Commentary on: Cultural evolution of genetic heritability (Uchiyama, Spicer & Muthukrishna, 2021)

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Going Beyond Heritability: Mechanisms of Gene-Culture Coevolution

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The target article offers an important cautionary note on the interpretation of the heritability index. However, it does not directly address how culture and genes might interact. Here, we suggest that one allele of the dopamine D4 receptor gene promotes the acquisition of cultural values and practices and likely has co-evolved with the human culture over the last 50,000 years.

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The Uchiyama et al. article takes a cultural evolutionary approach to argue that genetic effects on behavioral traits depend on culture. In particular, the authors show how the heritability index might take different values, depending on cultural contexts. This point offers an invaluable cautionary note on how to interpret the heritability index. However, beyond this, the authors' effort does not directly address the original question that motivated it, namely, how culture and genes have co-evolved and have interacted. As the authors note, "culture and genes are interwoven in the construction of many behavioral traits, making separation effectively impossible (page 46)." Unfortunately, much of the current knowledge on gene-culture coevolution pertains only to genetic evolution that took place far before culture as we know it today emerged (e.g., how the invention of cooking shortened the human guts). Some isolated examples, such as the effect of herding culture on the evolution of lactose tolerance (Tishkoff et al., 2007) and that of rice farming on the evolution of "Asian flush" (Peng et al., 2010), are arguably more recent. However, beyond the consumption of milk and alcohol, little else is known about the coevolutionary dynamic for cultural traits.

Here, we seek to readdress this blind spot of the field by focusing on one gene. For a while, it has been known that one varying length polymorphism of the dopamine D4 receptor gene (*DRD4*) likely coevolved with human cultural evolution over the last 50,000 years, which took place in the Eurasian continent (a similar process must have occurred in Africa, but today, little is known). Crucially, the population-level frequency of a key allele of *DRD4* (called the 7- or 2-repeat allele, or 7/2-R allele for short) increases systematically as a function of distance from Africa (Chen et al., 1999; Matthews & Butler, 2011). This 7/2-R allele is known as a plasticity allele since carriers of this allele are strongly influenced by the quality of parenting (Belsky & Pluess, 2009). Recent evidence shows that this plasticity effect is likely to result from the function of this allele to upregulate the fidelity of computing reward contingencies (Glazer et al., 2020).

Although much of the *DRD4* literature focused on the genetic modulation of parenting quality effects, we wanted to see if we could extend this evidence to cultural influences. Since reinforcement-mediated learning processes constitute a powerful mechanism of cultural learning, the carriers of the 7/2-R allele might acquire, internalize, and thus “carry” mainstream cultural traits. In our work, we have focused on a contrast between European Americans (who tend to be independent) and East Asians (who tend to be interdependent) (Markus & Kitayama, 1991). For example, compared to European Americans, East Asians feel happier when connected with others (Kitayama et al., 2006) and take another’s perspectives more readily (Wu & Keysar, 2007).

In one earlier study, we assessed these cultural traits with validated self-report measures and found European Americans are relatively more independent, and East Asians, relatively more interdependent. Importantly, however, this cultural difference was significantly more pronounced among the carriers of the 7/2-R allele than for non-carriers (Kitayama et al., 2014). Indeed, the non-carriers showed no such cultural difference. In more recent work, we tested cultural differences in brain structures that would support cultural traits among carriers and non-carriers. We had earlier observed that independence (vs. interdependence) positively predicts the gray matter (GM) volume of the orbitofrontal cortex (OFC) (Kitayama et al., 2017). As may be expected, the OFC GM volume was larger for European Americans than for East Asians. Again, however, this cultural difference was evident only among the carriers (Yu et al., 2018). Similar evidence exists for the temporal-parietal junction. Its GM volume increased by interdependence (vs. independence). As may be expected, it was greater for East Asians than for European

Americans as long as they carried the crucial 7/2-R allele (Kitayama et al., 2020; see Kitayama & Yu, 2020, for a review).

We may argue that the 7/2-R allele of *DRD4* emerged over the last 50,000 years to "turbo-charge" the acquisition of culturally sanctioned behaviors suitable for survival (e.g., interdependence in East Asian regions that was suitable for rice-farming) (Talhelm et al., 2014). Bear in mind, however, that this "turbo-charging" could backfire since culture sometimes does require changes and innovations. For this reason, we suspect this 7/2-R allele might account only for 30-40% of the population.

The work summarized above has begun to clarify how culture and genes might have co-evolved. By the time humans spread out of Africa approximately 50-60,000 years ago, humans have been fully equipped with massive genetic networks underlying component processes involved in reinforcement learning (e.g., detection of reward cues and computation of reward contingencies). We suspect that the 7/2-R allele served as a hub of these existing gene networks to amplify the fidelity of reward processing, which, in turn, helped the carriers acquire the most mainstream cultural traditions (as long as they are properly socialized). They may thus have become carriers in double, that is, carriers of both the 7/2-R allele and the mainstream culture of different ethnic groups. Meanwhile, noncarriers might well have remained agnostic to the viability of the mainstream culture, which might have enabled them to innovate and change that culture when such changes were called for.

In sum, Uchiyama et al. show that the heritability index of various traits takes different values depending on the cultural environment. This is a valuable contribution. However, this analysis stops short of directly addressing the dynamic interaction between culture and genes. We have offered the hypothesis that even though cultural traits are entirely contingent on ecological (i.e., environmental) factors, they may still be modulated by *DRD4*. This gene likely helped the human species acquire and sustain cultural traditions over the last 50,000 years. Future work may perform the heritability analysis separately for the carriers and non-carriers of the 7/2-R allele of *DRD4*. In combination, a day may come when we can better understand how genes and culture might have co-evolved to produce contemporary cultural and individual variations.

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