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Effect of Family Socioeconomic Status on Brain Structures Involved in Statistical Learning in
Children

by

Leyla Eghbalzad

Under the Direction of Şeyda Özçalışkan, PhD & Christopher Conway, PhD

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of

Doctor of Philosophy

in the College of Arts and Sciences

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2021

ABSTRACT

Children's early ability to implicitly learn the underlying patterns in their environment, also known as statistical learning (SL), is a crucial component of typical cognitive development. SL is essential for visual perception and language processing in infants, children, and adults. However, previous studies have not explored the association between children's environment and underlying neural mechanisms of SL ability in children. Socioeconomic status (SES) is one of the most important indicators of the quality of this environment. Children who live in low SES families have less exposure to cognitive and linguistic stimulation and show atypical structural and functional neural patterns compared to those with high SES. In this study, I explored the influence of SES (i.e., parental education level and household income) on gray matter volume of brain regions involved in SL ability in 232 healthy children ages 5-12 years recruited by the Human Connectome Project. These brain regions consisted of sensory/perceptual (primary visual and auditory cortices) and frontal/subcortical (Broca's area and caudate nucleus) regions previously reported to be involved in SL. In addition, I investigated the role of age in the potential interaction of SES with differences in these brain structures. The findings showed neither SES measure to be a predictor of variance in the volume of sensory/perceptual brain regions. In contrast, parental education was a strong predictor of variance in volume of one of the frontal/subcortical regions, namely caudate nucleus. Age, however, did not influence the association between SES measures and either region of interest. This study is the first to explore the influence of various SES factors on gray matter volume of sensory/perceptual and frontal/subcortical regions involved in SL in children.

INDEX WORDS: Socioeconomic status (SES), Structural magnetic resonance imaging (sMRI), Statistical learning, Cognitive development, Parental education, Household income

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August 2021

DEDICATION

I dedicate this dissertation project to my family and friends for their endless love and support during my doctoral training.

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1 INTRODUCTION

One important early emerging cognitive ability in children is the ability to detect and encode statistical patterns in the environment—a process known as *statistical learning*—which allows children to predict upcoming sensory events (Conway, 2020; Saffran et al., 1996). Statistical Learning (SL) can take place without conscious awareness (Cleeremans & McClelland, 1991) and the detection of underlying patterns in the environment may be processed either simultaneously in the visual domain (e.g., pictures; Fiser & Aslin, 2001) or sequentially in the auditory domain (e.g. musical tones; Creel, Newport, & Aslin, 2004). SL is a crucial component of visual perception (Fiser & Aslin, 2002; Turk-Browne, Jungé, & Scholl, 2005), music perception and production (Creel, Newport, & Aslin, 2004), and language processing in infants (Saffran, Aslin & Newport, 1996; Shafto, Conway, Field & Houston, 2012), children (Kidd & Arciuli, 2016; Lum et al., 2012), and adults (Christiansen, Conway, & Onnis, 2012; Misyak, Christiansen, & Tomblin 2010). Even though earlier research suggests that SL ability plays an important role in various cognitive abilities, there is no work—except for Eghbalzad, Deocampo, and Conway, 2020—that has explored the influence of social and environmental factors on SL ability, highlighting it as an important domain in need of further research. The main goal of this study is to fill in this important gap by examining the relationship between social factors and morphology (specifically gray matter volume) of brain regions associated with SL in children ages 5-12 years, using the Human Connectome Project-Development (HCP-D) archived dataset.

1.1 Role of Statistical Learning in Language and Perception

Over the past few decades, various studies have demonstrated the importance of SL ability in development of language. For instance, in a well-known word-segmentation study conducted by Saffran, Aslin, and Newport (1996), after only 2 minutes of exposure to novel speech input, 8-

month-old infants demonstrated an ability to segment words from the auditory speech stream by learning the transitional probabilities between the syllables, suggesting that young infants can detect these probabilities in the auditory input. Shafto and colleagues (2012) take these findings one step further investigating the relationship between SL, auditory perception (i.e., language) and visual perception (i.e., gesture comprehension) in 8- to 13-month-old infants. Using infants' looking time onset at the appropriate location of the upcoming stimulus as an index of their reaction time, they showed that the infants' SL ability on this visual serial reaction time task was correlated with their vocabulary comprehension at the time of testing (at 8 months) and with their gesture comprehension 5 months later demonstrating the essential role of SL in children's acquisition of age-relevant language skills.

Focusing on the role of SL in perceptual domains, numerous studies have examined the effect of statistical learning in visual and auditory domains. In a study by Fiser and Aslin (2002), examining the role of SL in visual perception, adult participants viewed an animation of moving shapes across the screen for 6 minutes without any specific task. These participants were not aware of the embedded sequences underlying presentation of these shapes as 'triplets'; however, in a surprise forced-choice familiarity task, they correctly identified 95% of shape-triplets as familiar, suggesting that statistical visual sequences can be learned with only 6 minutes of exposure. In a similar study by Turk-Browne, Jungé, & Scholl (2005), adult participants were able to learn underlying statistical patterns between shapes that were presented in temporal sequences even when instructed to only identify repetitions of presented shapes. Their results thus suggest that adults learn embedded statistical patterns in visual stimuli without explicit instructions.

As part of a larger study, Conway and Christiansen (2005) conducted an experiment to investigate auditory SL ability in adults. During the training phase, the participants listened to sequences of pure tones of varying frequencies with underlying embedded patterns. During testing, the participants listened to new sequences as well as sequences with same underlying patterns as the training phase; they were then asked to report whether any of the sequences sounded familiar to them. The authors reported that participants correctly recognized 75% of auditory sequences as familiar without having explicit knowledge of the underlying patterns, suggesting that SL plays an important role in perception of patterns embedded in tonal sequences. Overall, the existing studies, thus, demonstrate the essential role SL plays in various processes—from audition and vision to language.

1.2 Developmental Trajectory of Statistical Learning

Various studies have explored the role of age in SL ability from childhood to adulthood (Arciuli, 2017; Arciuli & von Koss Torkildsen, 2012; Arciuli and Simpson, 2011; Arciuli and Conway, 2018; Raviv and Arnon, 2017; Daltrozzo & Conway, 2014; Janacsek, Fiser, Nemeth, 2012). However, the results are not consistent across these studies. For example, Arciuli and Simpson (2011) found an increase in visual SL ability with age in a sample of children ages 5 to 12 years and suggested that late period of neural development of fronto-parietal regions involved in SL ability may underlie their findings. In a cross-sectional study investigating the influence of age on SL ability, Raviv and Arnon (2017), in their sample of 5- to 12-year-olds, reported that older children performed better on a visual SL task, whereas performance on linguistic auditory SL task remained unchanged across this age range. In a follow-up study, Shufaniya & Arnon (2018) investigated the effect of age on SL ability in 5- to 12-year-old children. Different from earlier work, however, they changed the auditory SL task from linguistic to a non-linguistic task.

Their results showed that visual and auditory SL ability both improved with age. Accordingly, they concluded that lack of age-related change reported in the original study (Raviv & Arnon, 2017) was related to the linguistic nature of the auditory task but not the modality-specific input. These findings suggest that in non-linguistic stimuli, regardless of input modality, SL ability shows an effect of age with steady improvements from age 5 to 12 years.

In a related vein, Janacsek, Fiser, and Nemeth (2012) found that across 400 individuals with ages between 4 to 85, 4- to 12-year-olds showed the highest statistical learning effect, as measured by their reaction time in a serial reaction time task. This learning effect started to decline after age 12 through late adulthood. However, accuracy scores showed a different trajectory. The accuracy scores on the serial reaction time task were lowest in children and older adults, with middle age adults showing the highest accuracy. Thus, they suggested that SL may consist of distinct, but related, learning systems with different developmental trajectories. Related to these findings, in an extensive review of the literature on age-related changes in SL, Conway (2020) proposed that SL consists of 2 distinct mechanisms with different developmental trajectories. One is the *implicit/bottom-up* mechanism which is involved in learning simple patterns and associations in various modalities (e.g., visual, auditory). This system is present during infancy (Saffran et al., 1996; Pelucchi et al., 2009) and involves automatic processing of stimuli without needing much attention. This system must be available early in development to create a foundation for learning more complex regularities in the environment later on (Daltrozzo & Conway, 2014). The second system is the *explicit/top-down* mechanism which is present during early childhood (Cameron-Faulkner et al., 2003; Thomas et al., 2004) and is involved in learning more complex/abstract patterns which require attention and executive function

processes. Following this framework, it is important to consider SL ability as a multi-mechanism system with different developmental trajectories evident in each mechanism.

1.3 Neural Mechanisms of Statistical Learning

Most of the earlier work that focused on SL used behavioral measures (e.g., reaction time) and only a few have investigated neural mechanisms associated with SL—a difference that is particularly pronounced in studies with children. Neuroimaging studies on adults have highlighted involvement of 2 types of neural networks during SL which map onto those proposed by Conway (2020): *sensory/perceptual networks* (Karuza, et al., 2013; McNealy, et al., 2006; Turk-Browne et al., 2009, 2010) that rely on bottom-up processing and *frontal and subcortical networks* (Conway & Pisoni, 2008; Karuza, et al., 2017; McNealy et al., 2006; Schapiro, Gregory, Landau, McCloskey, & Turk-Browne, 2014; Turk-Browne et al., 2009) that use more top-down processing. Research examining *sensory-specific networks* in SL processing in adults showed involvement of temporal regions such as the superior temporal gyrus in auditory SL tasks (Karuza, et al., 2013; McNealy, et al., 2006) and involvement of medial occipital (Turk-Browne et al., 2010) and lateral occipital areas (Turk-Browne et al., 2009) in visual SL tasks. Another study, also with adult participants, examining top-down associations in *frontal and subcortical networks* showed involvement of the prefrontal cortex (Conway & Pisoni, 2008; McNealy et al., 2006; Turk-Browne et al., 2009), Broca's area (Bahlmann, Schubotz, & Friederici, 2008; Petersson, Folia, & Hagoort, 2012; Uddén, Ingvar, Hagoort, & Petersson, 2017) as well as subcortical regions such as basal ganglia (Conway & Pisoni, 2008; Hikosaka et al., 1999; Ulanet et al., 2014; Karuza, et al., 2017) and hippocampus (Karuza, et al., 2017; Schapiro, Gregory, Landau, McCloskey, & Turk-Browne, 2014) during SL tasks. In addition to magnetic resonance imaging studies mentioned above, Christiansen et al. (2012) reported possible overlap

between neural mechanisms utilized for top-down cognitive abilities (i.e., processing syntactic rules of English) and SL ability in adults by using electroencephalography (EEG). They reported evidence of the same ERP component (P600; elicited by a “grammatical” error) during both an English reading task and an SL task suggesting involvement of higher-order networks during SL.

Studies investigating the neural basis of SL ability in children remain relatively scarce. Of the few existing studies, Finn, Kharitonova, Holtby, and Sheridan (2019) conducted a structural MRI study investigating the morphometric differences (i.e., gray matter thickness and volume) underlying SL in 5- to 8-year-old children on *a priori* regions of interest (ROIs), namely hippocampus, Broca’s area (left inferior prefrontal cortex), and the caudate nucleus (a subsection of basal ganglia). They reported that cortical thickness—a morphometric measure highly associated with gray matter volume—of Broca’s area and volume of the right hippocampus predicted SL ability in children. They also found an interaction between age and cortical thickness, showing that in older children (older than 6;11) the right hippocampus thickness strongly predicted performance on SL tasks compared to younger children (younger than 6;11). The authors concluded that differences in SL ability can be explained by neural mechanisms underlying memory and learning processes associated with hippocampus as well as language and top-down control processes associated with prefrontal cortex (Leung, Gore, & Goldman-Rakic, 2002; Xang, Leung, & Johnson, 2003)—a finding that is consistent with aforementioned studies with adults (e.g., Conway & Pisoni, 2008; Karuza, et al., 2017; McNealy et al., 2006; Schapiro, Gregory, Landau, McCloskey, & Turk-Browne, 2014; Turk-Browne et al., 2009) . Another study examining neural basis of SL in children (ages 9;6-10;7) by McNealy, Mazziotta, and Dapretto (2010) employed fMRI to explore brain activity in children during a visual task consisting of statistical regularities and random items. They reported increased activity of temporal cortices

and left inferior frontal cortex in association with processing statistically regular items in the task, suggesting the involvement of these regions in SL.

In a more recent fMRI study (Conway et al., 2020), which also forms the basis for the proposed study, researchers investigated underlying neural structures involved in processing errors in SL patterns in adults. Adults were presented a visual artificial grammar-learning task in which sequences of printed nonsense syllables containing adjacent (e.g., "A-B") versus nonadjacent (e.g., "A-X-B") dependencies were presented—with the assumption that the latter impose cognitive demands (Gómez, 2002; Newport & Aslin, 2004). After incidentally learning these grammatical sequences, 20 healthy adults made familiarity judgments on either novel *grammatical* sequences with no adjacent dependency violations or novel *ungrammatical* sequences with adjacent dependency violations. The results showed that violation of adjacent dependencies (i.e., ungrammatical sequences with adjacent dependency violations) was associated with increased blood oxygen-level dependent (BOLD) activation in both occipital and frontal regions compared to grammatical sequences. Activation of these modality-specific sensory regions, such as the lateral occipital cortex, during implicit SL has also been reported in previous studies (e.g., Conway & Pisoni, 2008; Frost et al., 2015). In addition, results showed increased activation in prefrontal cortex, specifically Broca's area and frontal pole, which previously has been associated with language production (Caplan, 2006; Gewe et al., 2005; Rodd, Davis, & Johnsrude, 2005) working memory (Sarnthein et al., 1998), goal-directed positioning and maintenance of attention (Hopfinger, Buonocore, & Mangun, 2000), as well as directing attention and detection of unexpected stimuli (Conway & Pisoni, 2008; Corbetta, Kincade, Ollinger, McAvoy, & Shulman, 2000; Folia & Petersson, 2014). These results suggest that learning and processing of adjacent sequential dependencies (i.e., SL) involve a distributed

network that mediates both sensory/perceptual and higher-order operations in frontal/subcortical networks. Conway and colleagues (2020) added that violation of nonadjacent dependencies (i.e., ungrammatical sequences with nonadjacent dependency violations) was associated with increased BOLD activation in subcallosal and paracingulate cortices as well as anterior cingulate cortex (ACC). Previous studies have reported activation of these regions to be associated with error detection, inhibition, and distribution of attention resources (e.g., Nebel et al., 2005; Nobre et al., 1997; Woodward et al., 2006). In sum, the detection of violations of dependencies appear to involve distinct neural networks, consistent with recent proposals that statistical-sequential learning is not a unified construct but depends on the interaction of multiple neural mechanisms acting together (Conway, 2020; Daltrozzo and Conway, 2014). The results from Conway et al., (2020), in addition to providing possible answers to questions on the underlying neural mechanisms of SL ability in adults, also raise new questions about the development and plasticity of brain regions involved in SL.

The reviewed neuroimaging results suggest that the underlying mechanisms of SL include a distributed network of neural processes involved in modality-specific perception, learning, memory, and executive function, all working together to detect and process statistical regularities in the input (Arciuli, 2017; Conway, Deocampo, Smith, & Eghbalzad, 2016; Daltrozzo & Conway, 2014; Frost, Armstrong, Siegelman, & Christiansen, 2015; Sawi & Rueckl, 2018; Thiessen, Kronstein, & Hufnagle, 2013). Collectively, the reported results also provide support for the idea that SL is mediated by two primary sets of neural networks (Arciuli, 2017; Conway & Pisoni, 2008; Daltrozzo & Conway, 2014; Frost et al., 2015; Conway, 2020): areas involved in *bottom-up* processes (i.e., sensory/perceptual regions involved in perception; Karuza, et al., 2013; McNealy, et al., 2006; Turk-Browne et al., 2009, 2010) and another that

comprises domain-general brain regions involved in *top-down* processes (frontal and subcortical regions involved in memory and attention; Conway & Pisoni, 2008; Karuza, et al., 2017; McNealy et al., 2006; Schapiro, Gregory, Landau, McCloskey, & Turk-Browne, 2014; Turk-Browne et al., 2009).

In summary, SL ability is found to play a critical role in typical development of language and perception (auditory and visual). This ability involves at least two underlying systems which include two primary sets of neural networks. The *bottom-up* system, present from birth, comprises modality-specific areas (sensory and perceptual regions) and facilitates learning sensory structures in the input. Conversely, the *top-down* system involves domain-general brain regions (frontal and subcortical) and facilitates learning more abstract structures of input which continues to develop through childhood and adolescence. The reviewed findings emphasize the importance of considering SL as a cognitive ability with multiple underlying neural components with distinct developmental periods, however, studies investigating the role of environmental factors on SL and its neural correlates are scarce.

1.4 Construct of Socioeconomic Status

Like any other cognitive ability, it is possible that SL ability is not just the product of multiple neural components working together. It may also be the outcome of these neural components interacting with environmental factors that children are exposed to, such as financial stability, nutrition, safety, medical access, and education. Among various such factors, one of the most important indicators of the quality of environment is family socioeconomic status (SES). SES consists of many distinct, but interrelated components which can individually and/or cumulatively influence children's development. These components include, but are not limited to, parental education level (e.g., Brito & Noble, 2014; Hoff, Tian, 2005; Hupp et al, 2011;

Mueller & Parcel, 1981; Noble et al., 2007; Roberts et al., 1999; Sheridan, et al, 2012; Stanton-Chapman, et al, 2002), household income (e.g., Betancourt, et al., 2016; Hanson et al, 2011; Hottenlocher et al, 2010; McLoyd, 1998; Noble et al., 2012; Noble et al., 2005; Petterson & Albers, 2001; Romeo et al, 2018; Sirin, 2005), home environment (Davis-kean, 2005; NICHD Early Childcare Research Network, 2000), neighborhood safety, maternal mental health (Pan, Rowe, Singer & Snow, 2005; Petterson & Albers, 2001), school type (Ardila, 2005), and stress level of the child (Brito & Noble, 2014; Noble et al., 2012; Sheridan, et al, 2012).

Numerous studies have found a relationship between children's SES level and academic outcomes mediated by behavioral and/or neural measures (Feldman et al., 2003; NICHD, 2000; Pan, Rowe, Singer, & Snow, 2005; Hoff et al., 2012). Children who live in low SES families are reported to have less exposure to cognitive and linguistic stimulation (Hart & Risley, 1995; Rowe and Goldin-Meadow, 2009) and experience more stress in their environment (Sheridan et al., 2012). This experience detrimentally impacts their language and cognitive development and leads to poor academic performance (U.S. Census Bureau, 2017). Therefore, it is of great importance to investigate the impact of SES on the neural structures underlying development of SL in children.

1.5 Neurocognitive Mechanisms Affected by Socioeconomic Status

SES impacts neurocognitive development in a number of ways. For instance, some studies have investigated the influence of SES on morphometric properties (e.g., volume, thickness, and surface area) of various brain regions in children. For instance, Noble and colleagues (2012) analyzed morphometric properties of the amygdala and hippocampal regions by using structural brain imaging in participants between ages 5 and 18 years from various SES level households. They measured SES by collecting data on parental education and calculating the participants'

income to need ratio (i.e., dividing total household income by the federal poverty level reported for a household of that size). The results showed that those with lower parental education displayed larger amygdala volumes. According to Tottenham et al. (2010), a larger amygdala volume in humans may be related to increased exposure to stress. Noble and colleagues (2012) posited that, from an evolutionary perspective, the brain needs a larger amygdala to learn more of what to fear since there is more fear to be discovered in the environment. Noble et al., also found smaller hippocampal volume in participants with lower SES, which they attributed to inhibition of neurogenesis caused by increased exposure to stress prenatally and during infancy. Looking further into the influence of SES on the brain, Betancourt et al. (2016) reported differences in gray matter volume in infants (ages 4-6 weeks) from high and low SES households. Infants with lower SES had smaller cortical gray and deep gray volumes, substantiating the influence of SES on subcortical regions such as basal ganglia and hippocampus. The authors also suggest that stressors that are more directly related to income, such as limited access to material resources, have a greater influence on the development of these subcortical regions compared to stressors that are more closely tied to parental education, such as parenting style or cognitive stimulation.

In addition to reported structural brain differences in children with various SES levels, Brito and Noble (2014) proposed a model with two main pathways by which functioning of certain brain regions relates to SES: linguistic exposure and stress. They suggested that SES is related to development of syntactic ability through the effect of linguistic environment on left inferior frontal gyrus. Furthermore, they proposed that SES is related to memory via the influence of stress on hippocampus, amygdala, and prefrontal cortex (Brito & Noble, 2014). In support of this model, there is increasing evidence suggesting that SES can impact brain regions that are

associated with executive function and language. For instance, Romeo et al. (2018) reported that children's SES, as measured by parental education level, was directly related to children's performance on lexical and syntactic tasks. More importantly, this relationship was mediated by activation in the left inferior frontal gyrus (IFG) during a narrative task. In this fMRI task, children (ages 4-6) passively listened to simple stories about events that children are likely to be familiar with. The participants were divided into 2 groups: those who heard normally-narrated stories and those who heard stories in reverse. The group with normal narration showed a higher activation in the left superior temporal sulcus. Notably, children who had more linguistic exposure at home showed higher activation in left IFG compared to those with less exposure. These results suggest that children with low SES, who are not receiving rich linguistic input from their environment, may be at higher risk of experiencing lower activation in certain brain regions involved in lexical and syntactic processing which provides support for the linguistic exposure pathway proposed in the model by Brito & Noble (2014).

Another fMRI study on 8- to 12-year-old children from low and high SES homes (Sheridan et al., 2012) provided further support for the model proposed by Brito & Noble (2014). During the fMRI task, children participated in a stimulus-response mapping task in which they had to learn to associate one of four buttons with a certain family of stimuli and another button with the second family of stimuli. This rule learning task has been associated with high prefrontal cortex activity. The results showed excessive activation of the prefrontal region in children with low SES which could be due to those children needing more time to learn the associations, thus resulting in greater reliance on the prefrontal brain region (Sheridan et al., 2012). Conversely, children from high SES homes were exposed to a more complex linguistic input, leading to improved prefrontal cortex function with lower activation levels. The authors added that children

from low SES homes had experienced more pronounced changes in their cortisol levels, likely to be an outcome of their exposure to greater stress during development which resulted in less efficient prefrontal cortex function. These results suggest that chronic exposure to high stress leads to a decrease in neural dendritic spines in prefrontal cortex. A decline in the number of these spines, in turn, makes it more difficult to transmit messages between neuronal networks in prefrontal cortex. Sheridan and colleagues (2012) refer to this phenomenon as “biological embedding” of SES. These results may further hint that the effects of environmental stressors, such as economic and social stressors, may cause physiological changes very early in children’s lives.

Surprisingly, given the extensive neuroimaging research exploring SES and neurocognitive mechanism, there is only one study that has investigated the relationship between SES and SL ability in children. Eghbalzad and colleagues (2016) used the EEG technique to measure SL ability during a visual predictor-target SL task. In this task, the participants were presented with sequences of flashing stimuli which consisted of “standard”, “predictor”, and “target” stimuli; predictors were followed by targets with varying transitional probabilities. Some predictors were followed by targets 80% of the time (high predictability condition) and others were followed by targets 20% of the time (low predictability condition). The participants were instructed to press a button as fast as they can to “catch” the targets, without being aware of the transitional properties underlying the sequences. SL performance (measured by the difference in ERP amplitude between 2 conditions) moderated the relationship between SES and syntactic comprehension scores in children. They reported that children with low SES appeared to have better syntactic ability only if they performed well on the SL task. In other words, the negative effect of low SES on syntactic ability appeared to be dampened by high SL ability. Thus,

children who were raised in households with lower SES showed more typical language scores if they had good SL skills. Conversely, for children with lower SL ability, their syntactic comprehension was more directly related to the level of their SES. Although this study addresses an important gap in the literature regarding the effect of social environment on neural processing of SL, it does not specify which underlying neural networks (involved in SL) are influenced by children's environment and in what way (e.g., structural vs. functional differences). Thus, new studies need to explore individual differences in development of neural structures underlying SL.

2 CURRENT STUDY

Most of the earlier work that investigated the neural basis of SL ability is focused on adults and very few studies have focused on children (Finn, Kharitonova, Holtby, & Sheridan, 2018; McNealy, Mazziotta, & Dapretto, 2010). Moreover, except for the study by Eghbalzad, Deocampo and Conway (2020), none of the previous studies have investigated the neural components of SL in children who are exposed to environmental adversity. This stands out as an important gap in the literature because SES is one of the most important indicators of the quality of environment and has a great influence on children's development. In this study, I investigated the influence of the two most commonly used indicators of SES (parental education and household income), on cortical and subcortical volume of brain regions associated with SL ability in children between 5;0-12;11 years of age.

2.1 Study Aims and Hypotheses

The first aim of this study was to examine the influence of SES on the morphology of two key systems associated with SL, namely the gray matter volume of *bottom-up* sensory-perceptual regions and *top-down* frontal/subcortical brain regions in school-aged (5-12) children, using structural imaging methodology. The second aim was to investigate whether children's age

played a role in the influence of SES on morphometric properties of brain regions involved in SL. Earlier research showed that non-linguistic SL ability improves with age during childhood (Arciuli & Simpson, 2011; Shufaniya & Arnon, 2018; Conway, 2020), but it is not clear whether age will influence underlying neural properties of regions associated with SL ability, particularly in the presence of environmental adversity (i.e., lower SES). I have attempted to answer 2 questions, each tied to a specific aim:

1. *How does SES influence the volume of sensory/perceptual regions (lateral occipital and primary auditory cortices) differently from the volume of frontal/subcortical brain regions (Broca's area and caudate nucleus) in young children?*

Previous studies conducted on the influence of SES on structural development of the brain do not report a direct effect of SES on sensory perceptual regions (see a review by Brito & Noble, 2014). The lack of a reported association may be due to the early developmental trajectory of these regions and shorter period of exposure to environmental adversity. This short time-window may be a protective factor, resulting in typical development of fundamental sensory areas in the brain. However, contrary to sensory/perceptual regions, research suggests a strong influence of SES on development of higher-order cognitive skills and the frontal/subcortical brain regions involved in these skills (D'Angiulli, Herdman, Stapells, & Hertzman, 2008; Betancourt, et al., 2016; Brito & Noble, 2014; Farah et al., 2006; Garcia-Sierra, Ramirez-Esparza & Kuhl, 2016; Hanson et al, 2011; Noble et al., 2012; Noble et al., 2007, 2005, 2006; Romeo et al, 2018; Sheridan, et al, 2012). Based on these findings, I predicted that there

will be no association between SES and volume of sensory/perceptual areas, however, based on earlier research (Sheridan et al, 2012), that showed impairments in the prefrontal cortex in children from low SES families due to excessive activation of HPA (hypothalamic-pituitary-adrenal) axis caused by chronic stress, I expected to see a negative effect of SES on the frontal/subcortical brain structures (Broca's area and caudate nucleus), resulting in smaller volumes in children from families with low SES.

2. *What is the added effect of age in the influence of SES on sensory/perceptual and frontal/subcortical brain regions involved in SL?*

Previous research (e.g., Brito & Noble, 2014) exploring differences in brain morphology of children from varying SES environments, showed no effect of SES on sensory/perceptual regions even after controlling for age. To my knowledge, there is no research that has yet examined the role age plays on the effect of SES on frontal/subcortical regions. One possibility is that in children with low SES, the brain regions that take longer to develop are also exposed to environmental deprivation for a longer period of time compared to those regions that are developed much earlier (e.g., prefrontal cortex, Petanjek et al., 2011; Tsujimoto, 2008); as such the negative effect of lower family SES on prefrontal areas may only be evident in later childhood or early adolescence (Brito & Noble, 2014). Based on these earlier findings, I predicted that the relationship between SES and sensory/perceptual regions would not be affected by child age. In contrast, I expected that age would play a mediating role in the association between SES and frontal/subcortical regions associated with SL.

3 METHOD

3.1 Participants

The data for this study were derived from an archival database of healthy participants collected by the Lifespan Human Connectome Project-Development (HCP-D)¹. HCP-D is a national project launched at 4 different sites in the United States (Somerville, et al., 2018) and is freely available under the approval of National Institute of Mental Health data archive (approval obtained by Leyla Eghbalzad on 11/5/2019; renewed on 11/5/2020). This database consists of demographic, neuropsychological, and neuroimaging data collected from 665 healthy participants, between ages 5-21. The structural imaging data were available for download in 2018 and the demographics data (e.g., SES) were released in the Spring of 2021. As depicted in Figure 1, out of 665 healthy participants, 244 were between ages 5;0-12;11 and had both imaging and parental education data available. Out of 244 participants, one participant was excluded due to poor quality of imaging data (see *section 3.3.3*) which resulted in a sample size of 243. From these 243 participants, 232 reported income data. In this database, the exclusion criteria for healthy participants included (1) presence of safety concerns (harming self or others) and (2) any atypicality in cognitive, behavioral, or neurological assessments. All participants provided written assent in addition to written consent from their parents or guardians.

The age range of 5;0 to 12;11 in this study provided an appropriate time window for two reasons: (1) at age 5, children show steady improvements in SL ability as reported in previous work (Arciuli and Simpson, 2011; Raviv and Arnon, 2017), and (2) age 12 is when the effect of

¹ Originally, I had proposed to use data from 2 datasets: HCP-D and Healthy Brain Network (HBN). However, after pre-processing brain images from HBN, I found majority of the images to be of low quality due to excessive motion in the scanner in this age range. Therefore, I decided not to include data from HBN database in my study. Even though this narrowed my originally proposed sample size from 331 to 232, a power analysis with one less control variable in the regression models (i.e., database) showed enough power to detect reliable effects (see *section 3.2* for more details).

age on SL ability is reduced, based on earlier work (Janacsek, Fiser, and Nemeth, 2012) that showed that implicit learning (e.g., SL) becomes stable and does not improve after age 12.

In this earlier work, researchers also argued that it was around age 12 that children begin to show sensitivity to more complex aspects of the environment and rely more on model-based interpretations of prior implicit learning experiences acquired during early childhood (Orban, Fiser, Aslin & Lengyel, 2008). At the same time, the significant changes in sensitivity to more complex aspects of environment around 12 years of age may be associated with structural changes in the brain beginning after age 12, further marking age 12 as the appropriate cut-off point in examining effect of age in this study.

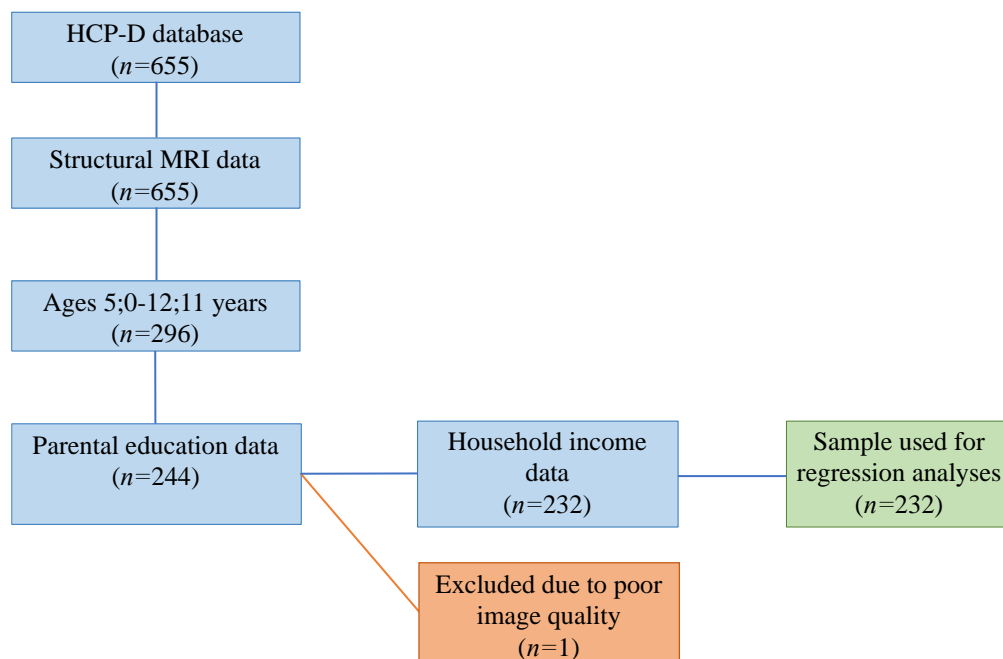


Figure 1. Flow Diagram of Available Data from HCP-D Dataset.

3.2 Power Analysis

According to a sensitivity power analysis using G*Power 3 tool (based on G*Power by Erdfelder, Faul, & Buchner, 1996), the sample size of $N = 232$ will give 95% power (alpha level of .05) to detect a marginally small effect size ($f^2 = 0.07$) for the proposed analyses of multiple hierarchical regression with 3 independent variables and 3 covariates (see section 4.3). In addition, previous studies have not reported significant volumetric differences between low vs. high SES groups in the set of brain regions (sensory/perceptual vs. frontal/subcortical) targeted in this study. However, an earlier comprehensive review on the associations between SES and brain (Brito & Noble, 2014) reported that most of the structural neuroimaging studies in children between ages 5 to 12 years used samples with 145 or fewer participants (e.g., Jednoróg et al., 2012; Luby et al., 2013; Raizada et al., 2008). Their results showed significant associations between SES and gray matter volume (ranges across studies: $t < 2.11-3.74 >$; p -values $< .05$) and significant two-way interactions (F -change $< 5.76 - 6.28 >$; $adjusted R^2 < .19 - .63 >$; p -values $< .05$). According to the power analysis and previous literature, the sample size of 232 provides adequate power to detect reliable differential effects of SES on sensory/perceptual vs. frontal/subcortical regions.

3.3 Procedure

3.3.1 Collecting Data Across Study Sites

In the HCP-D dataset, images were acquired at 4 different sites: Harvard University, University of California-Los Angeles, University of Minnesota, and Washington University in St. Louis. Imaging data were collected using a common platform with the same software version across all sites. To assure quality control across all 4 sites, the HCP team created a set of “standard operating procedures”, frequent communications across sites, and regular training

sessions for experimenters involved (Harms et al., 2018). All of the sites used a Siemens 3T Prisma scanner with a 32-channel head coil, except for 2 sites (Washington University and UCLA) that used a pediatric 32-channel head coil developed by Ceresensa in participants ages 5-7. Compared to the Siemens 32-channel coil, this coil has a smaller inner space which makes it more appropriate for pediatric head sizes and neck lengths (Supplemental Material for Hamers et al., 2018).

In addition to the potential confound created by using 2 different head coils across sites, it was important to consider that these data were collected at multiple locations, by different MRI technicians/experimenters, and in different environments; therefore, study site was included in the analyses as a categorical covariate to control for the potential effect of scanner location on outcome variables.

3.3.2 Magnetic Resonance Imaging (MRI) Acquisition Parameters

According to the HCP MRI parameters reported by Hamers et al (2018), all structural images were acquired by a single T1w scan with 0.8 mm isotropic voxels using a multi-echo magnetization prepared rapid gradient echo (ME-MPRAGE) sequence. The sagittal field of view (FOV) used was 256x240x166 mm with a matrix size of 320x300x208 slices. Slice oversampling of 7.7% was used with a pixel bandwidth of 744Hz/Px and 2-fold in-plane acceleration (GRAPPA) in the phase encoding direction. Specific T1w scan parameters include TR/TI=2500/1000, TE=1.8/3.6/5.4/7.2ms, and flip angle= 8 degree (up to 30TRs allowed for motion-induced reacquisition). To reduce signal from bone marrow and fat, water excitation was employed. In extension, subject motion was corrected for via embedded “volumetric navigators” (vNavs) by which motion-corrupted lines in *k*-space were selectively re-acquired. Through this process, 3D echo-planar imaging vNavs were collected, once for each TR period, and registered

in real-time. Positional information derived from these images were used to update the position of FOV for the scan duration (Hamers et al., 2008). This real-time motion correction technique is reported to reduce motion-related bias in interpreting imaging results (Reuter et al., 2015).

3.3.3 Image Preprocessing and Quality Assurance

Imaging data were downloaded from HCP-D database onto a secure server located at the Georgia State University/Georgia Institute of Technology/Emory University Center for Translational Research in Neuroimaging and Data Science (TReNDS). The image preprocessing and quality assurance procedures were conducted remotely through the TReNDS server by using MobaXterm software installed on a Mac computer with a Windows operating system (as recommended by GSU Psychology IT team).

Structural MRI images were used to measure differences in gray matter volume of 4 regions of interest (ROIs), 2 involving sensory/perceptual regions (bilateral transverse temporal gyrus, bilateral cuneus gyrus) and 2 involving frontal/subcortical regions (i.e., Broca's area: pars opercularis and pars triangularis; bilateral caudate nuclei as a subsection of basal ganglia) for each individual child. I used FreeSurfer v.6.0.0 image analysis pipeline (Fischl et al., 2002; <http://surfer.nmr.mgh.harvard.edu/>) to process and analyze structural brain imaging data. FreeSurfer has been widely used in investigations on morphometric properties in many populations due to its high rate of reproducibility, accuracy, and user-friendly composition (Fischl, et al., 2002; Tae et al., 2008; Bhojraj et al., 2011). In addition, FreeSurfer provides a set of fully automated analytic tools that are freely available to the public (see Fischl et al., 2002 and Fischl et al., 2004 for technical details of the analyses).

As the first step in pre-processing brain images, I visually inspected the quality of all the raw T1-w images. Although I had expected to exclude many T1 images in order to ensure high

quality of final images, I only excluded 1 participant due to blurred regions on the brain images potentially caused by radiofrequency artefacts, reducing the final sample size to 232. After this step, I used the *reconall* tool to run the images through a series of processing tools that generate estimates of morphometric measures of specific ROIs. First, the images were registered to a Talairach atlas space (<http://surfer.nmr.mgh.harvard.edu/>), which linearly transformed them into a common coordinate system. Following registration, FreeSurfer assigned an initial label to each voxel (basic building blocks of a 3-D MRI image, similar to pixels of a 2-D image) based on the voxel's intensity. Voxel intensity gradients were used to identify transition between gray matter to white matter to facilitate tissue segmentation (Fischl & Dale, 2000).

During tissue segmentation, non-brain tissues were removed by utilizing a fully automated algorithm. Then, subcortical structures were separated into white matter, gray matter, and cerebrospinal fluid depending on constraints and intensity of neighboring voxels. During a process called 'intensity normalization', the range of these voxel intensity values were changed to correct for variations across voxels. This step is helpful in processing images with low contrast which may have been caused by motion during the scan. Often, FreeSurfer fails to correctly label brain tissue during segmentation and/or intensity normalization steps. For example, in certain regions dura matter may be mistakenly marked as part of the pial surface or gray matter may be incorrectly included as white matter. Thus, I used *Freeview* tool to manually check and fix the results of brain registration and segmentation outcomes for all individuals with such errors. These edits included erasing mislabeled gray/white matter voxels and inserting control points to correctly identify the white matter voxels in coronal, axial, and sagittal views. Those images with manual edits (90% of images) were resubmitted through the automated *reconall* process and were rechecked to assure that the changes made were implemented.

3.4 Measures

3.4.1 Volume of ROIs

After manually correcting white matter and gray matter segmentation errors using *Freeview*, I used FreeSurfer's automated process to assign a final label to each voxel based on subject-dependent and subject-independent probabilities using the Destrieux atlas (Destrieux et al., 2010; Fischl et al., 2004). As a result, adjacent voxels that were assigned different labels created structural boundaries in the brain and the segmented images were transformed back to their native space. Similar to the first quality check step, I used *Freeview* to visually inspect the boundaries for all ROIs. None of the images needed extensive editing in this step. In the final stage of the processes, I used the *asegstats* (for subcortical regions) and *aparcstats* (for cortical regions) tools to automatically count the number of voxels contained within boundaries of each structure and generate the volume (mm^3) for bilateral transverse temporal gyrus, bilateral cuneus gyri, Broca's region, and bilateral caudate nuclei by rest. Volume of each structure (except for Broca's area: left pars opercularis and left pars triangularis) was calculated separately for each hemisphere. Then for each structure, volume of regions in both hemispheres were added to create total volumes of bilateral structures: bilateral transverse temporal gyri, bilateral cuneus gyri, and bilateral caudate nuclei. These are the values that were entered into SPSS for further analyses.

3.4.2 Estimated Total Intracranial Volume (eTIV)

In addition to volume of ROIs, FreeSurfer estimates the total volume of cranium which contains cerebrospinal fluid (CSF), gray matter, and white matter (<https://surfer.nmr.mgh.harvard.edu/fswiki/BrainVolume>). Total intracranial volume needs to be controlled for to account for head size variations among participants (Buckner et al., 2004). For example, a greater volume of caudate nucleus may be a result of having a larger head but not be

related to the effect of predictor variables. Therefore, including TIV as a control variable will help reduce its potential confounding effect (O'Brian et al., 2011).

3.4.3 *SES and Demographics*

SES is defined as a multi-dimensional construct, consisting of various components including parental education level, household income, home and school environment, and neighborhood safety—each of which can individually or cumulatively influence children's development. In this study, I used parental education and household income as the two measures for SES because these are the most commonly used indicators of SES in neuroimaging studies (see review by Brito & Noble, 2014). Parental education is reported to be related to children's verbal executive function (Ardila et al., 2005), working memory (Roberts, et al., 1999), and language (Hupp et al., 2011; Pan, Rowe, Singer & Snow, 2005; Romeo et al., 2018) through cognitive and linguistic stimulation (Brito & Noble, 2014). Household income has been shown to influence children's total gray matter volume (Hanson et al., 2013; Noble et al., 2012) and full-scale IQ (Lange et al., 2010) which is related positively to their access to educational resources and negatively to their stress levels (e.g., Luby et al., 2013; Noble et al., 2012; Romeo et al., 2018).

Given my interest in the investigation of the 'unique' influence of each of the two SES components (i.e., parental education and household income) on differences in morphometric properties of the brain, I avoided using a composite score for SES, as has been done in some of the earlier work (e.g., Betancourt et al., 2016; Dickinson, Adelson, 2014; Ensminger, Fothergill, 2014; Hoff, Laursen, & Bridges, 2012). Instead, I used parental education (average of both parents' education level) and household income, separately as indicators of SES in the current study. Parental education was reported for all participants and was averaged across two parents

on a scale of 0-6, as: 0 = Less than High School; 1 = High School; 2 = Some college; 3 = Associate's degree; 4 = Bachelor's degree; 5 = Master's degree; 6 = PhD/Professional degree. For single-parent households, I used the present parent's education level using the same scale. Household income was coded as raw total annual household income amount which ranged between \$5000 and \$500,000. A summary of SES measures is reported in Table 1.

3.4.4 *Handedness*

Differences in hand preference have been found to be related to differences in morphology of the brain (Amunts, Jancke, Mohlberg, Steinmetz, & Zilles, 2000; Good et al., 2001; Ocklenburg, Friedrich, Gunturkun, & Genc, 2016; Ocklenburg, Garland, Strockens, & Uber Reinert, 2015). In the HCP-D data set, handedness was assessed with the Edinburgh Handedness Inventory (EHI; Oldfield, 1971). In this inventory, handedness is calculated from answers to questions about hand preference in 10 daily activities. Each question is scored on a scale of -2 to +2, with score of '-2' being high preference for left hand and '+2' being high preference for right hand. Only 29 out of 232 participants were left-handed (see Table 1). I conducted Pearson correlation analysis to investigate whether handedness should be included as a control variable in further analyses and found that it was not significantly correlated with any of the measures and, therefore, was not included in the analyses. These correlation results are presented in Appendix A.

4 ANALYSIS

4.1 Test of Assumptions for Linear Regression

To investigate the assumptions of parametric statistical tests (linear regression), first I visually inspected the normality of distribution for each variable of interest using histograms. Second, I used 'stem and leaf' plots to identify extreme outliers (>3 standard deviations from the

mean; Hoaglin, Iglewicz, & Tukey, 1986) in the variables of interest. To avoid losing data, instead of excluding participants with extreme values, I replaced the extreme high or low values by the next highest or lowest value in the variable as advised by (Dixon, 1960; Dixon, 1980; Tukey, 1962). Third, I used Tolerance and variance inflation factors (VIFs) as indices of multicollinearity between predictors in the statistical models. Forth, the assumptions of linearity and homoscedasticity were tested using the scatterplots and histograms of standardized residuals of the data (Hair et al., 1998). Finally, all variables of interest were tested for the assumption of non-zero variance using the variance statistics.

4.2 Hierarchical Linear Regression Models

After processing structural data for all subjects using FreeSurfer (*section 3.3.1*), I used Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL) to conduct 4 hierarchical linear regressions (1 for each region of interest). In each model, parental education level was entered as the first predictor to determine whether it explains any variance in brain volume. Household income was entered as the predictor in the second step of the model to measure whether income adds or takes away from variance in brain volume explained by parental education. Given that household income was only reported for 232 out of 243 participants and 1 participant was excluded due to poor imaging data, the regression analyses were conducted with total of 232 participants. In the third step, the control variables: sex, study site, and estimated total intracranial volume (eTIV; calculated via FreeSurfer software) were entered to investigate whether these variables influence the effect of predictors entered into previous steps of the model. The same model was created for the volume of each region of interest as the outcome variable for a total of 4 models. Using hierarchical regression models allowed me to determine how much of variance in the outcome variable (volume of each region) is explained by each

predictor variable that is above and beyond the other predictors and control variables entered in each model. To address the issue of multiple comparisons caused by conducting 4 regression models, I adjusted for the family-wise error rate (FWER; probability of committing one or more Type I errors) using the Holm-Bonferonni method (Holm, 1979; Aickin & Gensler, 1996).

5 RESULTS

5.1 Sample Descriptive Statistics

Descriptive statistics for all participants ($n=243$) as well as those participants whose household income data were used in the regression analyses ($n=232$) are presented in Table 1. Given that 92.4% of participants were between ages 8-12 years, I presented the descriptive statistics for 2 separate age groups: ages 5;0-7;11 and ages 8;0-12;11. Table 1 shows that all participants in this study showed average linguistic and general intelligence shown by their performance on standardized neuropsychology assessments of receptive vocabulary (Peabody Picture Vocabulary Test -PPVT; Dunn & Dunn, 2007) and perceptual and abstract reasoning (Wechsler Intelligence Scale for Children -WISC; Kaplan et al., 2004). Appendix B shows the distribution of these variables across study sites.

Table 1. Sample Distribution and Descriptive Statistics.

	Total sample ^a	Sample used in regression analyses	Ages 5;0-7;11 years ^a	Ages 8;0-12;11 years ^a
<i>n</i>	243	232	18(7.6%)	214 (92.4%)
Age in years	10.18 ± 1.59	10.18± 1.57	7.13 ± 0.79	10.43 ± 1.34
Sex				
Female	136	130	12	118
Male	107	102	6	96
Edinburgh Handedness				
Left	31	29	1	28
Right	212	203	17	186
Race				

American Indian/Alaskan	1	1	0	1
Asian	11	10	1	9
Black or African American	10	10	2	8
White/Caucasian	171	166	6	160
More than one race	45	41	8	33
Unknown/Not reported	5	4	1	3
<hr/>				
Study site				
Harvard	71	69	0	69
UCLA	50	47	9	38
UMinn	70	64	0	64
WashU	52	52	9	43
<hr/>				
Annual household income \$/1000 (n=232)	142.55 ± 89.68	142.55 ± 89.68	94.85 ± 85.67	146.56 ± 89.03
<hr/>				
Parents' education average				
0. Did not graduate high school	2	2	1	1
1. High school diploma	8	7	2	5
2. Some college	27	25	2	23
3. Associate's degree	28	27	5	22
4. Bachelor's degree	94	90	4	86
5. Master's degree	71	69	4	65
6. Ph.D./ Professional degree	13	12	0	12
<hr/>				
Neuropsychological assessments				
PPVT (n=166)	113.72 ± 816.19	113.81 ± 16.01	108.43 ± 11.57	114.06 ± 16.17
WISC (n=238)	11.01 ± 3.25	11.03 ± 3.28	9.60 ± 2.87	11.13 ± 3.29

^a Mean ± SD for continuous variables, N for categorical variables

Abbreviations: UCLA=University of California Los Angeles; UMinn= University of Minnesota; WashU= Washington University in St. Louis; PPVT= Peabody Picture Vocabulary Test; WISC= Wechsler Intelligence Scale for Children

5.2 Test of Assumptions for Linear Regression

Household income data for two participants were identified as extreme outliers (> 3 standard deviations from the mean). These values were replaced by a score that was the next highest score in the distribution of each variable (Dixon, 1980; reflected in Table 1). No outliers

for any other variables of interest were identified. Tests exploring the assumption of collinearity showed that multicollinearity between predictor variables was not a concern (parental education level, *Tolerance* = 0.80, *VIF* = 1.25; household income, *Tolerance* = 0.80, *VIF* = 1.25). The assumptions of normality, linearity, and homoscedasticity were met according to the scatterplots and histograms of standardized residuals of the data (Hair et al., 1998). Finally, all variables of interest met the assumption of non-zero variance (*Variance* < 0).

5.3 Aim 1: How does SES influence the volume of sensory/perceptual regions (primary visual and auditory cortices) differently from the volume of frontal/subcortical brain regions (Broca's area and caudate nucleus) in young children?

5.3.1 SES and Sensory/Perceptual Regions

I first asked whether there was an association between each SES measure (parental education, household income) and cortical volume of **sensory/perceptual regions** in children. I tested this question with two separate regression analyses for each brain region as the outcome variable: one for cortical volume of primary visual cortex (bilateral cuneus gyri) and the other for primary auditory cortex (bilateral transverse temporal gyri). Each model included parental education average and household income as predictors in the first and second steps, respectively. Participants' sex, study site, and total intracranial volume were entered as control variables in the last step of the regression analysis.

In the model with **primary visual cortex (V1) as the outcome**, parental education level did not significantly predict variance in the volume of primary visual cortex $\beta = 0.09$, $p = 0.15$. Similarly, adding household income to the model did not explain any additional variance in volume of primary visual cortex $\beta = -0.75$, $p = 0.30$. Adding the control variables of sex, study site, total intracranial volume did not change the outcomes of the first model. However, total

intracranial volume was a significant predictor of variance in the volume of primary visual cortex $\beta = 0.39, p < 0.001, R^2_{adj} = .19, F(3, 226) = 11.60, p < 0.001$ (see Table 2 for regression results).

Table 2. Hierarchical regression analysis testing the effect of SES on gray matter volume of primary visual cortex.

	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	ΔR^2
	<i>b</i>	<i>SE</i>	β		
Step 1					0.009
V1 volume	7268.23	272.12		26.71**	
Parental education level	91.64	63.3	0.95	1.45	
Step 2					0.005
V1 volume	7280.48	272.34		26.73**	
Parental education level	122.12	69.85	0.13	1.75	
Household income	-0.001	0.001	-0.08	-1.03	
Step 3					0.191**
V1 volume	2576.02	971.44		2.65**	
Parental education level	43.16	64.09	0.05	0.67	
Household income	-0.001	0.001	-0.09	-1.39	
Sex	-170.06	168.43	-0.07	-1.01	
Study Site	117.87	65.83	0.11	1.79	
eTIV	0.003	0.001	0.39	5.33**	

N = 232

V1 = bilateral cuneus gyri (primary visual cortices)

eTIV = estimated Total Intracranial Volume

p* < .05, *p* < .01

The model with **primary auditory cortex (A1) as the outcome** showed similar results. Neither parental education level ($\beta = 0.11, p = 0.09$) nor household income ($\beta = 0.90, p = 0.22$) predicted variance in the volume of the primary auditory cortex. Adding the control variables to the model did not change the outcomes of previous steps in the model. Similarly to the volume of the primary visual cortex, total intracranial volume significantly explained variance in the

volume of primary auditory cortex $\beta = 0.52$, $p < 0.001$, $R^2_{adj} = .22$, $F(3, 226) = 13.8$, $p < 0.001$ (see Table 3 for regression results).

Table 3. Hierarchical regression analysis testing the effect of SES on gray matter volume of primary auditory cortex.

	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	ΔR^2
	<i>b</i>	<i>SE</i>	β		
Step 1					0.012
A1 volume	2278.32	104.26		21.85**	
Parental education level	41.21	24.25	0.11	1.7	
Step 2					0.007
A1 volume	2272.72	104.24		21.8**	
Parental education level	27.26	26.74	0.07	1.02	
Household income	0.0004	0.0004	0.09	1.23	
Step 3					0.215**
A1 volume	-85.02	365.79		-0.23	
Parental education level	0.41	24.13	0.001	0.02	
Household income	0.0003	0.0003	0.05	0.82	
Sex	92.24	63.42	0.1	1.45	
Study Site	-19.6	24.79	-0.05	-0.79	
eTIV	0.002	0.0002	0.52	7.25**	

N = 232

* $p < .05$, ** $p < .01$

A1 = bilateral transverse temporal gyri (primary auditory cortices)

eTIV = estimated Total Intracranial Volume

5.3.2 SES and Frontal/Subcortical Regions

Next, I asked whether there was an association between each SES measure (parental education, household income) and cortical volume of **frontal/subcortical regions** in children. I tested this question with two separate regression analyses for each brain region as the outcome variable: one for total cortical volume of left pars opercularis and pars triangularis (i.e., Broca's region) and the other for subcortical volume of bilateral caudate nuclei. Each model included parental education average and household income as predictors in the first and second steps,

respectively. Participants' sex, study site, and total intracranial volume (eTIV) were entered as control variables in the last step of the regression analysis. In the **model with Broca's region as the outcome**, neither parental education level ($\beta = 0.08, p = 0.23$) nor household income explained any variance in volume of Broca's area, $\beta = -0.01, p = 0.87$. As a control variable, sex did not explain any variance in the volume of Broca's area. However, total intracranial volume and study site were significant predictors of variance in the volume of the Broca's region, $\beta = 0.44, p < 0.001$ and $\beta = -0.12, p < 0.05$, respectively ($R^2_{adj} = .17, F(3, 226) = 10.43, p < 0.001$; see Table 4 for regression results). Although, these control variables were significant predictors of variance in the volume of Broca's area, they did not change the non-significant effect of SES measures in the model. Exploratory *post-hoc* comparisons using Tukey-HSD test did not show any significant differences in the mean volume of Broca's area between study sites ($F(3, 228) = 1.71, p = 0.17$).

Table 4. Hierarchical regression analysis testing the effect of SES on gray matter volume of Broca's area.

	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	ΔR^2
	<i>b</i>	<i>SE</i>	β		
Step 1					0.006
Broca's volume	7884.97	292.51		26.96**	
Parental education level	82.51	68.05	0.8	1.21	
Step 2					0.0001
Broca's volume	7887.02	293.41		26.88**	
Parental education level	87.63	75.25	0.09	1.16	
Household income	0.0001	0.001	-0.01	-0.16	
Step 3					0.181**
Broca's volume	2551.31	1053.72		2.42*	
Parental education level	25.6	69.51	0.03	0.37	
Household income	0.0005	0.001	-0.04	-0.53	
Sex	135.43	182.7	0.05	-0.74	
Study Site	-141.89	71.4	-0.12	-1.99*	

eTIV	0.004	0.001	0.44	5.98**
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$N = 232$

* $p < .05$, ** $p < .01$

Broca = left pars opercularis & pars triangularis

eTIV = estimated Total Intracranial Volume

In the **model with caudate nucleus as the outcome**, parental education level was a significant predictor, $\beta = 0.21$, $p < 0.01$, $R^2_{adj} = .05$, $F(1, 230) = 10.75$, $p < 0.01$. Even after adding household income to the model which did not show a significant main effect ($\beta = -0.07$, $p = 0.36$), parental education level remained a significant predictor of variance in the volume of caudate nucleus, $\beta = 0.21$, $p < 0.01$. Most importantly, adding the control variables to the model did not change the significant effect of parental education level, $\beta = 0.13$, $p < 0.05$, $R^2_{adj} = .40$, $F(3, 226) = 31.70$, $p < 0.001$. In addition to parental education level, total intracranial volume also served as a significant predictor of variance in volume of caudate nucleus $\beta = 0.65$, $p < 0.001$ (see Table 5 for regression results).

Table 5. Hierarchical regression analysis testing the effect of SES on gray matter volume of caudate nuclei.

	Unstandardized Coefficients		Standardized Coefficients	t	ΔR^2
	b	SE	β		
Step 1					0.05**
CN volume	7351.42	233.08		31.54**	
Parental education level	177.77	54.22	0.21	3.28**	
Step 2					0.004
CN volume	7360.79	233.38		31.54**	
Parental education level	201.07	59.86	0.24	3.36**	
Household income	-0.001	0.001	-0.07	3.36	
Step 3					0.36**
CN volume	505.88	728.29		0.7	
Parental education level	113.07	48.05	0.13	2.35*	
Household income	-0.001	0.001	-0.11	-1.9	

Sex	145.81	126.27	0.07	1.16
Study Site	35.88	49.35	0.04	0.73
eTIV	0.004	0.0004	0.65	10.4**

$N = 232$

* $p < .05$, ** $p < .01$

CN= *bilateral caudate nuclei*

eTIV= *estimated Total Intracranial Volume*

In order to further explore the main effect of parental education level on volume of caudate nucleus, I divided the parental education variable into two groups: those with a college degree and those without a college degree. In a review of the SES literature, Ardila and colleagues (2005) suggested that college-educated mothers are more likely to talk to their children, use more complex vocabulary, and read more books to their children which could, in turn, lead to children's increased exposure to linguistic and cognitive stimulation. Therefore, I conducted an exploratory *post-hoc* analysis to compare the volume of caudate nucleus between children of parents with a college degree and those without a college degree. The results indicated that the mean volume of caudate nucleus is significantly smaller in children with parents who did not earn a college degree ($N = 61$, $M = 7779.24$, $SD = 867.61$) compared to those children with parents who earned a college degree ($N = 171$, $M = 8194.21$, $SD = 1041.90$, $t(125.86) = -3.03$, $p = 0.003$, *equality of variances not assumed*). Figure 2 shows this significant group difference in the volume of caudate nucleus. It is important to mention that there were no sex group differences between those participants in the low parental education and those in the high parental education groups. In other words, both low and high education groups consisted of more female participants than male participants suggesting that participants' sex is not a potential confound in these analyses.

In summary, these results show that SES variables do not significantly explain the variance in the volume of the perceptual/sensory regions and Broca's area; however, parental education level does account for 5% of variance in the volume of bilateral caudate nuclei.

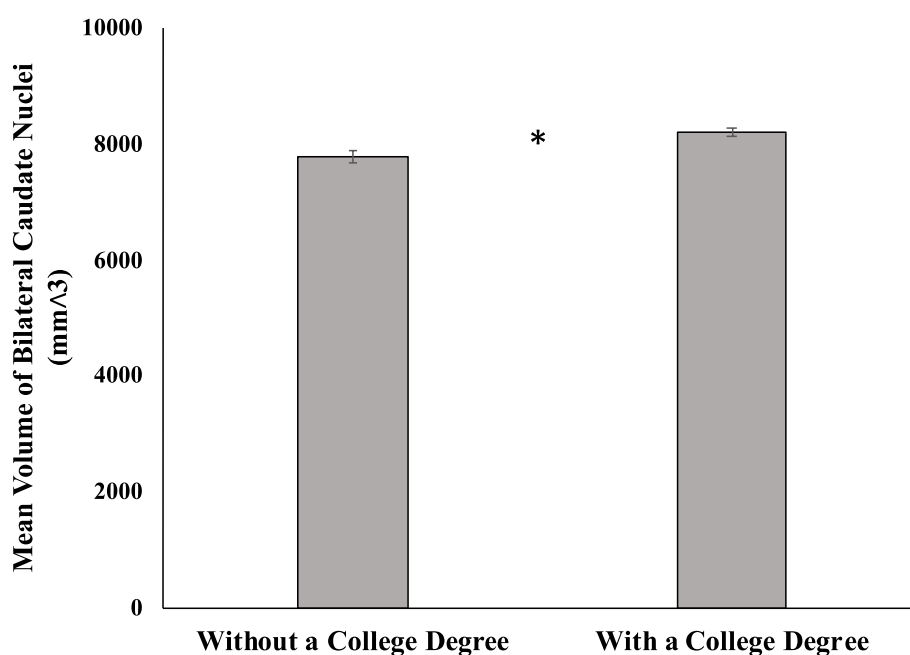


Figure 2. Significant Difference in Mean Volume of Bilateral Caudate Nuclei Across Parental Education Groups. Error bars represent standard error.

5.4 Aim 2: What is the added effect of age in the influence of SES on sensory/perceptual and frontal/subcortical brain regions involved in SL?

5.4.1 Contribution of age to the association between SES and Sensory/Perceptual Regions

To determine the influence of age on the effect of SES on volume of sensory/perceptual regions, I conducted the same hierarchical regression analyses outlined under *section 4.2*, with an additional predictor, namely child age, as the last step in the hierarchical regression model.

In the model with **primary visual cortex as the outcome**, age significantly predicted the variance in the volume of primary visual cortex ($\beta = -0.30, p < 0.001$). At the same time, however, age did not change the non-significant effect of parental education level on the volume of primary visual cortex ($\beta = 0.05, p = 0.44$). Similarly, the effect of household income on the volume of primary visual cortex remained non-significant ($\beta = -0.07, p = 0.24$; see Table 6 for regression results).

Table 6. Hierarchical regression analysis testing the effect of age on the association between SES and gray matter volume of primary visual cortex.

	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	ΔR^2
	<i>B</i>	<i>SE</i>	β		
Step 1					0.009
V1 volume	7268.23	272.12		26.71**	
Parental education level	91.64	63.30	0.10	1.45	
Step 2					0.005
V1 volume	7280.47	272.34		26.73**	
Parental education level	122.16	69.85	0.13	1.75	
Household income	-0.001	0.001	-0.07	-1.03	
Step 3					0.19**
V1 volume	2576.02	971.43		2.65**	
Parental education level	43.16	64.08	0.04	0.67	
Household income	-0.001	0.001	-0.09	-1.38	
Sex	-170.16	168.43	-0.07	-1.01	
Study Site	117.87	65.82	0.11	1.79	
eTIV	0.003	0.001	0.39	5.32	
Step 4					0.08**
V1 volume	3457.14	940.96		3.67**	
Parental education level	47.34	60.97	0.05	0.77	
Household income	-0.001	0.001	-0.07	-1.18	
Sex	-125.02	160.48	-0.05	-0.77	
Study Site	95.17	62.78	0.08	1.51	
eTIV	0.004	0.001	0.49	6.83**	
Age	-18.47	3.71	-0.3	-4.97**	

N = 232

* $p < .05$, ** $p < .01$

VI = bilateral cuneus gyri (primary visual cortices)
eTIV = estimated Total Intracranial Volume

Similarly, In the **model with primary auditory cortex as the outcome**, the results showed that age has a significant main effect on the volume of primary auditory cortex ($\beta = -0.23$, $p < 0.001$). At the same time, age did not change the non-significant effect of parental education level ($\beta = 0.004$, $p = 0.94$;) and household income ($\beta = 0.07$, $p = 0.29$) on the volume of primary auditory cortex (see Table 7 for the regression results).

Table 7. Hierarchical regression analysis testing the effect of age on the association between SES and gray matter volume of primary auditory cortex.

	Unstandardized Coefficients		Standardized Coefficients	t	ΔR^2
	b	SE	β		
Step 1					0.012
A1 volume	2278.32	104.26		21.85**	
Parental education level	41.21	24.25	0.11	1.07	
Step 2					0.007
A1 volume	2272.72	104.24		21.8**	
Parental education level	27.26	26.74	0.07	1.02	
Household income	0.0004	0.0004	0.09	1.23	
Step 3					0.215**
A1 volume	-85.02	265.79		-0.23	
Parental education level	0.41	24.13	0.001	0.02	
Household income	0.0003	0.0003	0.05	0.82	
Sex	92.24	63.42	0.1	1.45	
Study Site	-19.6	24.79	-0.05	-0.79	
eTIV	0.002	0.0002	0.52	7.25**	
Step 4					0.047**
A1 volume	177.43	361.52		0.49	
Parental education level	1.66	23.43	0.004	0.07	
Household income	0.0003	0.0003	0.07	1.06	
Sex	105.68	61.66	0.12	1.71	
Study Site	-26.36	24.12	-0.06	-1.09	

eTIV	0.002	0.0002	0.6	8.28**
Age	-5.5	1.43	-0.23	-3.86**

$N = 232$

* $p < .05$, ** $p < .01$

A1 = bilateral transverse temporal gyri (primary auditory cortices)

eTIV = estimated Total Intracranial Volume

5.4.2 Contribution of age to the influence of SES on Frontal/Subcortical Regions

To answer the second study question investigating the influence of age on the effect of SES on volume of frontal/subcortical regions, I conducted the same hierarchical regression analyses outlined under section 4.2, with an additional predictor, namely child age, as the last step in each hierarchical regression model.

In the model with **Broca's region as the outcome**, the results showed that age had a significant main effect on volume of this region ($\beta = -0.18$, $p < 0.001$), however, even after including age, parental education level and household income remained as non-significant predictors of variance in the volume of Broca's area, $\beta = 0.03$, $p = 0.68$ and $\beta = -0.03$, $p = 0.70$, respectively (see Table 8 for regression results).

Table 8. Hierarchical regression analysis testing the effect of age on the association between SES and gray matter volume of Broca's area.

	Unstandardized Coefficients		Standardized Coefficients	t	ΔR^2
	b	SE	β		
Step 1					
Broca's volume	7884.97	292.51		26.95**	0.006
Parental education level	82.51	68.04	0.08	1.21	
Step 2					
Broca's volume	7887.03	293.41		26.88**	0.0001
Parental education level	87.63	75.25	0.08	1.16	

Household income	-0.0002	0.001	-0.01	-0.16
Step 3				0.18**
Broca's volume	2551.31	1053.72		2.42**
Parental education level	25.59	69.51	0.02	0.36
Household income	-0.0005	0.001	-0.03	-0.53
Sex	135.42	182.69	0.05	0.74
Study Site	-141.89	71.40	-0.12	-1.98*
eTIV	0.004	0.001	0.44	5.98
Step 4				0.03**
Broca's volume	3130.03	1055.59		2.96**
Parental education level	28.34	68.39	0.02	0.41
Household income	-0.0003	0.001	-0.02	-0.38
Sex	165.07	180.03	0.06	0.91
Study Site	-156.79	70.43	-0.13	-2.22*
eTIV	0.004	0.001	0.50	6.67**
Age	-12.13	4.16	-0.18	-2.91**

N = 232

p* < .05, *p* < .01

Broca = left *pars opercularis* & *pars triangularis*

eTIV = estimated Total Intracranial Volume

However, in the **model with caudate nucleus as the outcome**, the results showed that age did not have a significant main effect on the volume of this region ($\beta = -0.01$, $p = 0.10$). More importantly, after adding age to the model, parental education level remained a significant predictor of variance in volume of caudate nucleus ($\beta = 0.14$, $p < 0.05$); however, household income remained a non-significant predictor ($\beta = -0.10$, $p = 0.07$; see Table 9 for the regression results).

In summary, the results showed that age is a significant predictor of volume of visual and auditory cortices as well as volume of Broca's area; however, there was no main effect of age on the volume of caudate nucleus. Interestingly, adding age to the models did not influence the effect of SES predictors on the volume of sensory/perceptual or frontal/subcortical regions. Thus,

parental education level remained a significant predictor of variance in volume of caudate nucleus.

Table 9. Hierarchical regression analysis testing the effect of age on the association between SES and gray matter volume of caudate nuclei.

	Unstandardized Coefficients		Standardized Coefficients	<i>t</i>	ΔR^2
	<i>b</i>	<i>SE</i>	β		
Step 1					0.05**
CN volume	7351.42	233.08		31.54**	
Parental education level	177.77	54.22	0.21	3.28**	
Step 2					0.004
CN volume	7360.78	233.37		31.54**	
Parental education level	201.07	59.85	0.23	3.36**	
Household income	-0.001	0.001	-0.06	-0.92	
Step 3					0.36**
CN volume	505.87	728.29		0.69	
Parental education level	113.06	48.04	0.13	2.35*	
Household income	-0.001	0.001	-0.11	-1.89	
Sex	145.81	126.27	0.07	1.15	
Study Site	35.88	49.35	0.04	0.73	
eTIV	0.004	0.0004	0.65	10.40*	
Step 4					0.007
CN volume	734.08	738.8		0.99	
Parental education level	114.14	47.87	0.13	2.38*	
Household income	-0.001	0.001	-0.10	-1.81	
Sex	157.49	126.005	0.08	1.25	
Study Site	30.003	49.29	0.03	0.61	
eTIV	0.005	0.0004	0.68	10.45*	
Age	-4.78	2.91	-0.09	-1.64	

N = 232

p* < .05, *p* < .01

CN = bilateral caudate nuclei

eTIV = estimated Total Intracranial Volume

6 DISCUSSION

SL ability plays an important role in the development of language and perception. At least two underlying systems with two primary sets of neural networks are involved in SL: the *bottom-up* system which facilitates learning sensory structures in the input and the *top-down* system that involves frontal and subcortical regions facilitating learning more abstract structures of input (Daltrozzo & Conway, 2014; Conway, 2020). This study is the first to investigate the association between SES and morphometric measures of brain regions involved in SL ability in children.

6.1 SES and Dual Mechanisms Underlying Statistical Learning

To determine if social environmental factors could play a role in children's cognitive development, the first aim of this study was to investigate the association between indices of SES and volume of the brain regions associated with *bottom-up* (primary visual and auditory cortices) vs. with *top-down* (Broca's area and caudate nucleus) processing of statistical patterns. The current results, in line with previous work (Brito & Noble, 2014), showed that neither parental education nor income explained any variance in the volume of sensory/perceptual regions. One possible explanation for lack of an association between SES and volume of sensory brain regions is that these regions are more developed relative to subcortical and frontal regions in this age range (e.g., Bishop et al., 2011; Litovsky, 2015;). Therefore, structural differences in sensory regions may be more affected by genetic indicators of SES (e.g., maternal physical and mental health pre- and during pregnancy; Evans, 2004; Shonkoff et al., 2009) rather than environmental factors such as parental education and income. These results, also in line with earlier work, showed some evidence of a significant association between measures of SES and volume of brain regions that are involved in complex learning processes. Specifically, parental education

level (not household income) significantly explained variance in the volume of caudate nucleus—but not Broca’s area. Similar to the findings of earlier work (e.g., Betancourt et al., 2016; Machlin, McLaughlin, & Sheridan, 2019), the results suggest that low SES—as indexed by parental education—is associated with smaller volume of subcortical regions in children ages 5-12. It has been reported that children who live in low SES families have less exposure to cognitive and linguistic stimulation in their environment. This lack of exposure can reduce children’s experience with behavior inhibition and regulation which are among the important functions of caudate nucleus (Padmanabhan, Geier, Ordaz, Teslovich, & Luna, 2011). Notably, caudate nucleus is reported to be involved in SL ability which is an essential component of language processing in infants (Saffran, Aslin & Newport, 1996; Shafto, Conway, Field & Houston, 2012), children (Kidd & Arciuli, 2016; Lum et al., 2012), and adults (Christiansen, Conway, & Onnis, 2012; Misyak, Christiansen, & Tomblin 2010). Seemingly, the influence of SES can last throughout the lifespan as smaller caudate volume has been reported in adults who were exposed to life stressors during early childhood (Cohen et al., 2006).

Contrary to the hypothesis, SES did not explain any variance in volume of Broca’s area—a finding that is in contrast to the earlier fMRI results reported by Romeo and colleagues (2018). A possible explanation is that although caudate nucleus and Broca’s area are both involved in learning, they are functionally distinct. According to Ullman and colleagues (2020), caudate nucleus is more involved in procedural memory and learning information by making predictions during perceptual learning. On the other hand, medial temporal lobe systems, including Broca’s area, are more involved in declarative memory and learning co-occurring stimuli and associations. It is possible that parental education level is more influential on regions associated with implicit learning as well as procedural memory, both of which are primarily processed by

the caudate nucleus. Furthermore, it is possible that effect of SES on language-related regions such as Broca's area in this sample is more pronounced in children raised in poverty and is not related to parental education (see *section 6.3* for further discussion).

6.2 Role of Caudate Nucleus in Learning

The results of this study suggest that volume of subcortical structures underlying SL, specifically caudate nucleus, is impacted by the social environment that a child is raised in. Importantly, in addition to its involvement in SL, caudate nucleus (as a subsection of basal ganglia) is also involved in learning skills/functions such as habit formation and procedural learning, to name a few (Ashby & Crossley 2012). Ullman et al., (2020), in his declarative vs. procedural learning model, explains how caudate nucleus is involved in gradual learning of associations which takes place through predictions and repeated exposures to stimuli. This model states that learning these associations involves procedural memory. Interestingly, learning grammatical rules in language also relies on procedural memory. That is, dependencies between elements in a sequence (e.g., noun and verb agreement in a sentence) are learned gradually and become automatic over time (Ullman, 2016). According to a meta-analysis by Hamrick and colleagues (2018), children and adults who showed better procedural learning also showed better grammatical knowledge compared to lexical knowledge. Finally, a meta-analysis on functional studies with adults reported activation in basal ganglia during grammar learning, but not during word learning (Tagarelli et al. 2019). Collectively, as reported previously, caudate nucleus is greatly involved in SL ability and also plays a critical role in learning linguistic (grammar) and nonlinguistic (e.g., habit formation) regularities; Therefore, according to Ullman's model of declarative vs. procedural learning (2020) these results can help explain delays and/or challenges in the development of language (specifically syntax) and other cognitive capacities in children

who are raised with low SES (e.g., Feldman et al., 2003; NICHD, 2000; Pan, Rowe, Singer, & Snow, 2005; Hoff et al., 2012; Rowe and Goldin-Meadow, 2009; Sheridan et al., 2012).

Consequently, the results of this study raise broader implications than SL ability in children. For instance, significant structural differences in caudate nucleus in children with low SES can shed light on the negative influence of adversity on other cognitive skills associated with this region such as motor learning, executive function, inhibitory control, and emotion regulation (Malenka, Nestler, & Hyman, 2009). These are valuable skills for academic success and building a career in adulthood. If we understand the neural differences associated with adversity, then we can have a better understanding of the underlying causes of the negative short-term and long-term consequences that will follow. The results of this study, along with those focusing on the association between adversity and neurocognitive development in children, can ultimately create the foundation for early intervention programs.

6.3 Construct of SES

Based on earlier work (e.g. Ardila, 2005; Betancourt, et al., 2016; Brito & Noble, 2014; Hanson et al, 2011; Hoff, Tian, 2005; Hupp et al, 2011), I predicted that parental education level would account for the largest variance in the volume of the caudate nucleus compared to household income. Parental education has been reported to influence brain regions involved in complex cognitive processes, such as language and executive function, through providing adequate linguistic and cognitive stimulation in children's environment (Ardila et al., 2005; Brito & Noble, 2014; Hupp et al., 2011; Roberts, et al., 1999; Romeo et al., 2018). According to Ardila and colleagues (2005), more educated parents tend to talk more to their children and use more complex language. More educated parents are also reported to use conversational parenting techniques as opposed to directive and punishment-based strategies (Hoff, Laursen, & Tardif,

2002). This enriched linguistic environment (or lack of) can change the neural function (Romeo et al, 2018) and structure (Merz et al., 2019) underlying complex cognitive abilities in children.

Income is also reported to be a strong indicator of availability of resources and overall quality of the environment, which, in turn, influences children's neural development (e. g. Lange et al., 2010; Noble et al., 2012; Noble et al., 2005; Romeo et al, 2018; Sirin, 2005). However, the results of the current study showed that household income did not explain any variance in the volume of the caudate nucleus. This lack of association may be explained by, first, low variability in household income in this sample. The mean annual household income for the sample in this study was \$142,551 and only 3% (n=7) of the participants reported living in poverty (calculated income-to-needs ratio based on the poverty threshold reported in 2019; U.S. Census Bureau, 2020); Second, 5% (n=11) of the participants did not report their income level which is reported to be a common issue among participants with lower incomes. Kim and colleagues (2007) report that social stigma, fear of judgment, and lack of privacy are potential reasons for difficulties in collecting income level data.

Aside from parental education level and household income, other various components of SES may be individually and cumulatively influencing these results. For example, on the family-level, previous research suggests that parental mental health (Wadsworth & Compas, 2002), parental stress level (Appleyard et al., 2005; Korat et al., 2007), and the quality of parent-child interactions (Dallaire et al., 2008) are all examples of how SES influences developmental outcomes in children and adolescents. Low SES could indirectly influence children via the mental health status of the parents (Pettersen & Albers, 2001). Parental anxiety has been associated with higher levels of stress in children (McLoyd & Wilson, 1990) which is reported to influence cortical volume of hippocampus, amygdala, and prefrontal cortex. Consequently,

higher stress levels lead to impairments in working memory and emotion regulation in children (Brito & Noble, 2014; Noble et al., 2012; Sheridan, et al, 2012). On the community-level, research suggests that SES affects development and academic achievement through neighborhood quality (Sirin, 2005) and opportunities for attending better schools (Ardila, 2005; Sheridan, et al, 2012).

6.4 Lack of Evidence for Influence of Age

The second aim of this study was to explore the influence of age on the possible influence of SES on volume of sensory/perceptual and subcortical/frontal regions. Lack of an association between SES factors and structure of sensory/perceptual regions in children remained unchanged even with the addition of child age as a predictor. These results support previous developmental studies exploring whole-brain differences in children from varying SES environments which did not report a significant effect of SES on sensory perceptual regions even after controlling for the age of the participants (see review by Brito & Noble, 2014). Similarly, age did not have a significant role on the association between parental education level and volume of caudate nucleus. Specifically, the main effect of SES remained significant across all ages. In line with earlier work, it is possible that SES and age may interact differently across development. For instance, cross-sectional studies focusing on a similar age range as this study have reported a stable effect of SES on cortical and subcortical gray matter volume across age groups (Lawson et al., 2013; McDermott et al., 2019; Noble et al., 2015). However, studies exploring this interaction in children younger than 4 years reported a strong interaction between SES and gray matter volume which increased by age (hippocampus; Hanson et al., 2013). Therefore, longitudinal studies are needed to explore the effect of age on the association between SES and brain morphometry.

6.5 Limitations and Future Directions

Even though this study is the first to investigate the association between SES indicators and brain morphometry in neural substrates of SL, it does not tell us about *how* parental education level influences children's neurocognitive development. To address this issue, as reviewed earlier, Brito and Noble (2006) proposed a theoretical model which describes how individual factors of SES can affect neurocognitive development in children through different pathways. The influence of SES factors on the brain structures may be mediated by levels of linguistic stimulation and stress level in the environment; this mediation varies depending on the specific brain structure. They propose that the well-known effect of SES on language-specific brain regions (e.g., language cortex) is mediated by the amount of linguistic stimulation present in children's environment. For instance, highly educated parents are reported to spend more time with their children (Guryan et al., 2008) and also engage in more varied and linguistically complex communication with their children (Hart & Risely, 1995; Hoff, 2003), compared to parents with lower education. This increased stimulation may, in turn, lead to larger gray matter volume of linguistic brain regions and better language skills in children with higher SES. Furthermore, Brito & Noble (2006) add that the effect of SES on neurocognitive development in children can also be mediated by their stress level. For instance, they suggest that the established relationship between SES and cognitive abilities such as memory, cognitive control, and socio-emotional processes are mediated by the direct effect of cortisol (stress hormone) levels on brain structures such as hippocampus, prefrontal cortex, and amygdala. Families with low SES tend to experience more financial and emotional hardship which, in turn, can lead to increased stress and consequently higher cortisol levels in children compared to high SES families. Therefore, it is of great importance for future neurocognitive studies to investigate not only *if* but also *how* SES can

influence underlying neural structures for SL in children by including parent-child interaction and stress-related measures in their designs. A related limitation is that the current study focused only on two of the several variables that define SES, namely parental education and household income. Future studies should focus on additional SES components related to children's schools and community environments and examine their effects on neural processes underlying SL. Nonetheless, by showing evidence of subcortical structural differences across SES levels in early childhood, the current study paves the way for future research to investigate the impact of various family-level and community-level factors on children's neurobiological development and, consequently, to develop more targeted interventions.

The analyses in this study tested the linear association between SES and gray matter volume. However, given the complex multifaceted construct of SES, it is also possible that SES influences brain morphometry in a nonlinear fashion. In other words, it is likely that SES is related to structural brain differences only in children with low SES and not in high SES, or vice versa. In a developmental study by Piccolo and colleagues (2016) they reported a curvilinear association between age and cortical thickness in children with low SES, however, in high SES participants there was only a linear association between age and cortical thickness. In addition, this nonlinear association was only evident in a global measure of cortical thickness and not region-specific thickness. It is also possible that not all brain regions show a linear association with SES. For instance, lack of an association between SES and gray matter volume in Broca's area in this study may be due to the nonlinear nature of the association between this structure and SES variables. Structure of Broca's area may only be impacted by greater exposure to adversity such as in low SES and/or extreme lack of exposure to adversity in high SES families, with middle SES not showing any associations with morphometry of Broca's area. Thus, it is

important to further explore the nonlinear interaction between SES and brain morphometry. Regarding measuring SES, it is important to note that parent's education level was collected by the HCP-D group as an ordinal variable which was then averaged across both parents/caregivers' education level to create the parental education level variable used in these analyses. As with any ordinal variable, the distance between categories in this variable is not equal; However, due to the lack of consensus regarding this issue and using previously collected data from an archived database, I assumed linearity between categories of this SES variable.

It is important to note that this study only relied on neural measures of SL, leaving behavioral measures of SL unexamined which could have provided a more complete picture of the differences across SES groups. An earlier study by Eghbalzad and colleagues, (2021) examining the association between SES (measured by parental education level) and SL (measured by ERPs and reaction time) in children, showed an effect of SES at the neural, but not the behavioral measures of SL, suggesting that neural indices might be better outcomes in detecting effects of SES on SL in children compared to behavioral measures. Nevertheless, future studies can use SL tasks from behavioral studies (i.e., the EEG study conducted by Eghbalzad et al., 2021) to create functional imaging tasks that help explore the relationship between behavioral correlates in addition to neural correlates of SL and SES in children.

Lastly, although the results of this study supported previous findings on the role of age in SES-related changes in morphology of the brain, the cross-sectional design of the current study prevented me from exploring within-subject changes over the course of development. In addition, as mentioned in *section 5.1*, the majority of the participants (92.4%) were between the ages 8 to 12;11 years which created an abnormal distribution. However, conducting the same analyses only with participants older than 8 years showed the same pattern of results as reported

for the analyses with all participants, suggesting that the small number of participants younger than 8 does not influence these results. Nonetheless, it is imperative for future research to conduct longitudinal studies from birth through childhood and adolescence in an attempt to shed light on the dynamic relationship between SES measures and brain morphology (especially subcortical/frontal regions) and work toward eliminating negative influence of adversity before it is developmentally too late.

6.6 Conclusion

This study showed that SES is associated with morphometry of brain regions associated with SL ability in children. However, this association was not homogenous across all neural substrates of SL. Specifically, the association between SES and gray matter volume was only evident in the caudate nucleus and not in Broca's area or sensory-perceptual regions in the brain. Understanding the neural differences associated with adversity can facilitate cognitive development in children who are raised in low SES families by minimizing the impact of being raised in a less than optimal social and linguistic home environment with the ultimate goal of mitigating the effects of unequal childhoods on children's development.

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APPENDICES

Appendix A

The table below shows the Pearson correlation statistics between all measures of interest. It is important to note that parental education level was positively correlated with eTIV ($r = 0.21$, $p = 0.001$) and volume of bilateral caudate nuclei ($r = 0.21$, $p = 0.001$). Those children of parents with higher average education level showed larger overall intracranial volume and larger subcortical gray matter volume in bilateral caudate nuclei. Also, the results show that eTIV is larger in older children in this sample ($r = 0.33$, $p < .001$).

	1	2	3	4	5	6	7	8	9	10	11
1. Age	--										
2. Sex (binary)	-0.098	--									
3. Household income	0.107	0.049	--								
4. Parental education average	0.120	-0.043	.423**	--							
5. eTIV	.325**	-.532**	0.124	.210**	--						
6. Bilateral A1 volume	-0.029	-0.172**	0.120	.132*	.479**	--					
7. Bilateral V1 volume	-.134*	-.289**	-0.021	0.107	.423**	.291**	--				
8. Broca's area volume	-0.020	-.184**	0.024	0.075	.412**	.393**	.266**	--			
9. Bilateral CN volume	0.124	-.298**	0.036	.206**	.623**	.324**	.244**	.322*	--		
10. PPVT	0.096	0.008	.163*	.289**	.171*	0.096	0.116	0.082	.228**	--	
11. WISC-Matrix Reasoning	.141*	0.052	0.121	.264**	.134*	-0.018	-0.077	0.054	0.121	.376**	--
12. Edinburgh Handedness (binary)	-0.109	0.083	-0.076	-0.030	-0.022	-0.015	0.016	0.041	-0.016	-0.074	-0.051

* $p < .05$, ** $p < .01$

Coefficients in **bold** remained significant after Bonferroni correction, $p = 0.004$

eTIV= estimated Total Intracranial Volume

A1= bilateral transverse temporal gyri (primary auditory cortices)

V1= bilateral cuneus gyri (primary visual cortices)

Broca's area= left pars opercularis & pars triangularis

CN= caudate nuclei

PPVT= Peabody Picture Vocabulary Test

WISC= Wechsler Intelligence Scale for Children

Appendix B

To further explore the sample characteristics, I grouped sample descriptive statistics across 4 study sites. The table shows that the younger participants between the ages 5;0-7;11 years were only recruited at UCLA and WashU. In addition, UCLA has the highest number of participants with low parental education level (no college degree = 22) and Harvard has the highest number of participants with high parental education level (with college degree = 59) with highest reported mean income ($M\$/1000 = 153.50$).

Study site	Harvard	UCLA	UMinn	WashU
<i>n</i>	69	47	64	52
Age in years ^a	10.53 ± 1.39	9.95 ± 1.81	10.31 ± 1.47	9.75 ± 1.61
5;0-7;11 years (<i>n</i>)	0	9	0	9
8;0-12;11 years (<i>n</i>)	69	38	64	43
Sex (<i>n</i>)				
Female	37	27	36	30
Male	32	20	28	22
Edinburgh Handedness (<i>n</i>)				
Left	12	3	8	6
Right	57	44	56	46
Race (<i>n</i>)				
American Indian/Alaskan	0	1	0	0
Asian	1	5	1	3
Black or African American	2	2	0	6
White/Caucasian	53	20	53	40
More than one race	13	16	9	3
Unknown/Not reported	0	3	1	0
Annual household income $\$/1000$ ^a	153.50 ± 73.52	121.75 ± 97.8	142.16 ± 92.76	147.31 ± 96.83
Parents' education average (<i>n</i>)				
0. Did not graduate high school	0	2	0	0
1. High school diploma	1	3	0	3
2. Some college	4	9	8	4
3. Associate's degree	5	8	5	9
4. Bachelor's degree	24	18	29	19

5. Master's degree	28	6	20	15
6. Ph.D./ Professional degree	7	1	2	2
<hr/>				
Neuropsychological assessments ^a				
PPVT	115.83 ± 18.23	111.65 ± 12.4	118.77 ± 17.12	111.10 ± 14.61
WISC	11.29 ± 2.80	10.67 ± 3.13	11.34 ± 3.77	10.58 ± 3.63
<hr/>				

^a *Mean ± SD*

Abbreviations: UCLA=University of California Los Angeles; UMinn= University of Minnesota; WashU= Washington University in St. Louis; PPVT= Peabody Picture Vocabulary Test; WISC= Wechsler Intelligence Scale for Children