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The Neuroscience of Socioeconomic Status: Correlates, Causes, and Consequences

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Keywords

socioeconomic status, poverty, development, individual differences, cognition, health disparities, hippocampus, morphometry, stress

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The Neuroscience of Socioeconomic Status:

Correlates, Causes and Consequences

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Summary

Human beings differ in their socioeconomic status (SES), with accompanying differences in physical and mental health as well as cognitive ability. Although SES has long been used as a covariate in human brain research, in recognition of its potential to explain behavioral and neural differences among people, only recently have neuroscientists made SES a topic of research in its own right. How is SES manifest in the brain, and how do its neural correlates relate to the causes and consequences of SES? This review summarizes the current state of knowledge on these questions. Particular challenges of research on the neuroscience of SES are discussed, and the relevance of this topic to neuroscience more generally is considered.

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Abstract

Neuroscience research on socioeconomic status (SES) has begun to characterize aspects of brain structure and function that vary with SES. This review summarizes our current state of knowledge concerning the neural correlates of SES, their likely consequences for human psychology and possible causes of these correlates, including relevant evidence from human and animal research concerning these causes. Challenges of research on the neuroscience of SES are discussed, and the relevance of this topic to neuroscience more generally is considered.

I. Introduction

As neuroscience has expanded to encompass the study of ever more complex social phenomena, socioeconomic status (SES) has become a topic of interest within human neuroscience. What was once a "nuisance variable," to be co-varied out of research results in psychiatry and cognitive neuroscience, has become a subject of study in its own right. What has neuroscience so far revealed about SES? What are the special challenges in the neuroscience of SES? And, what implications does this growing field of knowledge have for neuroscience more generally? The goal of this Review is to offer some preliminary answers to these questions.

What is (and what isn't) socioeconomic status?

One of the first tasks we face, when studying SES from the perspective of neuroscience -- or from any other perspective -- is to define what we mean by it. Before turning to measurement technicalities, an intuitive answer is in order. All societies have "worse off" and "better off" individuals, with those who are better off having more material resources and also more nonmaterial resources including education, occupational prestige and neighborhood quality. This dimension, from worst to best off, corresponds to SES. Its various aspects, material and nonmaterial, tend to be correlated with one another. More education, higher income, better neighborhoods and more prestigious jobs generally tend to go together. At the same time, the correlation among these aspects of SES is far from perfect. An adjunct professor will have more education than a plumber, but will make less money. A musician in a world-class orchestra may have less education than an office worker, but will have more professional prestige. A resident building superintendent may have little education, prestige or pay, but may benefit from the safety, convenience and sense of community in a good neighborhood. In short, SES corresponds to a complex bundle of social and economic factors that are generally, but imperfectly, correlated. Surveys have found only moderate correlations in the range of .2 to .7 and generally below .5, among measures of education, income, occupational status and neighborhood quality (Braveman et al., 2005; Chen & Paterson 2006; Winkleby et al., 1992). In addition to these

objectively measured aspects of SES, people have a subjective sense of where they stand in the social and economic hierarchies of their worlds. “Subjective social status” can also vary relative to objective measures.

Despite the breadth of SES as a concept, not all of life’s adversities should be considered socioeconomic adversities. For example, differences in exposure to domestic violence, child abuse and neglect are somewhat correlated with socioeconomic status, but are not generally considered to be part and parcel of the concept. Indeed, they may have different neural correlates (Lawson et al., 2017). The same is true of family differences, for example the higher prevalence of single mothers in lower SES homes and the higher rate of maternal depression in these homes. When social scientists combine measures of specifically socioeconomic deprivation with measures of interpersonal maltreatment, parental depression or absence, or other adversities, a broader designation such as “sociodemographic risk” or “adversity” is more often used. Exposure to environmental toxins such as lead, nutritional deficiencies, and other direct influences on the body are similarly viewed as important correlates of SES, and even as candidate mediators of the effects of SES on the brain, but not part and parcel of the SES concept. Finally, SES is correlated with race and ethnicity in many societies, but its effects can be separated from the effects of the latter, which include the effects of discrimination and cultural practices.

When researchers study SES they must specify the components of SES to be measured and, if more than one is measured, the ways in which they will be combined. The most commonly measured economic factor involves income. Of course, the number of mouths to be fed on a given income matters and therefore many researchers therefore use an income-to-needs ratio instead of income. The US federal government's “poverty line" is an income to needs ratio measure, with the current line equivalent to an income of $24,600 for a family of four (Federal Register, 2017). In addition, wealth influences one’s economic situation independently of income, and differs more sharply than income across racial and ethnic groups in the US. The focus of this article will be on the more general concept of SES, but findings with specific relevance to extremely low SES, or poverty, will be noted.

How and why to measure SES

Unless one has access to administrative data such as income tax returns, it can be challenging to obtain accurate income data from research participants. At all levels of SES, people may have difficulty recalling their own and their partners' salaries or wages, not to mention various other sources of income, such as tips, bonuses, help from family and informal cash arrangements with friends for childcare or room and board. In neuroscience research, therefore, SES is often measured in terms of social factors, specifically educational attainment and occupational status, which are more easily recalled, or in terms of neighborhood characteristics such as percent of neighborhood population living below the poverty line, which can be accessed from government databases using home address. Operationalizing SES with just one or two measures is not ideal, and prevents us from better understanding the contributions of different components of SES to the effects we observe (see Duncan &Magnuson, 2012, for an exposition of what is lost by cutting measurement corners), but given the at least moderate correlations among components of SES, and the practicalities of measurement, it is the most common approach in neuroscience research.

Given the complex and imprecise nature of the concept of SES, compounded by the difficulties and compromises involved in measuring it, why is it a focus of research in social science, medicine, and now neuroscience? The answer is that SES is predictive of an astonishingly broad range of important life outcomes. Physical health improves with higher SES; rates of heart disease, stroke, cancer, diabetes and many other serious illnesses go down as SES goes up, and life span is positively related to SES (Adler & Stewart, 2010). Mental health also increases with SES, with progressively less depression, anxiety and psychosis at higher levels of SES (Kessler et al., 2005; Lorant et al., 2003; McLaughlin et al., 2012). Intelligence and academic achievement both show positive gradients with SES. From the "school readiness" of kindergarteners to performance on standardized achievement and IQ tests throughout life, higher SES is associated with higher performance (Gottfried et al., 2003; Sirin, 2005). For example, a recent study found a 6 point difference in child IQ between the lowest and highest SES levels at the age of 2 years, which grew to more than a 15 point difference when assessed at age 16 (Von Stumm & Plomin, 2015). Understanding how SES interacts with human development is therefore an important goal from the perspective of public health and human capital.

Why a neuroscience approach to SES?

One might agree that understanding SES is an important goal but nevertheless question the relevance of neuroscience. Does it make sense to take a neuroscience approach to a phenomenon as complex and fundamentally societal as SES? Or is this like looking for why there are 9 innings in a baseball game by examining the materials and structure of a baseball? The realities of SES are far more complex than baseball, and I am not suggesting that neural explanations can replace explanations based on external structural features of people's social, economic and political situations. However, I am suggesting that neural explanations should be considered alongside structural societal explanations, and that in some cases neural explanations may be uniquely informative.

The brain is a major locus of integration and influence for the multitude of environmental factors that shape our lives, from physical factors (e.g. nutrition) to psychosocial factors (e.g. family stability). Let us set aside ways in which this is true in a trivial and uninformative way, such as when someone attends a high school without a knowledgeable history teacher and as a result has less history knowledge stored in his or her brain than people at better staffed schools. One gains no new explanatory traction on SES differences by recognizing the fact that history knowledge is represented in the brain, nor does this fact help suggest new ways of reducing educational inequality. In contrast, there are known mechanisms by which the physical and psychosocial environment affect the brain, which have no simpler or more straightforward explanations in purely psychological terms. These neural mechanisms constitute important candidate explanations for the relation between the socioeconomic environment and the brain. A clear example of this, to be discussed in more detail later, is the effect of chronic stress on the brain.

Furthermore, in addition to being shaped by environmental factors that vary across levels of SES, the brain has, in turn, a powerful influence on human capabilities known to vary with SES. These include cognitive ability and emotional resilience, which play an undeniable role in life outcomes in any socioeconomic context. It can therefore be viewed as a potential causal waystation whereby the socioeconomic environment leads to socioeconomic disparities in life course. Ultimately, the validity and usefulness of neuroscience for understanding SES is an empirical issue, and the proof will be in the pudding.

In this Review I take stock of what is known so far. In the next section I ask whether and how the brains of lower and higher SES individuals differ. In the section following that I examine the likely origins and practical significance of these brain differences. Finally, in conclusion I examine the ways in which SES is relevant for neuroscience more generally.

II. Neural Correlates of SES

The first question to be addressed, what differences are observable between the brains of lower and higher SES individuals, is primarily descriptive. Descriptive research is often denigrated for not advancing our understanding of the "why" questions, which most of us view as the proper concern of science. However, description is essential in the early stages of a scientific program. One of Hughlings Jackson's "laws," according to Ramachandran and Aronson (2012), was "The study of the causes of things must be preceded by the study of the things caused." One cannot frame "how" and "why" questions without knowing a certain amount about the "what" that is to be explained. In the case of SES research in neuroscience, simply establishing the "what" is challenging, given the complexity of the SES construct and the variability in how it is measured by different researchers. Indeed, while any psychological correlate of SES must ultimately be traceable to neural function, there is no guarantee that the correlates of SES will be related in ways that contemporary neuroscience can reveal. The most fundamental question we can ask regarding SES and the brain is therefore: Are there neural correlates of SES that can be captured by the current methods and theoretical frameworks of neuroscience?

If there are neural correlates of SES, then the next round of fundamental questions involves the nature of those correlates. For example, how general versus specific are they? Is SES related to brain function across the board, affecting all neurocognitive systems equally? Or, is there a jagged profile of SES disparity in brain function with some neurocognitive systems showing more SES disparity than others? If the latter is true then we can ask, which systems are most strongly linked to SES? The answers to these questions concerning the neurocognitive profile of SES disparities will position us to better address the

"how" questions, using what is already known about the determinants and developmental vulnerabilities of different neurocognitive systems.

Behavioral correlates of SES for specific neurocognitive systems

The earliest attempts to discover the neurocognitive profile of SES used behavioral tasks to assay a variety of neurocognitive systems. To reveal the neurocognitive profile of SES using behavioral tasks, it was necessary to identify tasks from cognitive neuroscience research that showed both functional (eg, working memory) and anatomical (eg, dorsolateral prefrontal cortex) specificity, and adapt them for use in a behavioral task battery. Such batteries were administered to kindergarteners (Noble et al., 2005), first graders (Noble et al., 2007) and middle schoolers (Farah et al., 2006), showing good, though not perfect, consistency of results across these different studies. SES, defined by a combination of parental income and education in these studies, was associated with overall performance as expected. Of greater interest was the pattern of SES disparities across the different neurocognitive systems tested; it was uneven, as demonstrated by statistically significant SES x system interactions in each study, with language, executive function (especially working memory and cognitive control) and declarative memory the most strongly related to SES. Other studies, focused on single systems, are generally accord with these results, finding language (Fernald & Marchman & Weisleder, 2013; Hart & Risley, 1995; Hoff, 2013), executive function (EF; Lawson, Hook & Farah, 2017; Raver et al., 2013; Turrell, 2002) and memory ability varying with SES (Fuhrer, Head & Marmot, 1999; Noble et al, 2015b; Hermann & Guadagno, 1997; Markant et al., 2017).

Functional correlates of SES in the healthy human brain

The behavioral findings suggest that we should expect to find SES correlations with more direct measures of brain function such as fMRI or ERP, and this has indeed been the case in a small but growing literature. In addition to increasing the sheer number of studies that assess SES disparities in various neurocognitive systems, these studies provide additional insights into the underlying nature of the disparities, in both anatomical and psychological terms. There are at least three ways that the functional brain correlates add to our understanding.

First, they add confirmation of the functional locus of SES disparities. For example, while disparities in performance of working memory tasks likely indicate a disparity in working memory per se, rather than disparities confined to other cognitive systems required for performing the task, the finding of disparities in dorsolateral prefrontal activation while performing the task provides an additional degree of confirmation for SES differences in working memory. Similarly, if SES disparities in syntactic parsing of sentences are reflected in an ERP component associated with syntactic parsing of sentences across a broad literature, this increases our confidence in the conclusion that the disparity involves syntax.

A second benefit of ERP and fMRI measures is that they are often more sensitive than behavioral measures; in many of the studies to be reviewed there was no disparity in behavioral performance (in some cases due to matching the groups on performance) yet disparities were present in the neural measures. Presumably a larger sample of behavior or a sample from different tasks would provide a more sensitive measure; indeed, the mere detection of differences in brain function would matter little without implications for behavioral differences. The advantage of brain function measures being highlighted here is their potential for predicting behavior better than available behavioral measures (Gabrieli et al., 2015). Therefore, even if our interest is solely in behavior, brain activity measures may add value above and beyond behavioral measures.

Third, neural activity can be informative concerning the nature of the differences in neurocognitive processing between levels of SES. Most studies of individual differences report differences in brain activity that parallel differences in task behavior; that is, there is either a positive or a negative relation between performance and a measure of brain activity (e.g., Yarkoni & Braver, 2010). On the basis of this, one would expect that, when high SES study participants perform better at a task than low SES participants, the difference in brain activity between these two groups would be the same as the difference in brain activity between higher and lower performing participants within a given level of SES. This would be consistent with higher SES participants performing better because they marshal more of the same neural processing resources than lower SES participants. However, it is possible that higher and lower SES participants are performing the task in different ways, and therefore high SES participants' success is correlated with one

pattern of activity, and low SES participants' success is correlated with a different one. Such an effect SES on the activity-performance relation, diagrammed in Figure 1a, is termed 'moderation' and is an important clue concerning the neurocognitive processing that underlies differences between SES. Several of the studies to be reviewed next find evidence of SES moderation and hence of differences in the way tasks are performed across levels of SES.

The ability to focus attention and ignore distraction, central to executive function, is reflected in ERPs showing enhanced processing of relevant information and/or suppression of irrelevant information, distributed over regions of the scalp consistent with prefrontal locations. In several studies, children of higher SES, as assessed by a variety of measures, show more evidence of this prefrontally mediated attentional focus (D'Angiulli et al., 2008, 2012; Kishiyama et al., 2009; Stevens et al., 2009). None of these studies found a significant SES difference in performance, even when performance was below ceiling, consistent with greater sensitivity of ERPs in these studies to disparities in attention compared to the concurrently collected behavior.

fMRI has also found differences in the way brain systems are deployed for executive function that have not been observed in behavioral studies. Using a rule-learning task that operationalized EF by rule novelty, Sheridan et al. (2012) found the expected SES difference in performance measures, and SES differences in, and moderation of, brain activity. Higher SES children showing overall less activity in several areas associated with executive function, including middle and inferior frontal gyri and anterior cingulate cortex but showed more activity in another area, the right superior frontal sulcus. This combination of both positive and negative relations between SES and brain activity suggests the possibility of different ways of performing the task across levels of SES. A working memory study by Finn et al. (2016) showed statistically significant moderation of task-activity relations by SES. As in Sheridan's study, the higher SES children performed better than their lower SES counterparts. When activation in the network of prefrontal and parietal working memory areas was examined, the higher SES children also showed a disproportionately larger increase in activation as working memory load was increased. This resulted in a cross-over in activation levels from least to most demanding working memory conditions, such that the lower-income

group exhibited more activation in the least demanding condition and less activation in the most demanding, again suggesting qualitative differences in the way higher and lower SES children performed the task.

SES and memory have been addressed in three studies of brain activity. In the first, older adults' judgements of the recency of memories, an ability dependent on prefrontal cortex, were more accurate for those of higher SES, and were associated with ERPs indicating more frontal activity (Czernochowski, Fabiani & Friedman, 2008). An fMRI study of young adults' recognition memory for pictures did not find an effect of childhood poverty on recognition performance after adult SES was covaried, but found a borderline significant effect of childhood SES on hippocampal activation during recognition. The most striking finding was that childhood SES significantly moderated the relation between performance and activation; those who had not been poor as children showed the expected positive relation between recognition accuracy and activation in the hippocampal region of interest (ROI), whereas those who had been poor showed an opposite effect. In a study of children, hippocampal activation during a paired-associate memory task was related to maternal subjective social status, although not to task performance or to maternal education or income-to-needs ratio (Sheridan et al., 2013).

Much of the work on SES and brain function has focused on academic skills in children, specifically mathematics and language skills, perhaps because of real-world importance of the socioeconomic achievement gap. Indeed, the working memory study mentioned earlier was undertaken in part to test the role of working memory in mathematical achievement. Finn and colleagues (2016) found that mathematics achievement, as assessed by a state test, was predicted by working memory ability, and again found moderation of the relation between brain activity and behavior by SES: Working memory-related brain activity in parietal cortex predicted math achievement in both lower and higher SES children, but activity in prefrontal cortex was predictive only for the higher SES children.

Demir et al. (2015) examined the neural correlates of children's arithmetic processing and found that brain activity varied by SES, measured by parental education and occupation. As in other studies, there was no overall effect of SES on performance in the subtraction task. However, there was variability in skill level within levels of SES, and SES moderated the relation between behavior and brain activation: In higher SES

children regions including left middle temporal gyrus, associated with verbal performance, tracked mathematical ability, whereas in lower SES children ability was more closely associated with regions including right intraparietal sulcus, associated with spatial processing. More recently this group examined the neural correlates of gains in arithmetic ability and again found differences with SES. In higher SES, student improvement was associated with increased activity in verbal areas including left inferior frontal gyrus whereas for lower SES students right parietal areas were related most strongly to progress (Demir-Lira et al, 2016).

SES disparities in literacy and associated language skills are at the heart of the socioeconomic achievement gap and several studies have investigated the functional neural correlates of these differences. Noble et al. (2006) scanned children of widely ranging SES, defined by parental education, occupation and income-to-needs ratio in a reading task. Specifically, the children were to match visually presented pronounceable nonwords, which engages phonological processing. Although there was no difference in phonological skill between the lower and higher SES children, the relation between performance and brain activity differed as a function of SES. Specifically, lower SES children's phonological ability was more predictive of activation in the left fusiform word area than higher SES children's. This was due to the higher left fusiform activity in higher SES children with low phonological skill, consistent with the availability for such children of literacy-related knowledge and abilities other than phonological processes for help with letter-string encoding. Raizada et al (2008) scanned children performing a rhyming task, which requires awareness of phonological structure and is an important foundational skill for reading. They found that the expected asymmetry in activity between Broca's area in left inferior frontal cortex and its right sided equivalent was less apparent in the lower SES children, and also that the degree of SES-related asymmetry exceeded that which would be predicted by the relations of SES and asymmetry to performance on a set of language tasks. Demir and colleagues (2015, 2016) also scanned children while performing a rhyming task with printed words as a verbal localizer task for their studies of arithmetic, and found that SES was negatively related to activation in the verbal ROIs in both cases. In contrast to the language studies just reviewed, Monzalvo et al.'s (2012) fMRI study of children did not find SES differences during the passive

perception of printed words or spoken language. The absence of a task to perform in this study may be responsible for the difference in result.

More elementary language processes related to speech perception have also been examined as a function of SES. Conant et al. (2017) scanned children during phoneme discrimination and found that that SES as measured by maternal education moderated the relation between brain activity and phonemic discrimination ability. For children with less phonemic discrimination ability, SES predicted the activation anterior left hemisphere regions. SES differences in the processing of speech by normal hearing adolescents was found by Skoe, Krisman and Kraus (2013) at the surprisingly early stage of auditory brainstem response. ERPs showed less distinct coding of the speech-relevant features of sound and what the authors referred to as noisier activity during silence. In an ERP study of higher levels of speech processing, Pakulak and Neville (2010) instructed adults to distinguish between sentences with correct and incorrect syntax, and the difference in ERPs between the two sentence types were compared. Exploratory analyses revealed that the left anterior negativity accompanying syntactic violations was larger in subjects with higher parental education and occupational status, even when controlling for language ability and other factors.

Finally, a number of studies have examined SES differences in emotion processing using fMRI. Greater amygdala reactivity to threatening or fearful faces, relative to neutral or happy faces, has been reported in lower SES adolescents (Muscatell et al., 2012) and adults (Gianaros et al., 2008; Javanbakht et al., 2015; see also Johnson, Riis & Noble, 2016, for a review of functional and structural differences in the amygdala in relation to SES and maternal depression). When the activity of prefrontal regions was also analyzed, mPFC was also found to be more reactive with lower SES (Javanbakht et al., 2015; Muscatell et al., 2012). Contrasting with greater cortical and subcortical response to negatively valenced stimuli, rewarding stimuli have been reported evoke less activity in frontal, ACC and striatal regions in lower SES adults (Gianaros et al., 2011; Silverman et al., 2009). Pilyoung Kim and colleagues have observed analogous patterns of response in first-time mothers exposed to affectively valenced stimuli related to infants. Medial frontal responses to the aversive sound of crying was enhanced in lower SES mothers (Kim et al., 2016), as

were amygdala responses to the sight infants with negative expressions, whereas responses to infants with positive expressions were dampened (Kim et al., 2017).

The functional connectivity among these areas while processing emotion has also been found to differ across SES, with less coupling between activity of cortical and subcortical areas (Gianaros et al., 2011; Javanbakht et al., 2015) and less prefrontal activation in response to instructed emotion regulation through cognitive reappraisal, along with less reduction in amygdala activity (Kim et al, 2013). In resting fMRI, both the amygdala and hippocampus were found to be less functionally connected at rest to a set of cortical regions including the right superior frontal cortex for lower SES children (Barch et al., 2016). The sample studied by Javanbakht, Kim and colleagues was found to have less default mode network connectivity in the low SES participants (Sripada et al., 2014), with a trend toward the same for 6 month-old infants studied by Gao et al (2015).

In sum, certain neurocognitive domains are particularly apt to show SES disparities on behavioral testing; these are language, executive function and memory. These same systems also show disparities in neural processing as revealed by ERPs and fMRI, including evidence of moderation whereby SES is associated with differences in the neurocognitive systems used. Differences between higher and lower SES mathematical problem-solving are consistent with SES disparities in language. Finally, functional imaging studies have documented differential engagement of neural systems for different aspects of positive and negative affect, and a few studies have noted diminished functional connectivity.

Structural correlates of SES in the healthy human brain

Does brain structure also vary with SES? This is a particularly interesting question for two reasons. First, unlike electrophysiology, fMRI and behavioral performance, brain structure as revealed by MRI is unaffected by momentary states of mind, which can affect the manner in which more trait-like abilities and inclinations are expressed. Motivation, distraction, or power relations between participant and researcher are among the possible factors that could confound measures of brain activity and behavior with different levels of SES. Indeed, the influential research program of Mullainathan and Shafir (2013) has shown that low SES can engender a "scarcity mindset" whereby preoccupation with pressing needs diverts attentional resources

from other cognitive processes. SES differences in brain structure indicate more trait-like differences alongside possible state differences.

Another virtue of structural, compared with functional, imaging is the comparability of findings across studies. The results of fMRI and ERP studies depend on the tasks and control conditions used, making it difficult to assess patterns of findings across differently designed studies. Although structural measures are not independent of methodological differences between studies, they are generally far more comparable.

Structural correlates of SES have been discussed in recent years by several authors (e.g., Blair & Raver, 2016; Brito & Noble, 2014; Gabrieli & Bunge, 2017; Holz et al., 2015; Johnson, Riis & Noble, 2016; Katsnelson, 2015; Lipina & Segretin, 2015). The growth of knowledge in this area is apparent from the near absence of findings on brain structure in early reviews of SES and brain development (Hackman & Farah, 2009; Raizada & Kishiyama, 2010) compared to dozens of relevant studies at the time of writing.

SES has been found to correlate with many aspects of brain structure. Cortical volume, surface area and thickness have all been studied and have been found to correlate with SES in many, but not all, studies (eg Gianaros et al., 2017; Mackey et al., 2015; Noble et al., 2015a; Figure 2). The volumes of subcortical structures, especially the hippocampus and amygdala, have been studied in relation to SES, yielding a mix of positive and null results (e.g. Butterworth et al., 2012; Hanson et al., 2011, Yang et al., 2015). White matter volume, and integrity as assessed by diffusion tensor imaging, have also been examined and found to relate to SES in some cases (e.g., Gianaros, et al., 2013; Johnson, Kim & Gold, 2013; Ursache & Noble, 2016) and, in another example of SES moderation of brain-ability relations, to interact with SES in predicting reading ability (Gullick, Demir-Lira and Booth, 2016). Brain regions showing structural differences include parts of the limbic system and the cerebral cortex, encompassing the frontal, parietal, temporal and occipital lobes. Two regions that are frequently reported to correlate with SES are the hippocampus and frontal cortex. This accords with the behavioral differences in memory and executive function summarized earlier.

The positive relation of children's hippocampal volume to SES was first reported by Hanson et al. (2011), and since then a number of other findings have appeared that are consistent with this in children (e.g.,

most recently, Noble et al., 2015a, Yu et al., 2017; Leonard et al., 2015). The literature on adults is more variable; a number of studies do replicate the hippocampal volume finding in adults (e.g., Butterworth et al., 2012; Janowitz et al., 2014; Staff et al., 2012; but some do not (e.g., Liu et al., 2012; Wang et al., 2016; Yang et al., 2015). Most recently, for example, Yu et al. (2017) found that SES predicted hippocampal volume in 8-12 year olds but not in 18-25 year olds. Studies of adults have the added dimension of complexity concerning whether adult SES or childhood SES are used in analyses, although that factor alone does not account for the variable findings.

Assessing SES differences in frontal regions is more difficult because studies may measure surface area, cortical thickness or their product, volume. These different dimensions index different developmental processes, with surface area assumed to reflect the development of cortical columns and cortical thickness reflecting the development of cells within a column as well as synapse formation and pruning and myelination (Johnson & De Haan, 2015). We should not, therefore, expect SES differences in the cortical thickness of a certain area to be "replicated" in surface area or vice versa. Further thwarting the effort to combine results on frontal structure across studies is the multitude of ways that subregions have been defined, including gyral and sulcal divisions, Brodman areas, other designations such as simply "dorsolateral" or "medial," or even the whole frontal lobe as an ROI. Only a minority of studies use whole brain analyses and the studies that test a priori ROIs rarely report findings concerning other regions. It should not be surprising that, with this heterogeneity of measures and analytic approaches in a nascent literature, firm generalizations are not yet possible. Indeed, while most of the studies that have looked have found anatomical correlates of SES within the frontal lobes, no specific area reliably varies with SES. For example, for studies that tested orbitofrontal cortex volume as an ROI, a positive effect of SES was reported by Holz et al. (2015) but null results were reported by Gianaros et al. (2007b), Hanson et al. (2010) and Kong et al. (2015). For those studies that tested the volume of inferior frontal gyrus as an ROI, a positive effect of SES was reported on the right side only by Krishnadas et al. (2013a). Raizada et al. (2008) and Noble et al. (2012a) tested the left side only, finding a borderline significant effect in the first case and no main effect of SES but an interaction of SES and age in the second.

In sum, a substantial body of research has revealed associations between SES and brain structure and function. However, it would be premature to make any grand generalizations about a brain signature of SES or poverty. The task of synthesizing this literature is made challenging by the diversity of research designs, sample sizes, ages, ranges of SES and aspects of brain structure and function measured, as well as the inevitable operation of statistical and inferential issues that affect the behavioral and neural sciences, including low power (Ioannides, 2005, 2011) and "researcher degrees of freedom (Simmons, Nelson & Simonsohn, 2011). We can be reasonably confident that SES is associated with hippocampus volume, based on a preponderance of results, which accords with the behavioral studies of memory mentioned earlier. Aspects of frontal structure and function have been frequently noted, consistent with behavioral studies of executive function mentioned earlier, although specific frontal regions do not line up especially reliably with SES in these studies. Furthermore, other regions are associated with SES in a number of studies. For example, Noble et al.'s (2015a) study of 1099 children, the largest study published to date, identifies several cortical areas outside the frontal cortex as showing highly reliable ($p<0.001$ FDR corrected) relations between cortical surface area and SES, including the insula, temporal pole, and anterior and posterior cingulate.

The current lack of a clear-cut brain signature of SES or poverty is disappointing but understandable for a science grappling with a complex phenomenon that is shaped by interacting social and biological causes over a prolonged developmental course. This is not a topic for a single "critical experiment" or a single definitive observational study, no matter how well designed! Consider that the literatures on childhood onset conditions such as autism or maltreatment are an order of magnitude larger yet generalizations about characteristic patterns of brain structure and function in these conditions are approached with caution (Bick & Nelson, 2016; Chen, Jiao & Herskovits, 2011; Hernandez et al., 2015).

SES and the brain: How early and how low?

Additional insight into the relation between SES and the brain emerges from studies that examine that relation at different ages and over different ranges of SES. Although these studies are still essentially descriptive, the parameters mapped out by them begin to put constraints on possible mechanisms. For

example, how early in life can neural correlates of SES be observed? The younger the age, the less likely that postnatal experience is the sole cause. Do neural disparities grow or narrow with age? The former is consistent with ongoing compounding of SES effects on the brain, the latter with a common developmental trajectory that is traversed at different rates, with lower SES children catching up to their higher SES counterparts at asymptote. Other, more complex, patterns of SES effects over time have other mechanistic interpretations, to be discussed shortly.

Surprisingly few studies speak to the emergence of SES correlates in the brain or their developmental trajectory, despite the use of samples with wide age ranges in some studies (e.g., Lawson et al., 2013; Noble et al., 2015a), perhaps because of the additional statistical power needed to contrast effect sizes at different ages in the available samples. The first explicit attempt to examine the issue was carried out by Hanson et al. (2013). They analyzed the brain development trajectories of a group of 77 young children under the age of 4 years who had been followed longitudinally, some starting as young as 5 months. When the lowest SES third of children was compared to the highest third, the authors found significantly more disparity in total grey matter with increasing with age, and frontal grey matter showed a borderline significant trend in the same direction. However, no direct tests of the SES effect were performed for any specific ages or age ranges, and there were relatively few children scanned as young as 5 months of age. The authors were therefore careful not to report any particular age at which SES disparities could be observed.

Other studies used measures of structure or function at various young ages and report mixed results. Brito et al. (2016) found no SES disparities in newborn EEG power across several frequency bands, whereas Tomalski et al (2013) found disparities in frontal gamma power at 6-9 months. Measuring resting fMRI longitudinally at 1, 3, 6, 9 and 12 months, Gao et al. (2015) assessed the development of 9 functional networks previously characterized in adults. They found SES disparities in the sensorimotor and default mode networks at 6 months, although after correction for multiple comparisons this finding was of only borderline significance. Finally, Betancourt et al. (2015) examined the structural MRIs of healthy, term 4-6 week olds of varying SES, including a substantial representation of infants from families below the poverty

line. At this age we found that SES was positively associated with cortical and subcortical grey matter volume.

Perhaps the difference between EEG at birth and at 6-9 months of age (Brito et al., 2016; Tomalski et al., 2013) reflects the effects of SES-linked differences in the early environment, or alternatively the effects of antecedent influences such as genetics or prenatal factors that are manifest only gradually. The same alternatives apply to the emergence of SES disparities in network strength at 6 months and growing volume differences in the preschool years (Gao et al., 2015; Hanson et al., 2013). If future research replicates the fleeting disparity noted by Gao et al. (2015) at 6 months, this would suggest different rates of maturation along a shared trajectory, as noted earlier. Finally, the early structural differences reported by Betancourt et al (2015) suggest that, whatever role SES plays later in life, some of the relevant processes take place early on. These could involve genetic or epigenetic inheritance or aspects of the prenatal and perinatal environment.

Brain changes at the other end of the life course have also been related to SES in some, but not all, studies. For example, Kim et al. (2015) found education to be positively related to cortical thickness in a number of regions, and this difference was larger at older ages, consistent with more rapid thinning for lower SES individuals. The relation between SES and brain structure among the elderly is complex, in part because of "cognitive reserve," the ability of some older adults to maintain cognitive abilities despite pathological changes associated with dementia (Barulli & Stern, 2013). Individuals of higher SES generally have more cognitive reserve, resulting in paradoxically more brain atrophy and other pathology when samples of clinically normal elderly are compared (Fontenos et al., 2008). In a cross-sectional study comparing participants spanning seven decades in age, Noble and colleagues (2012b) observed that the trend toward hippocampal volume loss in aging was steeper in adults with lower levels of educational attainment. A recent study by Elbejani and colleagues (2017) found that SES was related to hippocampal volume in older adults and, longitudinally, to volume loss. Given the cellular changes that underlie volume loss in aging (Barrientos et al., 2015; Mattson & Magnus, 2006) it is likely that SES differences reflect at least partially distinct mechanisms from those observed earlier in life.

A person's age is also likely to moderate the association between SES and brain structure. Brain development, from infancy through young adulthood, follows complex patterns that are regionally specific, with nonlinear and even nonmonotonic trajectories and, within certain general constraints, variable from person to person (Giedd & Rapport, 2010). An early clue that SES manifests differently in different aged children came from Noble et al's (2012a) study of 5-17 yo children. They found that, for two of the language-related ROIs examined, the left IFG and the left STG, age statistically moderated the SES effect, with positive SES-volume relations emerging at later ages. Noble and colleagues then examined the trajectory of structural development in a sample of 1148 children (Piccolo et al., 2016). They found that the normal thinning of cortex showed a precocious pattern in the lower SES children, with a steeper trajectory in early and middle childhood and then beginning to level off in adolescence, whereas thickness declines more linearly and for longer among the higher SES participants. This same pattern was observed in one of the authors' selected language-related ROIs, the left fusiform gyrus, and another such area, the left STG, showed linear effects of age at all levels of SES, but steeper (ie more) thinning overall for higher SES. In conjunction with the animal literature on early adversity and precocious brain development (e.g., Bath, Manzano-Nieves & Goodwill 2016), these findings begin to constrain the possible mechanisms by which SES comes to be correlated with brain structure. Although more studies, ideally with longitudinally collected data, would strengthen the initial clues to mechanism reported here, timing differences for cortical thinning can be related to plasticity and the precocious closing of sensitive periods of brain development in children of lower SES.

Turning to the question of "how low?," we can ask whether the neural correlates of SES are essentially the neural correlates of poverty, or whether increments of SES at any level predict brain differences. In the former case, one would see neural correlates below a certain socioeconomic threshold, but not at higher levels of SES, and the presumed causes would operate only within the lowest levels of SES. In the latter case one would see a gradient in brain measures across the entire range of SES, and the mechanisms that give rise to these differences would be similarly operational over that range.

One of the surprises of early health disparities research was that the statistical effects of SES operate across the whole SES continuum, generally showing a gradient rather than a threshold, although the gradient may be steeper at the lower end (Evans, Wolfe & Adler, 2012). The neural correlates of SES appear to share this property. Although some studies have examined the anatomical correlates of specifically low SES, or poverty, compared to higher levels of SES, many examine the effects of SES over the whole range, from poor to near-poor to varying levels of working and middle class and wealthy professional classes, and find a gradient. Two studies with large samples and continuous measures of SES show both graded effects and a steepening of the effect at the low end of SES. This is most clearly seen in the study of 1099 children by Noble et al. (2015a), where total brain surface area increased relatively steeply with family incomes below $25,000 per year and less steeply from that level to over $250,000 per year. In an analysis of the brain volumes of 389 children, Hair et al (2015) found that comparisons between poor and near-poor children revealed larger differences than near-poor and higher SES children. The interpretation of gradient and threshold effects is far from straightforward but may reflect differently weighted combinations of causes operating at different levels of SES, "diminishing returns" as the causal drivers of these effects increase at higher levels of SES, or simply nonlinearity in the scaling of SES measures used in the studies and the true drivers of the effects. The existence of such threshold-like effects indicates that poverty and SES are not interchangeable constructs, and research results based on analyzing broad ranges of SES or extreme group designs should be interpreted accordingly.

III. Causes and consequences of the neural correlates of SES

The neural correlates of SES are of interest primarily for what they can tell us about their causes and consequences. If their consequences for real-world health, wellbeing and achievement are minimal, then there is little point in studying them. On the assumption that they do play a role in life outcomes of interest, then they are of potential value as clues to the causes of these SES disparities.

<u>Are the neural correlates of SES consequential?</u>

Turning first to the consequences of the neural correlates of SES, the question is whether the associations just reviewed, between SES and brain, help to explain the better known and socially significant associations between SES and important life outcomes. Are these neural epiphenoma with little importance for understanding and improving the life outcomes that we ultimately care about? Or, might they embody part of the pathway through which SES shapes those outcomes, as shown in Figure 1b? Although it is plausible that SES-linked brain differences explain SES differences in outcomes, it is not necessarily the case. SES-linked differences in structure and function need not predict SES-linked differences in health and behavioral outcomes, and they need not do so above and beyond SES-outcome relations that are already expected. Although the observational data that make up this literature prevent direct tests of the causal role of the brain in the shaping of life outcomes by SES, they can certainly constrain the causal possibilities by determining whether SES-linked brain differences predict the relevant outcomes and, using statistical mediation analysis, whether that relation accounts for some or all of the SES-outcome relation.

A number of studies have so far collected SES, brain and behavior measures in the same participants and some include a mediation analysis. For example, Noble et al. (2015a) related SES to cortical surface area in children, as already described, and also related each of these variables to performance on a set of cognitive ability tests. They found that SES predicted test performance as well as overall surface area, and that surface area accounted for a significant portion the SES-ability relation for two of the four tests they examined, the executive functions tested by the flanker task and a working memory task.

Two studies of SES and brain structure have examined participants' academic performance in relation to these variables. Mackey et al. (2015) found that SES predicted the thickness of wide swaths of cortex as well as achievement test performance. Cortical thickness also predicted performance, and in the regions most predictive of performance it was reported to account for almost half of the SES achievement gap in their small sample. Hair et al. (2015) examined the relations among SES, frontal and temporal lobe volume and achievement test performance and found that these volumes partially mediated the relation between SES and achievement. Romeo et al. (2017) measured cortical thickness in children with reading disability, spanning a range of SES, as part of a larger study on reading intervention. They found that SES

predicted cortical thickness in perisylvian and parietal cortex bilaterally, most strongly in the left inferior frontal gyrus. As expected, SES was correlated with vocabulary knowledge. Left IFG thickness was found to fully mediate this relation. In a functional MRI study, Finn et al (2016) found that brain activation during working memory partially mediated the relationship between income status and mathematics achievement.

Neural correlates of SES have also been explored as potential mediators of social-emotional health. Low SES is a risk factor for depression (Lorant et al., 2003) and three studies highlight the role of neural correlates of SES in accounting, statistically, for that risk. The study of Barch et al. (2016), mentioned earlier with regard to functional connectivity among amygdala, hippocampus and cortical regions in children, found that the SES relation to this connectivity mediated the SES relation to negative mood and depression. Swartz et al (2016) conducted an ambitious longitudinal study relating adolescent SES to change in methylation of the serotonin transporter gene, change in amygdala reactivity to fearful faces and change in depression symptoms as a function of family depression history. They found that the relatively larger increase in depression symptoms, from early to late adolescence, in teens of lower SES was accounted for by a pathway from SES to epigenetic change to amygdala reactivity to symptoms. Finally, Yang and colleagues (2015) used structural imaging with a large sample of healthy young adults and assessed a set of personality traits linked to depression. They found that the relation between family SES and depression-related traits was partially mediated by the volume of medial prefrontal and ACC cortex.

Neural mediators for the relation between SES and externalizing behaviors in childhood and adolescence have also been sought. In a study of three types of early life stress, low SES, abuse and institutionalization, Hanson et al., (2014) found that all types reduced hippocampal volume in childhood and, relevant to the present question, mediated the relation between early life stress and disruptive behaviors. However, the relation between SES and behavioral problems and the mediating role of hippocampal volume for that relation were not specifically examined. Holz et al. (2015) confirmed the expected relation between child poverty and adolescent conduct disorder, and found that the volume of orbital frontal cortex, measured in adulthood, fully mediated this relation.

Finally, parental behavior and its relations to SES and brain activity were assessed in the study of Kim et al (2017). The authors measured mothers' sensitivity and intrusiveness during a videotaped session with their infants, aspects of parenting behavior that have been related to later psychological development. They found that lower SES was associated with higher intrusiveness, and that this relation was mediated by the elevated amygdala activation associated with lower SES.

SES and the brain: From correlation to causation

As noted earlier, descriptive knowledge of SES-brain relations is of interest primarily as a first step toward understanding mechanism, the "how and why" of SES and the brain. At a general level, two different classes of account have been offered for the origins of SES disparities in psychological and neural traits. They differ in the direction of causality hypothesized to link the traits with SES, are notoriously difficult to tease apart empirically, and are likely to operate in concert. The relative strength of these processes, and the ways they interact, are challenging topics of study (Conger & Donnellan, 2007).

According to *social causation*, SES causes brain differences though environmental influences on brain structure, function and development. More specifically, conditions associated with lower versus higher SES environments would be the causes of the neural correlates. Given the importance of brain function for academic and occupational success and emotional wellbeing, which are themselves clearly causally related to SES, this would create a vicious cycle: A family's poverty would causally impact the capacities needed for socioeconomic success in the next generation.

Additional social relevance of social causation concerns its implications for intervention. If features of the low SES environment are found to impact the brain detrimentally then there is at least one intervention that could protect the brain, namely eliminating those features. This may of course be easier said than done, but it does establish the in-principle corrigibility of SES disparities in brain structure and function. Another implication concerns our ethical obligations to lower SES children and adults. To the extent that individuals' brain health suffers due to conditions caused by others, those others arguably have an obligation to reverse or remediate those conditions. Again, applying this in the real world would be far from straightforward, as the causal networks are complex.

According to *social selection*, the brain differences reviewed in this article are under genetic control and cause SES differences through lowered educational and occupational performance. One might wonder how childhood SES would correlate with neural and psychological traits according to this account, as children's SES is not caused by their own education and occupational success. The association with childhood SES is explained in terms of genetic transmission of neural and psychological traits within the family, such that children are raised in the environment of their parents' SES and inherit the genetic predispositions to the same level of SES. Although social selection theories do not logically rule out the possibility of effective interventions (genetic effects are amenable to environmental moderation, as in the medical treatment of genetic diseases), social scientists who hold a belief in social selection tend also to be skeptical about the effectiveness of interventions (e.g., Jensen, 1969). It should be added that our moral obligation to help does not logically depend on the resolution of the social causation versus social selection issue.

It seems likely that both types of process operate. On the one hand, it is hard to imagine how innately higher or lower abilities would not encourage upward or downward drift in SES over a lifetime. On the other hand, there is ample evidence that SES-linked environmental factors can cause SES disparities in brain and behavior. For example, an adoption study comparing within- and between-SES adoption found an influence of adoptive family SES on IQ (Capron & Duyme, 1989) and comparisons of adopted siblings to those remaining with their biological families demonstrate that the higher the education of the adoptive family the greater the rise in child IQ relative to siblings (Kendler et al., 2015). In addition, for families who experience a limited period of poverty, later academic attainment is more affected for children who were younger during this experience than for the older siblings (Duncan, Brooks-Gunn, Yeung & Smith, 1998), an effect that has no plausible explanation based on genetics alone. Finally, in rare circumstances it may come to pass that large groups of poor families receive increased income while otherwise similar groups of families do not, and social scientists can use these circumstances as "natural experiments." Such studies have shown a causal effect of income on life outcomes from academic achievement to mental health (see Duncan, Morris & Rodrigues, 2011, for a review). None of these approaches have so far been employed to study the

causal role of socioeconomic factors on brain structure or function, although one research group is planning a randomized income intervention with neural as well as behavioral outcome measures (Noble, 2017). Many other interventions have been designed, although few have focused on manipulating SES per se, but have instead sought to enrich the cognitive or emotional environment of poor children in ways that may alter some of the proximal causes of SES disparities (see Magnuson, 2013, for a review). Although some of these interventions have been studied with neural measures (e.g., Brody et al., 2017; Neville et al., 2013; Farah et al., 2017), they do not give us information about the causal role of SES per se.

If there is a causal effect of SES on behavior and hence the brain, the natural next question is which specific causal pathways are involved. Income per se and other conventional measures of SES do not impinge directly on the brain. Rather, they are distal factors that exert their effects on the mind and brain through more proximal factors, as shown in Figure 1c. The research just reviewed has generally not been able to confirm specific causal pathways through which income affects child development, although some natural experiments involving income have found that changes in parental behavior mediate the positive effects of income increases on children (e.g., Costello et al., 2003). For clues to the relevant proximal features of the socioeconomic environment affecting brain development, there are two literatures to which we can turn: animal research on environmental influences on the brain, and the observational studies of SES and the brain already reviewed.

A tremendous strength of animal research is that it allows experimental manipulations of the environment and is therefore a powerful approach for understanding causality. An equally tremendous weakness is that animals do not have socioeconomic status. However, animals do have many of the candidate proximal causes of SES differences in brain function, and can therefore test causal hypotheses about these proximal factors. Among the candidate proximal causes are prenatal and postnatal biological risk factors such as nutrition and toxin exposure, prenatal and postnatal psychosocial stress, differences in cognitive and linguistic stimulation and differences in parenting behavior during childhood. Abundant evidence associates the aforementioned differences with SES in humans (Evans, 2004; Shonkoff, Boyce & McEwen, 2009), and with the exception of linguistic stimulation, shows their causal impact in experimental

studies of animals (see Hackman, Farah & Meaney, 2010, for a review). Stress and parenting behavior are two candidate environmental causes that have been especially thoroughly explored in animal models. Stress during development or during adulthood causes numerous cellular and molecular changes in the brains of rodents and nonhuman primates; these changes have been most extensively documented in the hippocampus and frontal regions (McEwen & Gianaros, 2010). Parenting behaviors are affected by environmental factors such as stress (Murgatroyd & Nephew, 2013; Rosenblum & Paully, 1984) and play a causal role in buffering the effects of stresses experienced by the offspring (Francis, et al., 1999). A different and older literature on the effects of environmental complexity and variety is also relevant to the candidate proximal causes of SES effects and has shown similarly pervasive effects on brain development, structure and function (see van Praag, Kempermann, & Gage, 2000, for a review; see Kozorovitskiy et al., 2005, in primates).

The other main source of evidence on proximal causes of SES effects are observational studies that apply mediation analysis to measures of SES, candidate proximal mediators, and brain measures. Whereas these studies lack the power of animal models to test causal hypotheses directly, their relationship to SES is more straightforward than animal studies. Such studies test whether specific proximal factors are candidate causes by determining whether these factors statistically mediate the brain measures in question. Statistical mediation is a necessary, if not sufficient, condition for causal mediation and thus narrows the range of causal factors to be considered.

Some of the strongest and clearest findings of mediation from observational studies in humans concern stress. For example, Kim and colleagues (2013) found that chronic stressor exposure in childhood fully mediated the relation between childhood family income and prefrontal activity measured by fMRI in young adulthood. Consistent with animal findings relating both stress and parenting to hippocampal structure, Luby and colleagues (2013) found that life stress and parenting quality together fully mediated the relation between SES and hippocampal volume in children. Kim et al. (2016) found that mothers' perceived stress mediates the SES difference in frontal activation in response to the sound of an infant crying. In contrast, Holz et al (2015) found that stress did not mediate the effects of childhood poverty on adult orbital frontal volume. Molecular studies have also supported a stress-related pathway linking SES and brain

structure. Neuroendocrine measures and cardiometabolic risk factors (Gianaros et al, 2013; 2017) and inflammatory markers (Krishnadas et al., 2013a), themselves associated with chronic stress, have been found to statistically mediate the SES-brain structure relation. The longitudinal study of Swartz et al. (2016), mentioned earlier, demonstrated epigenetic mediation of the relation between SES and amygdala reactivity.

IV. Conclusions

"The neuroscience of socioeconomic status" is a phrase that would have drawn a "huh?" from most scientists as recently as ten years ago. It remains a small field, as measured by publications and participating researchers, but is growing rapidly and for good reason. No human brain exists outside a particular socioeconomic context. The research reviewed here suggests that this context cannot be ignored if we seek to generalize our findings from a given socioeconomic stratum to others or if we seek an understanding of individual variation itself.

A number of special challenges accompany the study of SES and the brain. SES is not a "natural kind" (Quine, 1969) but rather a complex abstraction that can be measured in many ways, with some people's SES changing substantially by different measurement definitions. There is probably no "ground truth" against which to evaluate any specific measurement, but rather more or less relevance or utility to the phenomena under study. This problem is familiar to social scientists, who make progress despite it, but will be disconcerting to neuroscientists.

My descriptions of the literature here have largely ignored the specific measures by which subjects' SES was assessed, a choice made to emphasize the forest over the trees, but which limits depth of understanding. Another important measurement issue concerns the distinction between poverty per se and SES more generally. The neuroscience literature is often imprecise on this difference. The lowest SES included in a sample varies across studies, with poor subjects scarce or nonexistent in some samples. Given SES distributions and sample sizes, studies are often underpowered to distinguish effects of poverty over and above SES. The alternative approach, of studies that use an extreme groups design with poor and middle class subjects, give us no way to determine whether differences found reflect an SES gradient or an effect of

poverty per se. Measurement issues are equally important for the scientific understanding of SES and applications to poverty alleviation. Depending on what is measured – income, education, or other dimensions of SES – proximal mechanisms may differ and different interventions may be indicated (Johnson, Riis & Noble, 2016).

Another set of challenges concerns the direction of causality. The fundamentally observational nature of the human evidence makes it near impossible to distinguish social causation, by which the socioeconomic environment affects the brain, and social selection, by which certain kinds of brain help carry people up or down in socioeconomic status. Within the realm of observational studies, those that test for statistical mediation of SES effects by specific proximal factors such as stress can narrow down possible causal accounts, without directly proving causality. Animal studies of the effects of these proximal factors on the brain provide direct evidence of the causal sufficiency of these factors. As noted earlier, the rare observational study that exploits a "natural experiment" can address causality in humans more directly, but none have so far included neural measures among the outcomes studied.

Finally, the socioeconomic environment is not a one-time "treatment" but a set of factors that impinge on the brain continually from prenatal life through maturity and senescence. Brain development involves different processes at different stages, and SES may shape the brain or, in noncausal language, many be manifest in the brain, in different ways at these different stages, further complicating research in this area.

Despite these challenges, progress has been made. The foregoing review includes dozens of studies relating SES to brain structure and function in normal healthy human subjects. Brain function varies with SES, sometimes in the absence of behavioral differences. As we saw, different brain systems may be engaged in task performance based on SES. Structural differences have also been observed, suggesting the existence of cumulative or lasting differences beyond what is seen in a particular research session. The mechanisms that give rise to these differences have been illuminated by a combination of human and animal studies. There is a degree of consistency among the studies reviewed here, but the robustness of findings in this area will not be known until much more research has been done.

How can we improve and accelerate research on SES and the brain? Several relatively painless methodological changes can advance the field and help resolve some of its ambiguities. First, we should collect and report as many distinct measures of SES as we can for each study. One can generally obtain income and needs, educational attainment, occupational status, neighborhood SES and subjective social status with a brief interview or questionnaire, adding minimally to participant burden. Although income information is sometimes considered by participants as too private to share, many studies include this measure without difficulty. By reporting the mean, variance and effect of each measure on outcomes of interest, we would increase the comparability of results across studies and eventually provide clues to the aspects of SES that matter most to different neural outcomes. Of course, one would need to control for the larger number of independent statistical tests being performed by either creating a composite of the SES measures or prioritizing one of them.

For children, SES measures are the same as their families' SES, with the possible exception of subjective social status. For adults, it is valuable to try to estimate some measure of childhood SES as well as concurrent SES and for elderly it makes sense to try to obtain childhood, mid-life and concurrent SES (see, eg., Elbejjani et al., 2017). Given the multiple pathways through which SES and the brain are linked, different relationships may be apparent with different SES predictor variables at different ages, hence SES age may also be critical for testing the generality of results across studies.

These suggestions apply equally to studies that are not undertaken specifically to understand SES. A wide range of human neuroscience research projects can be informative about SES with a modest addition to the study protocol of SES measures. While this may make more sense for some studies than others, all large samples going forward should include a thorough assessment of participant SES. Given that SES sometimes moderates the relations between brain measures and behavioral outcomes, taking SES into account may help clarify issues of interest beyond SES per se.

Second, structural imaging studies that report SES effects for ROIs can increase their value by reporting the results not only from a priori ROIs but from other regions as well, or from a whole brain analysis. The additional results could be reported in online supplementary materials, in an online repository

or as a document available from the authors. An additional measure, requiring somewhat more effort, would be to analyze and report effects on both cortical thickness and surface area when feasible (see, eg, Noble et al, 2015).

Finally, in SES studies, as in any area of neuroscience, our gifts to the meta-analysis authors of the future can be further enhanced by exploring of the effects of different covariates on findings. The studies reviewed here differ from one another in their use of covariates such as linear and nonlinear effects of age, race and whole brain size measures.

Are we inviting an increase in published false positive results if we expand the number of SES, brain measures and covariates analyzed? The risk seems minimal, provided the full range of measures and analyses are reported, even briefly (e.g., by statements such as "results were qualitatively similar with..." or "effects were nonsignificant with...).

A final recommendation, requiring substantial effort, is for studies to expand downward the range of participants' SES and perhaps even to over-sample at the lowest levels, in order to increase power to measure SES differences and resolve threshold versus gradient effects. Recruitment of low SES participants is challenging, in part because they tend to be more isolated from the institutions through which participants are most easily recruited (e.g., schools and workplaces, Wilson, 1987). They are also substantially more likely to meet health-related and other exclusionary criteria (see, eg., Waber et al, 2007), raising difficult questions about who and what is "normal," which must be addressed in study design and analysis.

Psychology, sociology, epidemiology and economics have all sought to understand the long-observed SES disparities in cognition, behavior and health. Will continued progress in the neuroscience of socioeconomic status enhance our understanding of these outcomes? I am optimistic. There is much that the social sciences do not yet know about SES, and it is hard to imagine that discovering biological pathways linking SES and these outcomes would not advance our overall understanding. Indeed, neuroscience has already begun to contribute, for example providing converging evidence for the roles of stress and parenting in the effects of childhood SES and indicating that qualitatively different processes may underlie performance differences between levels of SES. These are insights with the potential to inform policy as

well as theory, highlighting factors that may be important targets for prevention programs and cautioning us that interventions that work at one level of SES may not be as effective at another.

The specific ways that neuroscience will contribute to understanding SES in the future are difficult to anticipate. Consider an analogy with the role of neuroscience in understanding depression. Neuroscience research on depression has not followed a linear course by which new nosologies, diagnostic tests and treatments are anticipated as the predictable results of a specified program of research. Rather, a mix of exploration, serendipity and hypothesis testing has led neuropsychiatry research to insights about the pathophysiology and treatment of depression (e.g., Mayberg et al., 2005). In similar ways neuroscience can be expected to illuminate the processes by which SES becomes associated with a wide range of important life outcomes, and to suggest ways of improving outcomes for people of low SES.

Finally, the literature reviewed here suggests that SES has relevance to all of human neuroscience. SES has long been recognized as a source of variance in data, hence its frequent inclusion as a so-called nuisance variable in statistical analyses. However, we should also be alert to the possible lack of generalizability of research results beyond the predominantly middle-class backgrounds of most research subjects. The social psychologists Henrich, Heine and Norenzayan (2010) have called the subjects used in most psychology research "WEIRD," because they come from societies that are Western, Educated, Industrialized, Rich, and Democratic. They provide evidence that the behaviors of such subjects cannot be generalized to the large segments of humanity living under different circumstances. Falk and colleagues (2013) have called for the incorporation of population science into neuroscience to avoid similar failures of generalization. SES seems likely to be more relevant in some areas of inquiry than in others, but before concluding that sensory processes would be largely unaffected, recall the findings of Skoe et al (2013) on auditory brainstem responses cited earlier. At a time when neuroscience is being applied ever more widely, in education (e.g., Gabrieli, 2009), marketing (e.g., Arieli & Berns, 2010) and law (e.g., Jones & Shen, 2012) the generalizability of neuroscience research across levels of SES has never been more important.

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Figure Legends

Figure 1. Possible relations among the causes and consequences of SES and its neural correlates. (a) Moderation of brain-behavior relations by SES. (b) Mediation of behavioral consequences of SES by the brain. (c) Mediation of SES-brain relations by proximal factors associated with SES.

Figure 2. Visualizations of findings relating different aspects of SES to different aspects of brain structure. (a) VOLUME varying with NEIGHBORHOOD SES in adults (colored regions $q<0.05$, L and R collapsed). (b) CORTICAL THICKNESS varying with INCOME in children (Scale shows uncorrected p values). (c) SURFACE AREA varying with PARENTAL EDUCATION in children (Scale shows uncorrected p values).

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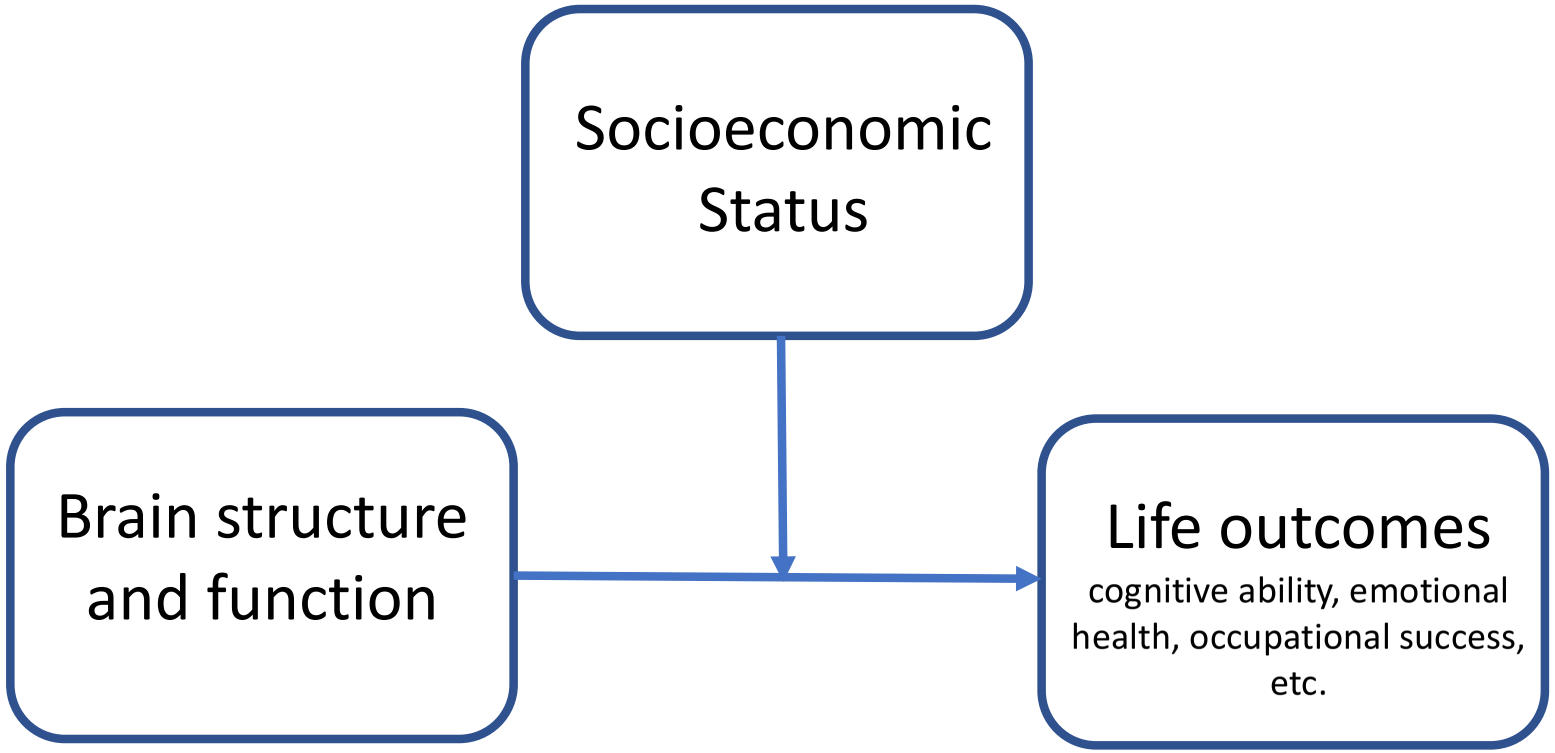
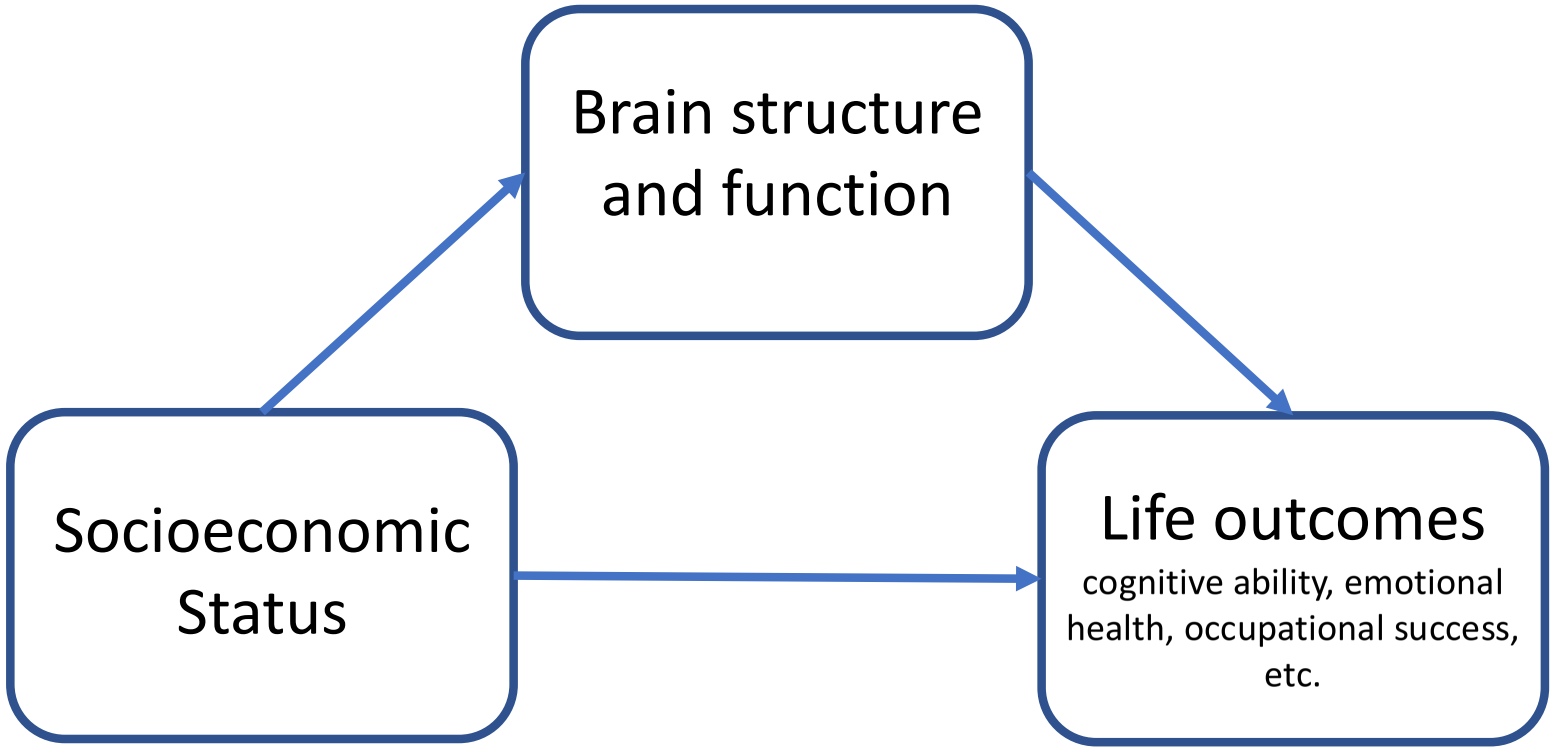
Figure

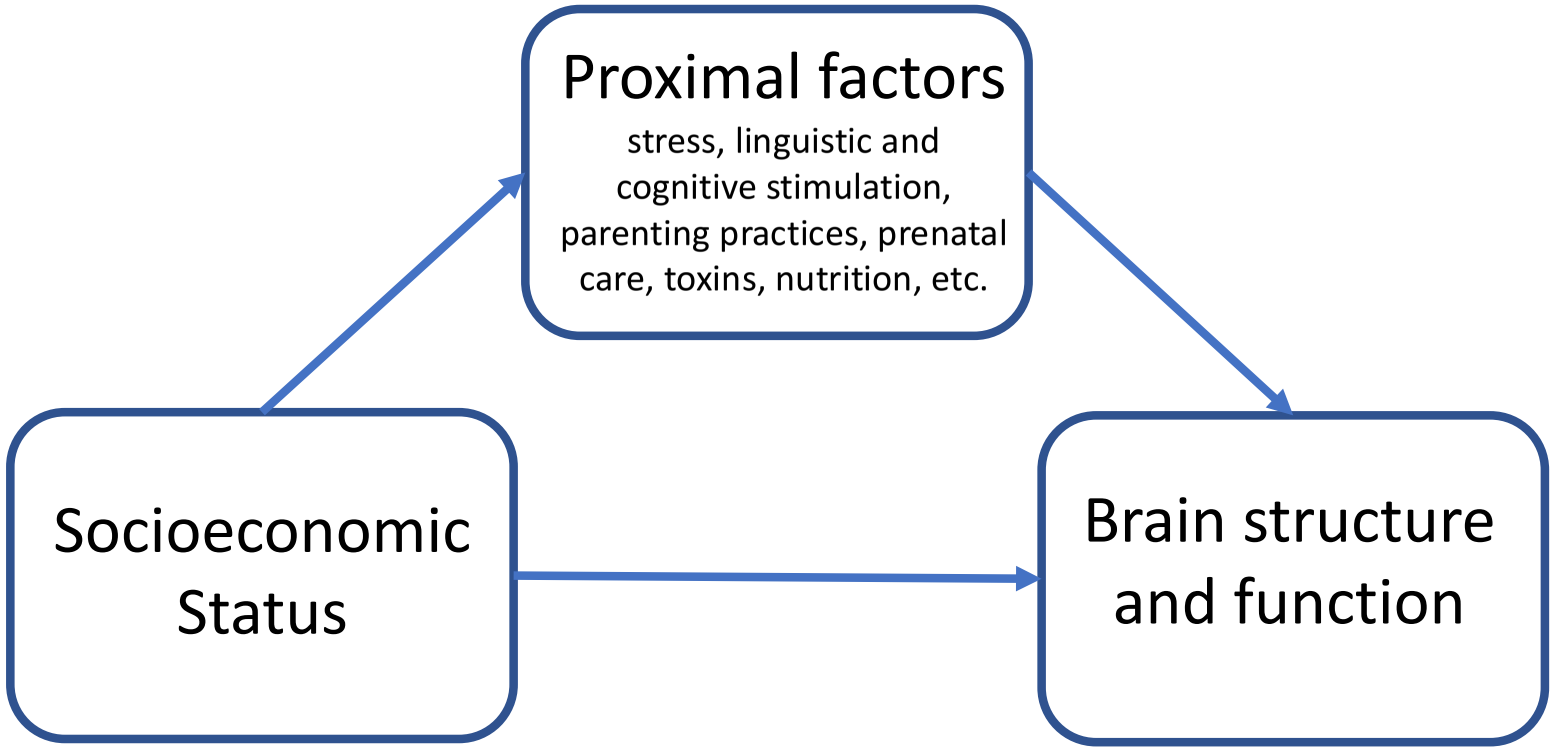
(a)


Socioeconomic Status
Brain structure and function
Life outcomes
cognitive ability, emotional health, occupational success, etc.

(b)


Brain structure and function
Socioeconomic Status
Life outcomes
cognitive ability, emotional health, occupational success, etc.

(c)


Proximal factors
stress, linguistic and cognitive stimulation, parenting practices, prenatal care, toxins, nutrition, etc.
Socioeconomic Status
Brain structure and function

Figure