Genetic Variation of the Serotonin Transporter Moderates the Socioeconomic Health Gradient and Hypertension

ABSTRACT

Genetic variation in the serotonin transporter (5HTT) is thought to influence reactivity to stressors and low social status. This study examines whether 5HTT moderates links in an SES-health gradient model predicting hypertension. Data come from Waves I and IV and the DNA subsample of Add Health. A multiple group comparison strategy was used to contrast the SES-health gradient model as applied to s-carriers and l/l-carriers. Consistent with expectations, results suggest that background experiences are more salient than later experiences: The effects of parental education, female status, African American status, and Hispanic status (reference=whites) were significantly different between the groups (in the expected directions). The respondent's own education had a protective effect among s-carriers. The effects of parental education and sex on respondent's own SES also differed significantly. These results suggest that 5HTT moderates many links in the SES-health gradient model as applied to hypertension.

EXTENDED ABSTRACT

Many studies have examined the socioeconomic and demographic correlates of health in adulthood (Adler, 2010; Berkman cite), including central indicators of cardiovascular disease such as hypertension (cite). These relationships are thought to reflect a wide range of social mechanisms that ultimately lead to biological distress, including differential exposures to and accumulation of stressors, social isolation, psychosocial hardships, demoralization, and poor health-related behaviors (Cohen et al., 2010). Among some racial and ethnic minorities (particularly African Americans), these distressful mechanisms may be yet more disadvantageous owing to discrimination, racism, and residential segregation (Matthews et al., 2010; Williams et al., 2010).

At the same time, a growing body of evidence supports the conclusion that variation in the serotonin transporter genotype (5HTT) is associated with stress reactivity and, consequently, moderates associations between stressors and distress. Indeed, 5HTT is the most investigated genetic variant in neuroscience, with a large body of experimental and observational data showing that carriers of the short variant (or "s-carriers") exhibit greater reactivity to stressors than people who possess two long variants ("l/l-carriers;" for a recent review, see Caspi et al., 2010). Indeed, because 5HTT is associated with stress reactivity, it may moderate many of the above-mentioned mechanisms that link socioeconomic factors with health (Gianaros et al., 2010; Way & Taylor, 2010a). Research with nonhuman primates also suggests that low social status, by itself, may be distressful for s-carriers (Watson et al., 2009), which likewise raises the possibility that 5HTT moderates the effects of socioeconomic status on health.

This paper joins these two literatures by examining the extent to which the SES-health gradient model is moderated by 5HTT in the prediction of hypertension. If s-carriers are indeed more reactive to stressors and low status incumbency, then perhaps social disadvantages are more detrimental to health for them compared to l/l-carriers. We focus on hypertension because people are often unaware of their condition (particularly in young adulthood), eliminating possibilities of self-report bias. Hypertension in young adulthood is also a precursor to more serious, common cardiovascular complications in later life (cites), suggesting that it is a pre-disease pathway of great significance (Ryff & Singer, 200x). Beyond its empirical focus, the paper also illustrates how genetic candidates may be productively integrated into models of long-standing interest in the sociology of health. Data come from Waves III and IV of the National Longitudinal Study of Adolescent Health, a nationally representative study of youth.

Hypothesis 1: Social disadvantages (i.e., social factors that typically increase hypertension) will be more deleterious among s-carriers when contrasted with l/l carrriers. These include being African American and coming from a family in poverty.

Hypothesis 2: Social advantages (i.e., social factors that typically decrease hypertension) will be more efficacious among l/l carriers when contrasted with s hemizygotes. These include parental education, parental income, female, Hispanic, and one's one socioeconomic status as indicated especially by education.

Hypothesis 3: Reflecting developmental mechanisms, it may be that background characteristics and socioeconomic indicators in the family of origin are moderated by the serotonin transporter, not socioeconomic status in young adulthood. That is, the effects of parental education, sex, race, and poverty will differ between s-carrier and l/l-carrier groups, but respondent's own income, education, and subjective status will not.

Hypothesis 4: As an alternative to Hypothesis 3, it may be that background characteristics are moderated by 5HTT such that risks are accentuated among s-carriers and assets are accentuated among l/l-carriers but assets in young adulthood may be protective (i.e., accentuated among s-carriers).

In analyses to date, we have examined a model positing that poverty, highest parental education, race (whether white, black or non-white Hispanic), and sex at Wave I predict respondent's income, status, and education at Wave 4, which in turn predict respondent's hypertension at Wave IV. The model is fully recursive, allowing for main effects from Wave I variables to hypertension. The model was estimated for the Wave III DNA subsample using M-Plus, and then for s-carrier and l/l-carrier subsamples in a stacked, multiple group comparison framework. Statistical contrasts were then used to assess whether effect sizes differed significantly between the s-carriers and the l/l-carriers. Prior to these analyses, descriptive

statistics were examined for outliers, kurtosis, and indicators of central tendency and dispersion.

Results from these analyses reveal a series of significant interactions that are largely consistent with expectations. First, consistent with Hypothesis 1 (that social disadvantages will have larger positive effects on hypertension for s-carriers when contrasted with l/l-carriers), results show that African-American status has a larger direct, positive effect on hypertension among s-carriers. As suggested, this may reflect the greater stressors faced by African-Americans because of racism, discrimination, and residential segregation.

Second, consistent with Hypothesis 2 (that social advantages will have larger negative effects on hypertension for l/l-carriers when contrasted with s-carriers), parental education, female, and Hispanic have larger direct, negative effects on hypertension among l/l carriers when contrasted with s/s carriers. Parental education and female also have larger positive effects on respondent's income, education, and subjective status among l/l carriers.

Third, consistent with Hypothesis 3, the respondent's own indicators of socioeconomic status have little effect on hypertension in either the total sample, the s-carrier subsample, or the l/l-carrier subsample. In contrast, parental education, female, and Hispanic (all characteristics that shape early experiences) proved significantly different between the two groups. However, consistent with Hypothesis 4, the respondent's own education had a protective effect, decreasing hypertension among s-carriers. This unique pattern suggests that background characteristics may alter stress reactivity, but the respondent's own achievements can act as protective factors.

Several limitations should be noted. First, because the research design is non-experimental, no strong conclusions can be reached regarding the causal nature of the observed associations. At the same time, there is a very solid evidentiary basis for the SES-health gradient model and also for the role of 5HTT in stress reactivity (including experimental studies). Second, the statistical contrasts do not adjust for multiple hypothesis testing, which may result in false positives. At the same time, the analyses are underpowered for the study of gene-environment interactions, the magnitude of the differences between groups was typically large, and the study is the first of its kind, suggesting that false negatives should be avoided and findings replicated.

Despite these limitations, the study draws on a large, nationally representative and a reliable and valid measure of hypertension to address a previously unexplored possibility: that the SES-health gradient model—which has informed many hundreds of studies—may be moderated by 5HTT because it is a marker for stress reactivity, including reactivity to social status incumbency. Indeed, despite the fact that gene-environment interactions are generally somewhat difficult to observe (owing to power, measures, and other factors), the analyses reveal a set of

interactions consistent with the hypotheses. Some interactions reflect the prediction of hypertension (by parental education, race, and education), and some reflect the prediction of the respondent's own socioeconomic status (by parental education, sex, and race). Hence, the SES-health gradient model, as applied to hypertension, shows numerous signs of moderation by 5HTT.

Replication is important and would be feasible (for example, with data from NHANES). It is unclear the extent to which these findings would generalize to other health outcomes and to other age groups. Thus, both close replications (i.e., replications referring to similar populations and using similar measures) and differentiated replications (i.e., referring to different populations and using different measures) would be informative.

This study suggests that, however, that 5HTT moderates many links in the SES-health gradient model for hypertension, likely reflecting the greater reactivity of s-carriers to stressors and low social status.