Hanson, Chandra, Wolfe, & Pollak, 2011; Hanson et al., 2013; Jednoróg et al., 2012; Luby et al., 2013; Noble, Grieve, et al., 2012; Noble, Houston, et al., 2012; Raizada, Richards, Meltzoff, & Kuhl, 2008; Staff et al., 2012). However, cortical volume is a composite measure of cortical surface area (SA) and cortical thickness (CT), two distinct properties of the cortex that have different cellular and genetic bases (Raznahan et al., 2011; Winkler et al., 2012). Both SA and CT have a dynamic and heterogeneous development throughout

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the lifespan and vary depending on a multitude of factors including an individual's age, IQ, and SES (Brito & Noble, 2014; Lawson et al., 2013; Mackey et al., 2015; Noble et al., 2015; Raznahan et al., 2011; Schnack et al., 2014; Shaw et al., 2006). Therefore, it is most appropriate to study these two cortical measures separately, as the composite metric of volume may oversimplify nuances in structural brain development. One study has reported a positive association between socioeconomic factors and SA (Noble et al., 2015), whereas the findings linking socioeconomic factors and CT have been mixed (Lawson et al., 2013; Mackey et al., 2015; Noble et al., 2015; Piccolo, Merz, He, Sowell, & Noble, 2016).

Secondly, the links between structural brain development and cognitive skills are also variable (Shaw et al., 2006). Cortical thickness has been related to cognitive outcomes, but not consistently, and associations are commonly specific to the particular brain region or cognitive function of interest. Indeed, longitudinal studies have demonstrated that it is the *trajectory* of cortical thickness, rather than the absolute value at any one time-point, that is most closely related to intelligence. In childhood, thinner cortices tend to be associated with higher IQ, whereas, in late childhood and beyond, thicker cortices tend to be related to higher IQ (Schnack et al., 2014; Shaw et al., 2006). Further, some studies have reported age-related localized cortical thickening in frontal and temporal regions during childhood and adolescence (Shaw et al., 2008; Sowell et al., 2004). In relation to brain and behavior, studies have observed an association between thicker cortices in the inferior frontal gyrus and better visual-motor processing in late adolescents/young adults (Menary et al., 2013), as well as an association between thicker cortices in the middle frontal gyrus and increased long-term verbal memory in adults (Walhovd et al., 2006). On the other hand, frontal lobe gray matter thinning has been predictive of better verbal learning (Sowell, 2001), verbal fluency (Porter, Collins, Muetzel, Lim, & Luciana, 2011), and working memory scores (Kharitonova, Martin, Gabrieli, & Sheridan, 2013; Tamnes et al., 2010) in children and adolescents.

Finally, when studies have examined whether SES and CT independently account for differences in cognitive performance, findings have been mixed. For example, Mackey et al. (2015) analyzed data from a sample of 58 adolescents and observed that higher family income was associated with greater CT in all lobes of the brain, with greater CT associated with better standardized test performance in reading and math. In contrast, in a sample of 1099 children and adolescents, Noble et al. (2015) did not find associations between either parental education or family income and CT. Further, although these authors reported that cortical surface area mediated links between family income and specific neurocognitive skills, cortical thickness did not.

These inconsistencies could potentially be explained if the relation between CT and cognition varies as a function of socioeconomic factors, as opposed to CT and SES each accounting for independent, unique variance in cognition. Indeed, past work has suggested that SES may serve as a moderating role in explaining age-related differences in brain structure (Noble, Grieve, et al., 2012; Piccolo et al., 2016) as well as in explaining links between brain function and behavior (Noble, Wolmetz, Ochs, Farah, & McCandliss, 2006). Therefore, using the same dataset as Noble et al. (2015), we hypothesized that, rather than CT mediating links between SES and cognitive performance, SES may moderate (either buffer or amplify) associations among brain structures and neurocognitive skills during childhood. In addition, we hypothesized that SES moderation may be most prominent in certain regions of interest (ROIs) in which CT has previously been related to cognitive function (Kharitonova et al., 2013; Lawson et al., 2013; Mackey et al., 2015; Menary et al., 2013; Porter et al., 2011; Walhovd et al., 2006). These included regions associated with vocabulary and oral reading (left inferior frontal gyrus, left superior temporal gyrus, and left fusiform gyrus), as well as those associated with working memory, attention/inhibition and cognitive flexibility (middle frontal gyrus and anterior cingulate cortex).

Table 1
Sample demographics (N = 1091).

	Mean (SD; Range) or N (%)
Age (years)	11.9 (4.9; 3.0–20.9)
Sex	
Male	562 (51.5%)
Female	529 (48.5%)
Parental education (years)	15.57 (2.23; 6–18)
Family Income	$97,878 ($76,756; $4,500–325,000)
Genetic ancestry	
African	0.12 (0.26; 0–1)
American Indian	0.05 (0.11; 0–1)
Central Asian	0.02 (0.12; 0–1)
East Asian	0.16 (0.31; 0–1)
European	0.64 (0.37; 0–1)
Oceanic	0.01 (0.03; 0–1)

Note. GAF data show mean, standard deviation, and range across all subjects of the estimated proportion of genetic ancestry for each reference population.

2. Methods

2.1. Participants

Data used in this study were collected as part of the multi-site Pediatric Imaging, Neurocognition, and Genetics (PING) study and obtained from the PING Study database (http://ping.chd.ucsd.edu). Participants were recruited through a combination of web-based, word-of-mouth, and community advertising at nine university-based data collection sites in and around the cities of Los Angeles, San Diego, New Haven, Sacramento, San Diego, Boston, Baltimore, Honolulu, and New York. Participants were excluded if they had a history of neurological, psychiatric, medical, or developmental disorders. In this study, analyses were conducted on the 1091 participants, ranging from 3 to 20 years old ($M = 11.9$, $SD = 4.9$). All participants and their parents gave their informed written consent/assent to participate in all study procedures, including whole genome SNP genotype, demographic and developmental history questionnaires, and high-resolution brain MRI (see Table 1 for demographics). Each data collection site's Office of Protection of Research Subjects and Institutional Review Board approved the study.

2.2. Measures

2.2.1. Socioeconomic status

Parents were asked to report the level of educational attainment for all parents in the home. Parents were also asked to report the total yearly family income. Data were not collected on the number of adults and children in the home, and therefore income-to-needs ratios were unable to be calculated. Both parental education and family income data were originally collected in bins, which were recoded as the means of each bin (Noble et al., 2015). Family income was natural log-transformed for all analyses due to the typically observed positive skew.

2.2.2. Genetic collection and analysis

Saliva samples were sent to Scripps Translational Research Institute for analysis. Once extracted, genomic DNA was genotyped with Illumina Human660W-Quad BeadChip. Replication and quality control filters (i.e., sample call rate > 99, call rates > 95%, minor allele frequency > 5%) were performed. To assess genetic ancestry and admixture proportions in the PING participants, a supervised clustering approach implemented in the ADMIXTURE software was used (Alexander & Lange, 2011). A genetic ancestry factor (GAF) was developed for each participant, representing the proportion of ancestral descent for each of six major continental populations: African, Central Asian, East Asian, European, Native American and Oceanic. Information on PING genetic collection and analysis is described in detail in