Both nature and nurture contribute to signatures of socioeconomic status in the brain

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Your education, your job, your income, the neighborhood you live in: Together these factors are considered to represent socioeconomic status

(SES) and contribute to a variety of health and social outcomes, from physical and mental health to educational achievement and cognitive capacities.

The brain acts as an obvious mediator between SES and many of these outcomes. But the mechanism by which it does so has remained hazy, and scientific studies have failed to show whether SES's impact on the brain is encoded in our genes or driven by the environment in which we live.

In a new report in *Science Advances*, an international research team led by scientists at the University of Pennsylvania and Vrije Universiteit Amsterdam take strides to tease apart the relative contributions of genes and environment. Using the largest dataset ever applied to this question, the team found evidence that both genetics and environmental influences contribute to SES's impact in a complex interplay with effects that span a variety of brain regions.

"What we saw in the study is that some of the relationship between the brain and socioeconomic status could be explained by genetics, but there is a lot more to that relationship that remains even after you account for genetics," says Gideon Nave, a marketing professor in Penn's Wharton School and a study coauthor. "This suggests that socioeconomic conditions get under the skin in some way, and can have additional negative influences on the social and economic disparities we see around us."

The work is a product of a large academic collaboration co-led by Nave and Vrije's Philipp Koellinger, a senior author on the study, called BIG BEAR, for Brain Imaging and Genetics in Behavioral Research. Martha Farah, another co-senior author on the work and a psychology professor at Penn, is a principal investigator in the collaboration.

Mapping SES's footprint in the brain

A significant body of research has shown that SES has a signature in the brain.

"I study the relation between SES and the brain," says Farah, "and a question that always comes up is: What causes these differences? Are characteristics of SES encoded in the genome, or does life experience at different levels of SES have these effects on the brain? We were able to show that it is both, and also that genes and environment seem to exert different effects on different parts of the brain."

In the work, the researchers used a massive dataset, the UK Biobank, to better understand those relative contributions. Earlier studies used smaller sample sizes to study the link between the brain and SES or were inconsistent in how they defined SES. In contrast, the UK Biobank encompasses a vast range of types of data, including brain scans and genomic sequencing as well as SES measures, all collected in a standardized fashion. As a result, the research team was able to search for patterns among SES factors and brain scan information for nearly 24,000 individuals.

Each individual was assigned two SES "scores," one combining income, occupation, and educational attainment, and a second combining neighborhood and occupation. Looking at the two scores together, they accounted for about 1.6% of variation in total brain volume—a finding that had been seen previously.

The researchers then dug more deeply into the brain scan data, looking for specific regions of the brain that tracked with SES. They found a whole host of different brain regions related to SES, including some surprises. Of note, the cerebellum, not analyzed by many previous studies, showed a substantial connection to SES. Located near the brainstem, the cerebellum is responsible for movement and balance as well as higher level functions involving cognition and learning.

"We see correlations popping up all over the brain between SES and gray matter volume," says Nave. "They're small, but with the large sample size of our study, we can be confident that they're real."

Adds Hyeokmoon Kweon, the study's first author and a doctoral student at Vrije Universiteit Amsterdam, "Importantly, these small regional correlations do not imply that the overall relationship between the brain and SES is also small. In fact, we can predict a sizable amount of SES differences by aggregating these small brain-SES relationships.

Nature vs. nurture

Because tens of thousands of individuals in the UK Biobank have also had their genomes sequenced, the researchers could look for evidence of the genetic influence of SES in the brain. For this analysis, they created a single index of SES and genetic linkages based on previous research that identified single nucleotide polymorphisms—variations of one "letter" of the DNA code—that correlate with SES.

Using this index, they found that genetics could explain a bit over half of the relationship between gray matter volume and SES in some regions. The prefrontal cortex and insula—responsible for capacities like communication, decision making and empathy—turned up as particularly strongly governed by genetic influence. However the relationship between SES and gray matter volume in other brain regions—the cerebellum and lateral temporal lobe, for instance—were less correlated with genetics, a sign that alterations there may instead be environmentally influenced.

Underscoring the influence that the environment can have, the researchers look at another variable in the data: body mass index (BMI). While genetics plays a role in BMI, BMI also arises from non-genetic factors, including nutrition and physical activity. Even after controlling for the known genetic linkages between brain anatomy and SES, they found BMI could account for an average of 44% of the relationship between SES and gray matter volume.

The finding suggests that the environmental factors, not just genetic determinants, that can contribute to elevated BMI—such as poor nutrition and insufficient physical exercise—may also manifest in brain structure.

A rationale for intervention

The researchers say that their findings, far from suggesting that there's nothing to be done to ameliorate the impact of SES on the brain, instead underscore that thoughtful policymaking could address health and social disparities connected to SES differences.

"The issue of genetic or environmental contributions to SES differences is controversial, in part because of its perceived implications for policy," Farah says. "Many people think that if the difficulties of low SES people are caused by the environment, then we can and should modify the environment, but then go on to an illogical conclusion: to the extent that they are genetic, there's nothing to be done. Genetically-caused problems can also be ameliorated with environmental interventions, for example dietary changes for people with the serious inborn metabolic syndrome PKU or eyeglasses for commonplace vision problems."

Policy interventions could be one solution, the researchers say, addressing, for example, environmental justice concerns that are linked with poorer neighborhoods. "If air quality is worse in lower-SES neighborhoods, that can be triggering inflammation and other negative effects in the brain," says Nave. "As just one example, regulations that mitigate air pollution could remove that harm and improve health and well-being across the board, no matter what neighborhood one lives in. Free, high-quality preschool can do the same thing. Genetics, in this case, is not destiny."

More studies are needed, the team says, to move from identifying correlations to pinning down causations in terms of understanding the environmental effects of SES on the brain. "With more and more data becoming available," says Kweon, "I expect we will be soon able to produce such studies, which will help shape targeted interventions."

More information: Hyeokmoon Kweon et al, Human brain anatomy reflects separable genetic and environmental components of socioeconomic status, *Science Advances* (2022). DOI: 10.1126/sciadv.abm2923. www.science.org/doi/10.1126/sciadv.abm2923

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