Biological Psychiatry: Celebrating 50 Years

Biological Psychiatry and Socioeconomic Status

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The basic science underlying biological psychiatry came first from animal models. For example, rodent studies established the pathways through which early-life experience and stress impact brain systems involved in anxiety and depression (1). With the advent of modern neuroimaging it became possible to study these systems as they function in healthy humans and in those with psychiatric disorders (2).

However, there is one potent risk factor for psychopathology that has been omitted by these otherwise fruitful approaches. This factor does not exist for nonhuman species, and it is rarely examined in studies of the human brain. The factor is socioeconomic status (SES), and in this issue of *Biological Psychiatry*, Merz *et al.* (3) exemplify a new and much-needed focus on the relevance of SES to the health of the mind and brain.

To gain an intuitive understanding what SES is and how we are affected by it, consider epidemiologist Michael Marmot's parade analogy (4): If we were to line everyone up in order of their income, with the lowest-paid people at the front of the parade and the highest-paid people at the back, while watching the procession we would notice changes in what Marmot describes as "demeanor…comportment and confidence…and a healthy glow increasing in radiance with those going past." If we were to reorganize people in terms of educational attainment or occupational prestige, we would observe the same trends in signs of well-being as the people file past—and indeed, most people would be at roughly the same point between front and back as they were in the income parade.

Perhaps not surprisingly, the incidence of psychiatric disorder follows the same trend as Marmot's "demeanor" and signs of health. Psychiatric disorders are more common with low SES, particularly for affective disorders (5)—and while the existence of the trend might not be surprising, the magnitude of it is. A recent Canadian government survey (6) found that disabling mental health problems were twice as common among those without a high school diploma compared with college graduates (Figure 1). A review of studies of childhood mental health found that children from low-SES families were as much as three times more likely to suffer from disorders than their higher SES counterparts (7).

These epidemiological findings raise a fundamental question for basic research: how does SES impact mental health? It goes without saying that there will not be one right answer to this question. Myriad factors are likely to be at work, including differences in nutrition, toxin exposure, prenatal health, parenting practices, cognitively stimulating experience, and stress. Concerning the last factor, traumatic experiences are more likely for people of low SES, and daily struggles are more intense. With less education and less access to material resources, life problems are harder to avert and may instead grow and compound. Animal studies and clinical research show us that this surplus of stress impacts a number of brain structures, including the hippocampus. The hippocampus is the most consistently associated with SES in the small but growing literature on the neuroscience of SES, with higher SES linked to larger hippocampi (8). The hippocampus is also an essential brain structure for the regulation of the brain's stress response, and hippocampal abnormalities are found in most mood and anxiety disorders.

In an early study of SES and the hippocampus, Luby *et al.* (9) found that the number of psychological stressors experienced by a child partially mediated the relation between the family's SES and the child's hippocampal volume. The Merz *et al.* study (3) seeks the corresponding biological pathway in the form of a neuroendocrine mechanism. Their hair cortisol findings are essentially the smoking gun implicating cumulative exposure to cortisol as a mechanism underlying the SES–hippocampus relation.

Their work also adds anatomic specificity to the SAS–hippocampus relation by relating it to dentate gyrus and CA1 subfield volumes (and also larger CA3 subfield volumes, in the same direction with comparable effect size, albeit with only borderline significance). In addition, cumulative cortisol exposure was significantly related to CA3 and dentate gyrus volume, in the expected direction of higher exposure predicting smaller volumes.

Finally, and crucially, a statistical mediation analysis showed that cumulative cortisol exposure accounted significantly for the relation between parental education and both CA3 and dentate gyrus volume [as conveyed graphically in Figure 5 in Merz *et al.* (3)]. While only a randomized experiment can definitively test the causal role of cortisol exposure in the SES–hippocampus relationship (a difficult if not impossible experiment), the present results make a strong case that SES-linked differences in cumulative stress are responsible for reducing hippocampal volumes in low-SES children.

The task of understanding how SES shapes our psychiatric health is a daunting one and has only recently been addressed within biological psychiatry. The present study is in excellent but meager company. This company includes the work of Luby *et al.* (9), already mentioned, and work by Swartz *et al.* (10), who used a longitudinal study design to relate SES to changes in methylation of the serotonin transporter gene, which in turn affected amygdala function and rates of depression for individuals with a family history of depression. The current knowledge is limited, making well-designed studies such as the present one especially valuable.

At this early stage of research, it is to be expected that some findings will neatly answer new questions, while others will simply confirm expected patterns, and still others may

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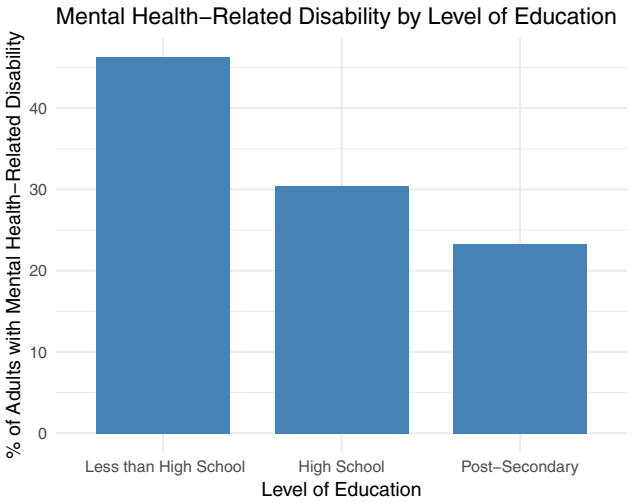

Figure 1. Proportion of adults with a mental health–related disability, by highest level of education in Canada, 2012.

turn out to be unexpected and even perplexing. Merz *et al.*'s findings (3) on the direction of relations between SES and anatomic measures of the anterior cingulate cortex can probably be placed in the last category. At a time of heightened concern over publication bias and its distorting effect on scientific knowledge, the publication of both the interpretable and perplexing findings from this study is commendable.

What are the implications of SES for biological psychiatry research more generally? Given the important influence of SES on the biological substrates of mental health, investigations of those substrates should include an examination of the results in view of participants' SES. Although SES is often included in analyses as a "nuisance variable" because it is indeed understood to predict variance in many outcome variables, authors sometimes simply report that it was covaried, without reporting its effects. By allocating a few more lines of journal space to the effects of SES in studies that do not explicitly focus on this factor, we can accelerate the growth of empirical knowledge about SES. Finally, by recruiting socioeconomically diverse research samples, as Merz *et al.* (3) did, the power to observe SES influences will be amplified and the generalizability of findings enhanced.

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