

UC Berkeley

UC Berkeley Previously Published Works

Title

Dopamine-system genes and cultural acquisition: the norm sensitivity hypothesis

Permalink

<https://escholarship.org/uc/item/9p24k3n0>

Authors

Kitayama, Shinobu

King, Anthony

Hsu, Ming

et al.

Publication Date

2016-04-01

DOI

10.1016/j.copsyc.2015.11.006

Peer reviewed

Dopamine-system genes and cultural acquisition: the norm sensitivity hypothesis[☆]

Shinobu Kitayama¹, Anthony King¹, Ming Hsu², Israel Liberzon¹ and Carolyn Yoon¹

Previous research in cultural psychology shows that cultures vary in the social orientations of independence and interdependence. To date, however, little is known about how people may acquire such global patterns of cultural behavior or cultural norms. Nor is it clear what genetic mechanisms may underlie the acquisition of cultural norms. Here, we draw on recent evidence for certain genetic variability in the susceptibility to environmental influences and propose the norm sensitivity hypothesis, which holds that people acquire culture, and rules of cultural behaviors, through reinforcement-mediated social learning processes. One corollary of the hypothesis is that the degree of cultural acquisition should be influenced by polymorphic variants of genes involved in dopaminergic neural pathways, which have been widely implicated in reinforcement learning. We review initial evidence for these predictions and discuss challenges and directions for future research.

Addresses

¹ University of Michigan, United States

² University of California, Berkeley, United States

Corresponding author: Kitayama, Shinobu (kitayama@umich.edu)

Current Opinion in Psychology 2016, 8:167–174

This review comes from a themed issue on **Culture**

Edited by **Michele Gelfand** and **Yoshi Kashima**

<http://dx.doi.org/10.1016/j.copsyc.2015.11.006>

2352-250/© 2015 Elsevier Ltd. All rights reserved.

Introduction

The last two decades of research in cultural psychology shows that cultures vary in social orientations of the self as independent or interdependent [1–3]. Western cultures (e.g. European American cultures) value the independence of the self from others. In contrast, Eastern cultures (e.g. Asian cultures) value the interdependence of the self with others. The social orientation dimension of independence versus interdependence has systematic influences

on cognition [4,2,5], emotion [6–8], and motivation [9[•],10,11]. So far, however, it remains unclear what mechanisms might underlie the acquisition of the culturally sanctioned social orientations of independence and interdependence — in particular, the learning of explicit and implicit rules governing these orientations [12[•]], notwithstanding some initial evidence suggesting that culture-typical behavioral characteristics emerge after six or seven years of age and become more pronounced over the course of adolescence [13–15].

Here, we explore a novel perspective on the acquisition of explicit and implicit rules of social behavior, or cultural norms, by drawing on recent advancements in social genomics — a new field of research that investigates ways in which genetic and epigenetic processes are dynamically linked to socio-cultural processes to constitute various phenotypes including health and other psycho-social outcomes [3,16[•],17,18]. Evidence suggests that individuals are genetically variable in terms of their sensitivity to environmental influences [16,17,19[•]]. Extending this work, we propose the norm sensitivity hypothesis [20^{••}], which holds that people are genetically variable in their sensitivity to global patterns of cultural behaviors or social norms.

Mutual influences between culture and genes

Recent research in population genetics suggests that over the past 10 000 years of human history, numerous polymorphic genetic changes have been positively selected. Moreover, the rate of positive selection appears to have accelerated [21–23]. This exponential increase of genetic change seems likely to be related to the massive increase in human population and exposure to new environments (including domesticated animals and plants) and the resulting diversity in both infectious diseases and available nutrition. This is consistent with ideas in evolutionary biology and biological anthropology that genetic evolution and cultural evolution have proceeded in tandem as suggested by theories of dual inheritance [24] or gene–culture co-evolution [24–27]. Initial evidence for the gene–culture co-evolution came from effects of herding and milk production on emergence of genetic mutations that support the digestion of lactose — the milk

[☆] Writing of this paper was supported by a National Science Foundation grant (SES 1325881) and an Air Force grant (FA955-01-41-0020) to SK and a National Institute of Health grant (RO1 MH098023) to MH.

sugar [28], leading to rapid incorporation of these mutations and supporting the growth of dairying culture.

One intriguing recent proposal is that some genetic variants may lend themselves to plasticity of behavior [17]; that is, carriers of certain alleles could be differentially susceptible to environmental influences [17,29,30]. Such individuals might be more susceptible to early childhood adversity or maltreatment. Indeed, early life traumas increase the risk of depression and posttraumatic stress disorder later in life, but particularly in carriers of specific alleles in the serotonin transporter gene (5-HTTLPR) [29], glucocorticoid receptor chaperone gene (*FKBP5*) [31], and beta-2 adrenergic receptor gene (*ADRB2*) [32].

Extending this literature, Kim and colleagues argued that culture is but one element of one's eco-social environment that encourages certain behaviors and inhibits others. It would then seem to follow that genetic alleles that increase behavioral plasticity might also amplify cultural differences in behavior [16]. For example, it is normative to seek emotional or social support at times of distress in European American cultural contexts, but not in Korean cultural contexts; Kim and colleagues found cultural differences tended to be larger for carriers of the G allele of the oxytocin receptor gene (*OXTR*) polymorphism rs53576, previously linked to increased socioemotional sensitivity [33].

So far, work has focused on isolated behavioral traits such as social support [33] and emotion suppression [34], leaving open the question of whether genetic polymorphisms might modulate each individual's readiness to acquire global phenotypic traits such as norms and behavioral patterns of independence and interdependence. Although social learning has long been argued to be central in maintaining long-lasting cultural traditions [35,36,37*] (see also the Tomasello article in this Special Issue), rarely has this line of reasoning considered genetic factors that foster social learning.

The norm sensitivity hypothesis

Reinforcement-mediated social learning and dopaminergic system genes

The norm sensitivity hypothesis suggests that acquisition of global behavioral patterns and norms of culture, such as independence and interdependence, is influenced by reinforcement-mediated social learning. This type of learning is based on a set of mechanisms that enable the organism to select behavioral options that maximize anticipated rewards [38]. These mechanisms include discerning of behavioral patterns, selection of one's behaviors, and tracking of the reinforcements given to these behaviors [39,40]. Major components of reinforcement-mediated social learning (e.g. social rule learning and reinforcement tracking) involve dopamine-mediated

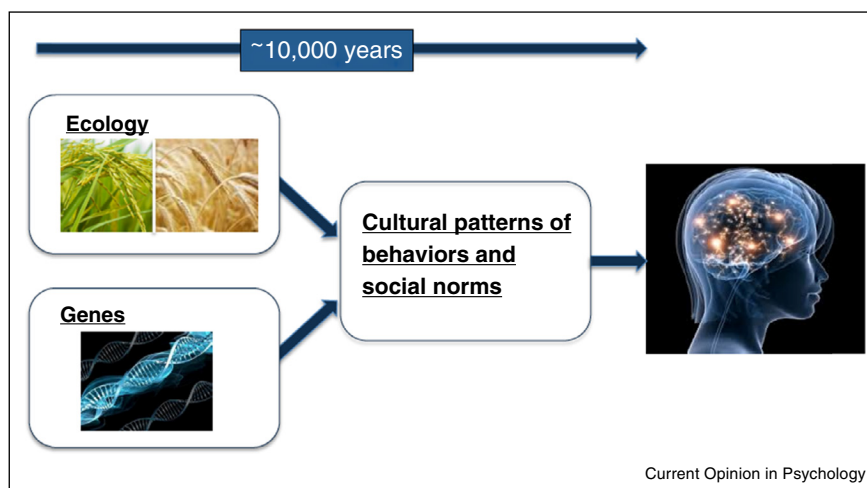
brain substrates (e.g. frontal cortex and striatal reward processing area) [41,42]. By highlighting the role of rewards in social learning, we hypothesize that cultural and social learning is not merely cognitive, but also inherently motivational. We may therefore anticipate that cultural acquisition would be facilitated by gene variants that increase the efficiency of central dopaminergic pathways.

To illustrate, children in any society must infer the rules governing their 'street' by trial and error. The emerging cognitive representation of others' response patterns constitutes the perceived norm for the community. Individuals respond to such norms by formulating their own responses, which may in turn be reinforced either positively (i.e. complimented and praised) or negatively (i.e. punished and ignored). This social mechanism is universal, although cultures vary in terms of how tight or loose in application of social norms [43]. The individuals must track reinforcement history to assess validity of inferred social norms. Resulting behaviors tend to be consistent with group norms, some aspects of which are culture-specific (e.g. independence versus interdependence) and others are more universal (e.g. within-group cooperation and altruistic behavior); although culture-unique socioecological conditions such as mobility and strength of within-group ties are likely to influence the extent of such behaviors [44].

Our theoretical framework, illustrated in Figure 1, explains contemporary cultural variations in terms of large-scale ecological considerations. Anatomically modern humans evolved in Africa approximately 200 000 years ago [45], spread out of Africa approximately 50 000 years ago, and started farming and herding approximately 10 000 years ago. One factor that initially differentiated Eastern versus Western regions of the Eurasian continent is the type of crops available and successfully domesticated (e.g. wheat versus rice) [46**]. This differentiation might have imposed a strong constraint on divergent paths of cultural evolution in the two broadly demarcated regions of the continent.

As a result of sedentary forms of living afforded by newly-emerged subsistence systems, human groups became increasingly large and started to incorporate non-kin members. We may assume social norms were utilized to breed much-needed within-group cooperation and coordination [47,48]. Dopaminergic system genes may therefore have played an instrumental role in facilitating the norm-based system of cooperation and coordination—the system we call culture. Given that human groups expanded in size over the last 10 000 years since the inception of sedentary living, the evolution of norm sensitivity must have been critical over this recent evolutionary past [49,50]. As argued by recent theorists [51], complex traits influencing social learning are likely to be

Figure 1



The norm sensitivity hypothesis is based on an observation that since the inception of sedentary forms of living, people have organized their groups by certain patterns and norms of social behavior that are afforded and constrained by the forms of subsistence (e.g. farming different crops such as rice and wheat and herding different animals). Acquisition of these cultural patterns and norms is hypothesized to have been facilitated by certain polymorphic variants of dopaminergic (DA) system genes, including those of the dopamine D4 receptor gene (*DRD4*), that increase the dopamine signaling efficiency.

highly polygenic, and to involve variations in multiple genes within the dopaminergic as well as other systems. However, it is plausible that individual mutations directly influencing dopaminergic functioning may have particularly pronounced effects on norm sensitivity.

Evidence for the norm sensitivity hypothesis

Dopamine D4 receptor gene (*DRD4*)

One candidate in the context of gene–culture co-evolution is the dopamine D4 receptor gene (*DRD4*). Exon 3 of *DRD4* has a variable number tandem repeat (VNTR) polymorphism (2–11 repeats), with 2, 4, and 7 repeat alleles (2R, 4R, and 7R) being the most frequent. Receptors coded by 7R alleles show less in vitro dopamine functioning and poorer response to agonists than 4R alleles [52,53], whereas the 2R allele is intermediate. Physiologically, diminished dopamine inhibitory feedback in 7R and 2R alleles carriers [23] is thought to lead to relatively higher physiological dopamine signaling capacity relative to 4R carriers [54].

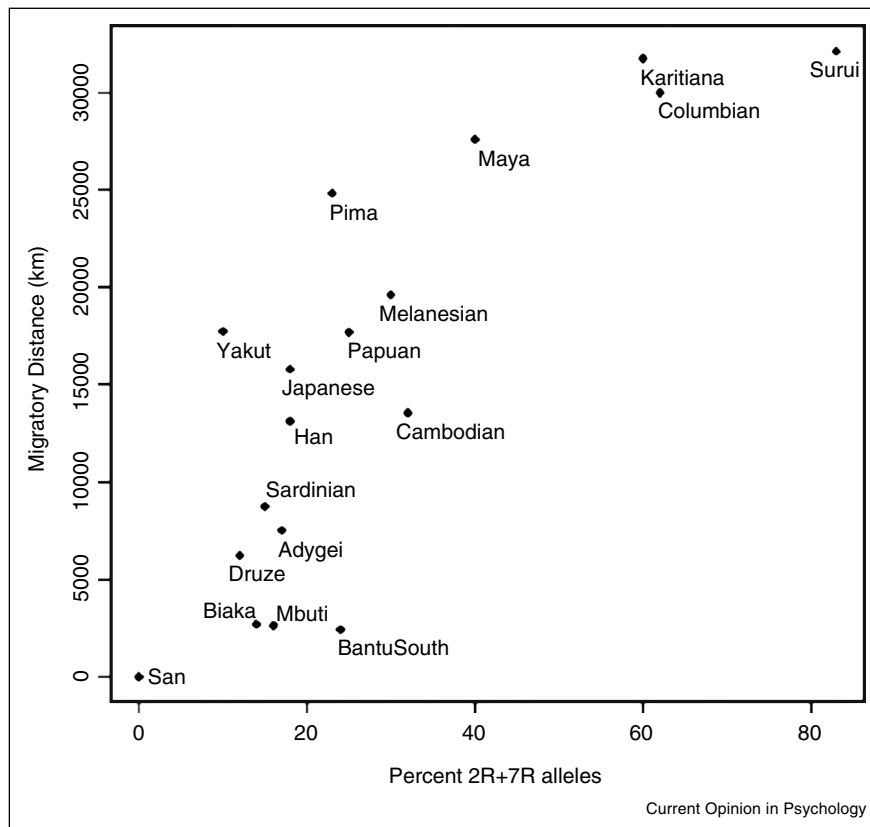
Haplotype linkage disequilibrium (LD) patterns suggest the *DRD4* 7R allele was likely derived from the ancestral 4R allele 40 000–50 000 years ago, when humans started to expand their territory [23]. The 2R allele is more recent, purportedly appearing ~10 000 years ago, when humans started herding and farming. Herding and farming, as well as the kind of crops farmed, all have systematic influences on cultural patterns of behavior [46,55,56]. Moreover, the 7R and 2R alleles may be under selection pressures associated with migration [57,58**]. The 7R allelic frequency increases as a function of migratory

distance as humans spread over the globe (see Figure 2), suggesting that *DRD4* variants linked to altered dopamine signaling capacity could have co-evolved with cultural forms of human adaptation. Specifically, the population-level frequency of 7R and 2R alleles of *DRD4* might have increased over the last 10 000–50 000 years as different groups underwent a series of challenges to survive in ‘frontier-like’ social and ecological conditions fraught with a variety of life-threats [59]. A recent simulation suggests that such social and ecological conditions conduce to the emergence of strong social norms for cooperation and coordination within an ingroup [60**].

DRD4 and environmental sensitivity

Previous work reported associations between the 7R allele of *DRD4* and certain behavioral traits including novelty seeking [61], heavy drinking [61], and financial risk taking [62], although these associations are not always replicable [63]. Other evidence indicates that 7R allele carriers are sometimes relatively better socialized, with superior attention control [30] and greater prosocial orientations [19,64*]. The seemingly conflicting pattern could reflect environmental sensitivity of the *DRD4* 7R/2R alleles [17,19]. That is, under adverse environmental conditions (e.g. neighborhoods dominated by gangs), the 7R/2R alleles may be associated with more negative outcomes (e.g. impulsive, antisocial behaviors). The norm sensitivity hypothesis suggests that the behaviors that are considered less desirable or even explicitly anti-social may be rewarded and thus fostered in such adverse conditions. In contrast, under desirable environmental conditions, these alleles may be associated with more

Figure 2



Migratory distance out of Africa as a function of the prevalence of the 7R/2R allele of *DRD4*. Taken from Matthews & Butler, 2011, *American Journal of Physical Anthropology*, 145, 382–389.

advantageous outcomes because such environments enforce norms encouraging desirable behaviors. In support of this analysis, developmental work shows that children with these alleles are influenced more by the quality of caregiving [65–68]. Consistent with the norm sensitivity hypothesis, children with 7R/2R alleles of *DRD4* might more readily infer informal behavioral norms from their caregivers.

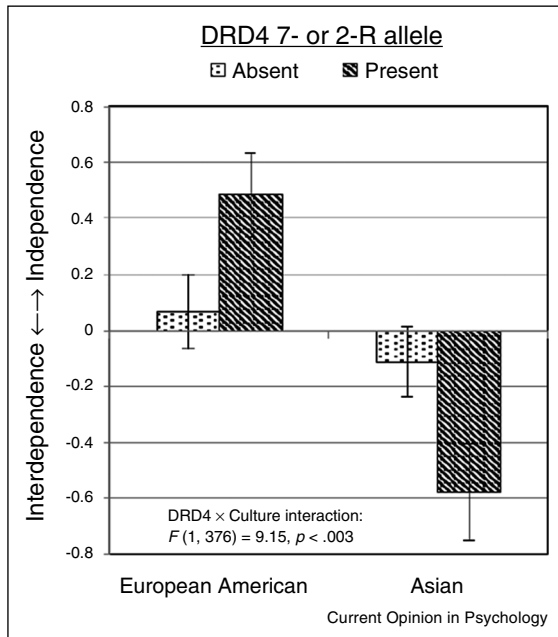
***DRD4* × culture interaction**

Culture is an environment that is constituted by beliefs, values, and human behaviors derived from these beliefs and values [69]. On the basis of the norm sensitivity hypothesis, we may anticipate that higher dopamine signaling variants of *DRD4* (7R and 2R) will accentuate the cultural difference in the social orientations of independence and interdependence. In our recent work [20], 194 European Americans and 204 Asians completed several scales assessing independence (e.g. independent self-construal, self-efficacy) or interdependence (e.g. interdependent self-construal, holistic cognitive style). As summarized in Figure 3, the predicted *DRD4* × culture interaction was significant. Overall, Asians tended to be more interdependent or less independent than European

Americans. Importantly, whereas this cultural difference was sizable for the 7R/2R allele carriers of *DRD4*, it was negligible for the 7R/2R allele non-carriers. Within each cultural group, the 7R/2R allele carriers showed to a greater extent the social orientations typical for their respective cultures. This finding resonates with an earlier study showing that when the prevalent norms are made salient through induction of accountability, individuals from individualistic and collectivistic societies behave in diametrically opposite ways in a social negotiation task. Whereas individualists become more competitive, collectivists become more cooperative [70].

If carriers of high dopamine signaling variants of *DRD4* acquire and internalize social norms, they may show more pronounced effects of priming of such norms. Consistent with this hypothesis, a recent study demonstrates that priming of religious ideas increases pro-social behaviors only among the carriers of these gene variants [19]. Consistent with the norm sensitivity hypothesis, this result might show that carriers of the high dopamine signaling variant of *DRD4* acquire religious ideas (which encourage altruism) more deeply. Also consistent is a recent review indicating that these gene variants are often

Figure 3



Composite measure of independent versus interdependent orientation (independent factor score — interdependent factor score) as a function of culture and DRD4 VNTR polymorphisms. Taken from Kitayama et al., 2014, *Psychological Science*, 25, 1169–1177.

associated with greater altruism — a behavior that is positively sanctioned in all societies [64].

Challenges and future directions

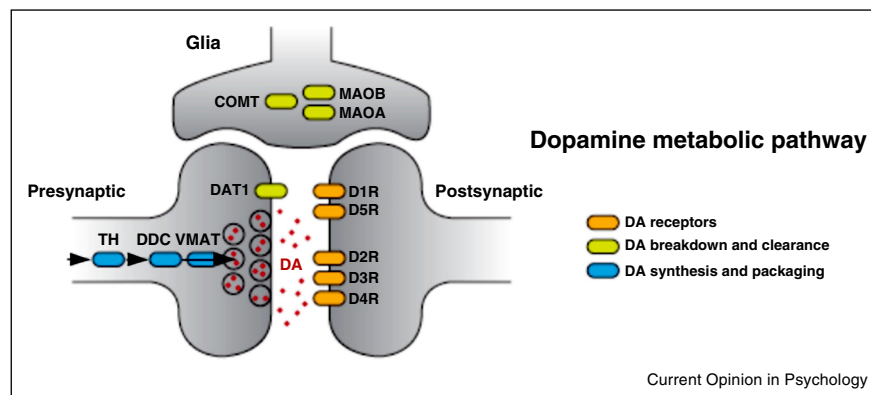
There are important challenges and directions for future work. Future research should examine the function of genes within biological pathways and their interactions. In the context of dopamine, for example, this would include dopamine receptors (*DRD1* through *DRD5*),

and those involved in dopamine synthesis (*TH*, *DDC*, *VMAT*), update (*DAT*), and clearance (*COMT*, *MAOA*, and *MAOB*) (Figure 4). These genes are assumed to work in highly interactive fashion [71*,72] to influence social cognition and behavior [73]. One important research agenda is to combine information from multiple genes for phenotypic traits including norm sensitivity [71*,74,75].

As compared to complex personality traits such as extraversion and neuroticism and disease categories such as anxiety disorder and schizophrenia, the dimension of norm sensitivity is relatively unitary. Thus, it may be seen as an endophenotype, or intermediate trait, that links the operation of genes to actual behaviors [76]. Nevertheless, as should be clear from our discussion, the norm sensitivity itself could be divided into various component processes (e.g. norm induction, reward sensitivity, and reward tracking), each of which could be influenced by different genes implicated in dopamine signaling. These processes may also be influenced by myriad background mutations that might produce certain perturbations and biases in genetic signaling [51,77]. Posing a major challenge to future work is the inherently polygenic nature of psychological parameters of social behavior, including norm sensitivity.

It is equally important to assess norm sensitivity directly. One promising approach may be to use economic games and test the degrees to which participants learn response patterns of other participants (rule induction) and change their own behaviors accordingly (reinforcement tracking) [71*]. Initial evidence shows that certain dopaminergic system genes are systematically related to relevant parameters (rule induction and reward tracking) estimated from such a behavioral experiment [71*]. Another promising approach may be to use a reinforcement learning paradigm and assess a rate with which individuals learn

Figure 4



Dopaminergic (DA) pathway genes. Adapted from Set et al., 2014, *Proceedings of National Academy of Sciences*, 111, 9615–9620.

from performance feedback (e.g., approval or disapproval of own actions by others) [78,79]. This rate, called the learning rate, may be tied to the norm sensitivity.

There may be other mechanisms of gene \times culture interaction. As noted above, oxytocin (associated with enhanced sensitivity to certain socially relevant cues [80]) is likely to moderate certain cultural differences [33,34]. In another example, serotonin innervates cortico-limbic systems of emotion processing. Serotonergic genetic variants may then amplify culture-typical emotional response patterns [81,82] as well as other processes that are linked to them [83,84]. Further, any effect of gene variants must be understood within a larger context in which genes are transcribed and expressed in response to a variety of environmental cues including significant social signals such as hierarchy and social inclusion or exclusion [18,85].

To conclude, although in its infancy, the social genomic analysis of cultural acquisition suggests some new avenues of research [3,16,18]. We assert that some people may be genetically more sensitive to cultural norms than others. The norm sensitivity hypothesis sheds light on a genetic source of within-culture individual differences by examining biologically based reinforcement-mediated social learning mechanisms that are likely influenced by dopaminergic system genes.

Conflict of interest statement

Nothing declared.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
 - of outstanding interest
1. Markus HR, Kitayama S: **Culture and the self: implications for cognition, emotion, and motivation.** *Psychol Rev* 1991, **98**:224-253.
 2. Masuda T, Nisbett RE: **Attending holistically versus analytically: comparing the context sensitivity of Japanese and Americans.** *J Pers Soc Psychol* 2001, **81**:922-934.
 3. Kitayama S, Uskul AK: **Culture, mind, and the brain: current evidence and future directions.** *Annu Rev Psychol* 2011, **62**:419-449.
 4. Kitayama S, Duffy S, Kawamura T, Larsen JT: **Perceiving an object and its context in different cultures A cultural look at new look.** *Psychol Sci* 2003, **14**:201-206.
 5. Hedden T, Ketay S, Aron A, Markus HR, Gabrieli JDE: **Cultural influences on neural substrates of attentional control.** *Psychol Sci* 2008, **19**:12-17.
 6. Uchida Y, Kitayama S: **Happiness and unhappiness in east and west: themes and variations.** *Emotion* 2009, **9**:441-456.
 7. Murata A, Moser JS, Kitayama S: **Culture shapes electrocortical responses during emotion suppression.** *Soc Cognit Affect Neurosci* 2013, **8**:595-601.
 8. Tsai JL: **Ideal affect: cultural causes and behavioral consequences.** *Perspect Psychol Sci* 2007, **2**:242-259.
 9. Kitayama S, Tompson S: **A biosocial model of affective decision making: implications for dissonance, motivation, and culture.** In *Advances in Experimental Social Psychology*. Edited by Zanna, Olson J. Elsevier; 2015:71-137.
- The authors propose a brain mechanism by which preference is produced through management of behavioral conflict, with implications for affective and motivational commitment people acquire to cultural symbols.
10. Kitayama S, Park J: **Error-related brain activity reveals self-centric motivation: culture matters.** *J Exp Psychol Gen* 2014, **143**:62-70.
 11. Heine SJ, Lehman DR, Markus HR, Kitayama S: **Is there a universal need for positive self-regard?** *Psychol Rev* 1999, **106**:766-794.
 12. Morris MW, Hong Y-Y, Chiu C-Y, Liu Z: **Normology: integrating insights about social norms to understand cultural dynamics.** *Organ Behav Hum Decis Process* 2015, **129**:1-13.
- This paper provides a review of the current literature on how cultural diversity and cultural behaviors may be explained by dynamic social psychological mechanisms underlying social norms.
13. Greenfield PM, Keller H, Fuligni A, Maynard A: **Cultural pathways through universal development.** *Annu Rev Psychol* 2003, **54**:461-490.
 14. Rothbaum F, Pott M, Azuma H, Miyake K: **The development of close relationships in Japan and the United States: paths of symbiotic harmony and generative tension.** *Child Dev* 2000, **71**:1121-1142.
 15. Keller H: *Cultures of Infancy*. Lawrence Erlbaum Associates Publishers; 2007.
 16. Kim HS, Sasaki JY: **Cultural neuroscience: biology of the mind in cultural contexts.** *Annu Rev Psychol* 2014, **65**:487-514.
- This recent review of empirical work in cultural neuroscience summarizes recent findings on gene \times culture interaction effects.
17. Belsky J, Pluess M: **Beyond diathesis stress: differential susceptibility to environmental influences.** *Psychol Bull* 2009, **135**:885-908.
 18. Cole SW: **Social regulation of human gene expression.** *Curr Direct Psychol Sci* 2009, **18**:132-137.
 19. Sasaki JY, Kim HS, Mojaverian T, Kelley LD, Park IY, Janušonis S: **Religion priming differentially increases prosocial behavior among variants of the dopamine D4 receptor (DRD4) gene.** *Soc Cognit Affect Neurosci* 2013, **8**:209-215.
- Drawing on the hypothesis that 7R/2R variant of DRD4 constitutes a plasticity allele, the authors show that carriers of these alleles show more pronounced religious priming effect of prosocial behavior.
20. Kitayama S, King A, Yoon C, Tompson S, Huff S, Liberzon I: **The dopamine D4 receptor gene (DRD4) moderates cultural difference in independent versus interdependent social orientation.** *Psychol Sci* 2014, **25**:1169-1177.
- This cross-cultural genetic research provides the first evidence that the global cultural difference in independence and interdependence is moderated by DRD4. 7R/2R carriers show culture-typical social orientations, but noncarriers do not.
21. Hawks J, Wang ET, Cochran GM, Harpending HC, Moyzis RK: **Recent acceleration of human adaptive evolution.** *Proc Natl Acad Sci U S A* 2007, **104**:20753-20758.
 22. Ding Y-C, Chi H-C, Grady DL, Morishima A, Kidd JR, Kidd KK, Flodman P, Spence MA, Schuck S, Swanson JM et al.: **Evidence of positive selection acting at the human dopamine receptor D4 gene locus.** *Proc Natl Acad Sci U S A* 2002, **99**:309-314.
 23. Wang E, Ding YC, Flodman P, Kidd D, Kidd KK, Grady DL, Ryder MA, Spence MA, Swanson JM, Moyzis RK: **The genetic architecture of selection at the human dopamine receptor D4 (DRD4) gene locus.** *Am J Hum Genet* 2004, **74**:931-944.
 24. Richerson PJ, Boyd R: *Not by Genes Alone: How Culture Transformed Human Evolution*. The University of Chicago Press; 2004.
 25. Feldman MW, Laland KN: **Gene-culture coevolutionary theory.** *Trends Ecol Evol* 1996, **11**:453-457.
 26. Laland KN, Brown G: *Sense and Nonsense: Evolutionary Perspectives on Human Behaviour*. Oxford University Press; 2011.

27. Chiao JY, Blizinsky KD: **Culture-gene coevolution of individualism–collectivism and the serotonin transporter gene.** *Proc R Soc B: Biol Sci* 2010, **277**:529–537.
28. Tishkoff SA, Reed FA, Ranciaro A, Voight BF, Babbitt CC, Silverman JS, Powell K, Mortensen HM, Hirbo JB, Osman M *et al.*: **Convergent adaptation of human lactase persistence in Africa and Europe.** *Nat Genet* 2006, **39**:31–40.
29. Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, Harrington H, McClay J, Mill J, Martin J, Braithwaite A *et al.*: **Influence of life stress on depression: moderation by polymorphism in the 5-HTT gene.** *Science* 2003, **203**:288tw–288.
30. Sheese BE, Voelker PM, Rothbart MK, Posner MI: **Parenting quality interacts with genetic variation in dopamine receptor D4 to influence temperament in early childhood.** *Dev Psychopathol* 2007, **19**:1039–1046.
31. Binder EB, Bradley RG, Liu W, Epstein MP: **Association of FKBP5 polymorphisms and childhood abuse with risk of posttraumatic stress disorder symptoms in adults.** *J Am Med Assoc* 2008, **299**:1291–1305.
32. Liberzon I, King AP, Ressler KJ, Almlil LM: **Interaction of the ADRB2 gene polymorphism with childhood trauma in predicting adult symptoms of posttraumatic stress disorder.** *J Am Med Assoc* 2014, **71**:1174–1182.
33. Kim HS, Sherman DK, Sasaki JY, Xu J, Chu TQ, Ryu C, Suh EM, Graham K, Taylor SE: **Culture, distress, and oxytocin receptor polymorphism (OXTR) interact to influence emotional support seeking.** *Proc Natl Acad Sci U S A* 2010, **107**:15717–15721.
34. Kim HS, Sherman DK, Mojaverian T, Sasaki JY, Park J, Suh EM, Taylor SE: **Gene–culture interaction: oxytocin receptor polymorphism (OXTR) and emotion regulation.** *Soc Psychol Pers Sci* 2011, **2**:665–672.
35. Mathew S, Perreault C: **Behavioural variation in 172 small-scale societies indicates that social learning is the main mode of human adaptation.** *Proc R Soc B: Biol Sci* 2015, **282**:20150061.
36. Tomasello M: *A Natural History of Human Thinking.* Harvard University Press; 2014.
37. Whiten A, Caldwell CA, Mesoudi A: **Cultural diffusion in humans and other animals.** *Curr Opin Psychol* 2016, **8**:15–21.
This paper provides a concise review of recent developments in human and non-human research on social learning processes involved in cultural transmission.
38. Sutton RS, Barto AG: *Reinforcement Learning.* MIT Press; 1998.
39. Frank MJ, Claus ED: **Anatomy of a decision: striato-orbitofrontal interactions in reinforcement learning, decision making, and reversal.** *Psychol Rev* 2006, **113**:300–326.
40. Kitayama S, Tompson S: **A biosocial model of affective decision making.** *Advances in Experimental Social Psychology.* Elsevier; 2015: 71–137.
41. Holroyd CB, Coles MGH: **The neural basis of human error processing: reinforcement learning, dopamine, and the error-related negativity.** *Psychol Rev* 2002, **109**:679–709.
42. Glimcher PW: **Understanding dopamine and reinforcement learning: the dopamine reward prediction error hypothesis.** *Proc Natl Acad Sci U S A* 2011, **108**:15647–15654.
43. Gelfand MJ, Raver JL, Nishii L, Leslie LM, Lun J, Lim BC, Duan L, Almaliaich A, Ang S, Arnadottir J *et al.*: **Differences between tight and loose cultures: a 33-nation study.** *Science* 2011, **332**:1100–1104.
44. Roos P, Gelfand M, Nau D, Carr R: **High strength-of-ties and low mobility enable the evolution of third-party punishment.** *Proc R Soc B: Biol Sci* 2014, **281**:20132661.
45. Cann RL, Stoneking M, Wilson AC: **Mitochondrial DNA and human evolution.** *Nature* 1987, **325**:31–36.
46. Talhelm T, Zhang X, Oishi S, Shimin C, Duan D, Lan X, Kitayama S: **Large-scale psychological differences within China explained by rice versus wheat agriculture.** *Science* 2014, **344**:603–608.
Within-China regional variation provides initial evidence for the hypothesis that rice (versus wheat) played a significant role in shaping more interdependent social orientation in Eastern, relatively temperate regions of the Eurasian continent over the last several thousand years.
47. Herrmann B, Thoni C, Gächter S: **Antisocial punishment across societies.** *Science* 2008, **319**:1362–1367.
48. Henrich J, McElreath R, Barr A, Ensminger J, Barrett C, Bolyanatz A, Cardenas JC, Gurven M, Gwako E, Henrich N: **Costly punishment across human societies.** *Science* 2006, **312**:1767–1770.
49. Nowak MA, Tarnita CE, Wilson EO: **The evolution of eusociality.** *Nature* 2010, **466**:1057–1062.
50. Boyd R, Richerson PJ: **Culture and the evolution of human cooperation.** *Philos Trans R Soc B: Biol Sci* 2009, **364**:3281–3288.
51. Keller MC, Miller G: **Resolving the paradox of common, harmful, heritable mental disorders: which evolutionary genetic models work best?** *Behav Brain Sci* 2006, **29**:385–404.
52. Asghari V, Sanyal S, Buchwaldt S, Paterson A, Jovanovic V, Van Tol HHM: **Modulation of intracellular cyclic AMP levels by different human dopamine D4 receptor variants.** *J Neurochem* 1995, **65**:1157–1165.
53. Seeger G, Schloss P, Schmidt MH: **Marker gene polymorphisms in hyperkinetic disorder — predictors of clinical response to treatment with methylphenidate?** *Neurosci Biobehav Rev* 2001, **31**:35–48.
54. Nikolova YS, Ferrell RE, Manuck SB, Hariri AR: **Multilocus genetic profile for dopamine signaling predicts ventral striatum reactivity.** *Neuropsychopharmacology* 2011, **36**:1940–1947.
55. Uskul AK, Kitayama S, Nisbett RE: **Ecocultural basis of cognition: farmers and fishermen are more holistic than herders.** *Proc Natl Acad Sci U S A* 2008, **105**:8552–8556.
56. Edgerton RB: *The Individual in Cultural Adaptation: A Study of Four East African Peoples.* University of California Press; 1971.
57. Chen C, Burton M, Greenberger E, Dmitrieva J: **Population migration and the variation of dopamine D4 receptor (DRD4) allele frequencies around the globe.** *Evol Hum Behav* 1999, **20**:309–324.
58. Matthews LJ, Butler PM: **Novelty-seeking DRD4 polymorphisms are associated with human migration distance out-of-Africa after controlling for neutral population gene structure.** *Am J Phys Anthropol* 2011, **145**:382–389.
Population-level prevalence of 7R/2R alleles of DRD4 increases as a function of migratory distance over the last few thousand years, likely mediated by positive selection processes.
59. Kitayama S, Conway LG III, Pietromonaco PR, Park H: **Ethos of independence across regions in the United States.** *Am Psychol* 2010, **65**:559–574.
60. Roos P, Gelfand M, Nau D, Lun J: **Societal threat and cultural variation in the strength of social norms: an evolutionary basis.** *Organ Behav Hum Decis Process* 2015, **127**:14–23.
Using an agent-based simulation inspired by an evolutionary game theoretic framework, this study investigated conditions in which strong norms for cooperation and coordination in an ingroup might emerge and found that the presence of external threats is a major determinant of such norms.
61. Laucht M, Becker K, Blomeyer D, Schmidt MH: **Novelty seeking involved in mediating the association between the dopamine D4 receptor gene exon III polymorphism and heavy drinking in male adolescents: results from a high-risk community sample.** *Biol Psychiatry* 2007, **61**:87–92.
62. Dreber A, Apicella CL, Eisenberg DTA, Garcia JR, Zamore RS, Lum JK, Campbell B: **The 7R polymorphism in the dopamine receptor D4 gene (DRD4) is associated with financial risk taking in men.** *Evol Hum Behav* 2009, **30**:85–92.
63. Munafò MR, Yalcin B, Willis-Owen SA, Flint J: **Association of the dopamine D4 receptor (DRD4) gene and approach-related personality traits: meta-analysis and new data.** *Biol Psychiatry* 2008, **63**:197–206.
64. Jiang Y, Chew SH, Ebstein RP: **The role of D4 receptor gene exon III polymorphisms in shaping human altruism and prosocial behavior.** *Front Hum Neurosci* 2013, **7**:1–7.

This paper provides a review of existing studies seeking to link *DRD4* VNTR to prosocial behavior and altruism and concluded that whereas evidence for the main effect of *DRD4* is inconsistent, the existing findings support a more nuanced gene \times environment hypothesis that the alleles of *DRD4* linked to high dopamine signaling capacity are linked to prosocial behavior in environments that support such behavior.

65. Nikitopoulos J, Zohsel K, Blomeyer D, Buchman AF, Schmid B, Jennen-Steinmetz C, Becker K, Schmidt MH, Esser G, Brandeis D *et al.*: **Are infants differentially sensitive to parenting? Early maternal care, *DRD4* genotype and externalizing behavior during adolescence.** *J Psychiatr Res* 2014, **59**:53-59.
 66. Bakermans-Kranenburg MJ, van IJzendoorn MH: **Differential susceptibility to rearing environment depending on dopamine-related genes: new evidence and a meta-analysis.** *Dev Psychopathol* 2011, **23**:39-52.
 67. Berry D, McCartney K, Petrill S: **Gene-environment interaction between *DRD4* 7-repeat VNTR and early child-care experiences predicts self-regulation abilities in prekindergarten.** *Dev Psychol* 2014, **56**:373-391.
 68. Belsky J, Pluess M: **Genetic moderation of early child-care effects on social functioning across childhood: a developmental analysis.** *Child Dev* 2013, **84**:1209-1225.
 69. Kitayama S: **Culture and basic psychological processes – toward a system view of culture: comment on Oyserman *et al.* (2002).** *Psychol Bull* 2002, **128**:89-96.
 70. Gelfand MJ, Realo A: **Individualism-collectivism and accountability in intergroup negotiations.** *J Appl Psychol* 1999, **84**:721-736.
 71. Set E, Saez I, Zhu L, Houser DE, Myung N, Zhong S, Ebstein RP, Chew SH, Hsu M: **Dissociable contribution of prefrontal and striatal dopaminergic genes to learning in economic games.** *Proc Natl Acad Sci U S A* 2014, **111**:9615-9620.
- Using an economic game, the authors identified distinct cognitive parameters involved in social rule learning and then relates these parameters of distinct polygenic profiles of polymorphic loci in multiple dopamine system gene.
72. Saez I, Set E, Hsu M: **From genes to behavior: placing cognitive models in the context of biological pathways.** *Front Neurosci* 2014 <http://dx.doi.org/10.3389/fnins.2014.00336/abstract>.
 73. Yacubian J, Buchel C: **The genetic basis of individual differences in reward processing and the link to addictive behavior and social cognition.** *Neuroscience* 2009, **164**:55-71.
 74. Bogdan R, Hyde LW, Hariri AR: **A neurogenetics approach to understanding individual differences in brain, behavior, and risk for psychopathology.** *Mol Psychiatry* 2012 <http://dx.doi.org/10.1038/mp.2012.35>.
 75. Hyde LW, Bogdan R, Hariri AR: **Understanding risk for psychopathology through imaging gene-environment interactions.** *Trends Cognit Sci* 2011, **15**:417-427.
 76. Kendler KS, Neale MC: **Endophenotype: a conceptual analysis.** *Mol Psychiatry* 2010, **15**:789-797.
 77. Gibson G: **Rare and common variants: twenty arguments.** *Nat Rev Genet* 2012, **13**:135-145.
 78. Frank MJ, Moustafa AA, Haughey HM, Curran T, Hutchison KE: **Genetic triple dissociation reveals multiple roles for dopamine in reinforcement learning.** *Proc Natl Acad Sci U S A* 2007, **104**:16311-16316.
 79. Walsh MM, Anderson JR: **Modulation of the feedback-related negativity by instruction and experience.** *Proc Natl Acad Sci U S A* 2011, **108**:19048-19053.
 80. Bartz JA, Zaki J, Bolger N, Ochsner KN: **Social effects of oxytocin in humans: context and person matter.** *Trends Cognit Sci* 2011 <http://dx.doi.org/10.1016/j.tics.2011.05.002>.
 81. Lee BT, Ham BJ: **Serotonergic genes and amygdala activity in response to negative affective facial stimuli in Korean women.** *Genes Brain Behav* 2008, **7**:899-905.
 82. Long H, Liu B, Hou B, Wang C, Li J, Qin W, Wang D, Zhou Y, Kendrick KM, Yu C *et al.*: **The long rather than the short allele of 5-HTTLPR predisposes Han Chinese to anxiety and reduced connectivity between prefrontal cortex and amygdala.** *Neurosci Bull* 2013, **29**:4-15.
- The typical Caucasian finding linking the short allele of 5-HTTLPR to poor connectivity between regulatory regions of the brain to the limbic regions (a measure of the competence in emotion regulation) may be reversed, with the short allele associated with better emotion regulation.
83. Ma Y, Li B, Wang C, Shi Z, Sun Y, Sheng F, Zhang Y, Zhang W, Rao Y, Han S: **5-HTTLPR polymorphism modulates neural mechanisms of negative self-reflection.** *Cereb Cortex* 2014, **24**:2421-2429.
 84. Kim HS, Sherman DK, Taylor SE, Sasaki JY, Chu TQ, Ryu C, Suh EM, Xu J: **Culture, serotonin receptor polymorphism and locus of attention.** *Soc Cognit Affect Neurosci* 2010, **5**:212-218.
 85. Robinson GE, Fernald RD, Clayton DF: **Genes and social behavior.** *Science* 2008, **322**:896-900.