Title: Developmental noise is an overlooked contributor to innate variation in psychological traits

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Abstract:

Stochastic developmental variation is an additional important source of variance – beyond genes and environment – that should be included in considering how our innate psychological predispositions may interact with environment and experience, in a culture-dependent manner, to ultimately shape patterns of human behaviour.

Main Text:

The target article (Uchiyama et al., in press) presents a very welcome and much-needed overview of the importance of cultural context in the interpretation of

heritability. The authors discuss a range of complex interactions that can occur between cultural and genetic effects, illustrating how already complicated gene-environment correlations and interactions can vary at a higher level as a function of cultural factors or secular trends.

However, the framing with genes and environment as the only sources of variance ignores an extremely important third component of variance, which is stochastic developmental variation (Vogt, 2008). Genetic effects on our psychological traits are mainly developmental in origin, but genetic differences are not the only source of variance in developmental outcomes (Mitchell, 2018). The genome does not specify a precise phenotype – there is not enough information in the three billion letters of our DNA to encode the position of every cell or the connections of every neuron. Rather, the genome encodes a set of biochemical rules and cellular processes through which some particular outcome from a range of possible outcomes is realized (Mitchell, 2007).

These processes of development are intrinsically noisy at a molecular and cellular level (Raj and van Oudenaarden, 2008), creating substantial phenotypic variation even from identical starting genotypes (Kan et al., 2010). The importance of chance as a contributor to individual differences was recognised already by Sewall Wright in a famous 1920 paper (Wright, 1920) and is ubiquitously observed for all kinds of morphological and behavioural traits across diverse species (Honegger, 2018; Vogt, 2019). For brain development in particular, the contingencies and non-linearities of developmental trajectories mean that such noise can manifest not just as quantitative, but sometimes as

qualitative variation in the outcome (Honegger, 2018; Linneweber et al., 2020; Mitchell, 2018).

The implication is that individual differences in many traits are more (sometimes much more) innate than the limits of the heritability of the trait might suggest. In other words, not all of the innate sources of variation are genetic in origin, and not all of the non-genetic components of variance are actually “environmental”. Indeed, a sizeable proportion of the confusingly named “non-shared environmental” component of variance may have nothing to do with factors outside the organism at all, but may be attributable instead to inherently stochastic developmental variation (Barlow, 2019; Kan et al., 2010; Mitchell, 2018). This may be especially true for psychological traits, where heritability tends to be modest, but systematic environmental factors that might explain the rest of the variance have remained elusive (Mitchell, 2018). Proposals that idiosyncratic experiences should somehow have more of an effect than systematic ones (Harris, 1995) provide no convincing evidence that this is the case, nor any persuasive arguments for why it might be so.

This does not overturn any of the important points that the authors make but does suggest an important reframing. Rather than thinking solely of genetic versus environmental sources of variance, and the interaction between them, we can think of the interplay between innate predispositions – which reflect both genetic and developmental variation – and experience. Culture can have a huge influence on this interplay, especially on how much scope it gives for individual differences in psychology to be expressed or even amplified through experience.

However, if such predispositions do not solely reflect genetic influences then the implications of such effects for heritability become less obvious. If genetic variance predominates at early stages, then heritability may increase across the lifespan, as is observed for cognitive ability. On the other hand, if the influence of stochastic developmental variance (included in the non-shared environment term) is larger, then heritability may decrease with age, as observed for example for many personality traits (Briley and Tucker-Drob, 2017). In both cases, innate differences may be amplified, as observed in mice (Freund et al., 2013).

An already complicated picture of interactions and meta-interactions thus becomes even more so. In addition, there may be further interactions at play, as the degree of developmental variability is often itself a genetic trait. This has been observed in various experimental systems, which have found that variability of a trait can be affected by genetic variation and even selected for, with no concomitant effect on the phenotypic mean (e.g., Ayroles et al., 2015). More generally, the developmental program has evolved to robustly produce an outcome within a viable range (Wagner, 2015). However, that robustness depends on all of the elements of the genetic program and the multifarious feedforward and feedback interactions between them. Increasing genetic variation is therefore expected to not just affect various specific phenotypes, but also to degrade the general robustness of the overall program and thus increase the variability of outcomes from some genotypes more than others.

This is illustrated by the special case of increased variance in many traits in males compared to females, observed across diverse phenotypes in many different species (Lehre et al., 2008). A proposed explanation is that hemizyosity of the X chromosome in males reduces overall robustness of the programs of development and physiology and thus increases variance in males. Strong support for this hypothesis comes from the evidence that the direction of this effect is reversed in species, including birds for example, where females are the heterogametic sex and show increased phenotypic variance (Reinhold and Engqvist, 2013). Sex is thus another factor that may affect patterns of variation of human traits through this kind of general influence on developmental variability. In addition, of course, cultural factors differ hugely between the sexes, which may differentially influence how innate predispositions are expressed by males and females.

One final complication is that environmental conditions may either buffer or further challenge the developmental program, reducing or exposing variability, as demonstrated in classic experiments (Waddington 1957; Wagner, 2007). Overall then, the already complex interactions very thoroughly discussed by the authors should be expanded to include the often overlooked but hugely important third component of variance: noise inherent in the developmental processes by which genotypes become realized as specific phenotypes.

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