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Tools of the Trade

Theory and methods in cultural neuroscience

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Cultural neuroscience is an emerging research discipline that investigates cultural variation in psychological, neural and genomic processes as a means of articulating the bidirectional relationship of these processes and their emergent properties. Research in cultural neuroscience integrates theory and methods from anthropology, cultural psychology, neuroscience and neurogenetics. Here, we review a set of core theoretical and methodological challenges facing researchers when planning and conducting cultural neuroscience studies, and provide suggestions for overcoming these challenges. In particular, we focus on the problems of defining culture and culturally appropriate experimental tasks, comparing neuroimaging data acquired from different populations and scanner sites and identifying functional genetic polymorphisms relevant to culture. Implications of cultural neuroscience research for addressing current issues in population health disparities are discussed.

Keywords: cultural neuroscience; cultural psychology; neuroscience; molecular genetics; gene × environment interaction; culture–gene co-evolution

INTRODUCTION

'There is nothing so practical as a good theory.'
– Kurt Lewin (1951)

Cultural neuroscience is an emerging research discipline that investigates cultural variation in psychological, neural and genomic processes as a means of articulating the bidirectional relationship of these processes and their emergent properties. Research in cultural neuroscience is motivated by two intriguing questions of human nature: how do cultural traits (e.g. values, beliefs, practices) shape neurobiology (e.g. genetic and neural processes) and behavior and how do neurobiological mechanisms (e.g. genetic and neural processes) facilitate the emergence and transmission of cultural traits?

The idea that complex behavior results from the dynamic interaction of genes and cultural environment is not new (Johnson, 1997; Li, 2003; Caspi and Moffitt, 2006); however, cultural neuroscience represents a novel empirical approach to demonstrating bidirectional interactions between culture and biology by integrating theory and methods from cultural psychology (Kitayama and Cohen, 2007), neuroscience (Gazzaniga *et al.*, 2002) and neurogenetics (Canli and Lesch, 2007; Green *et al.*, 2008, Hariri *et al.*, 2006). Similar to other interdisciplinary fields such as social neuroscience (Cacioppo *et al.*, 2000) or social cognitive neuroscience (Ochsner and Lieberman, 2001), affective neuroscience (Davidson and Sutton, 1995) and neuroeconomics (Glimcher *et al.*, 2008), cultural neuroscience aims to explain a given mental phenomenon in terms of a synergistic product of mental, neural and genetic variables of interest. Cultural neuroscience shares overlapping research goals with social neuroscience, in particular, as understanding how neurobiological mechanisms facilitate cultural transmission involves investigating primary social processes that enable humans to learn from one another, such as imitative learning. However, cultural neuroscience is also unique from related disciplines in that it focuses explicitly on ways that mental and neural events vary as a function of cultural traits (e.g. values, practices and beliefs) in some meaningful way (Chiao, 2009a). Additionally, cultural neuroscience illustrates how cultural traits may shape the emergence of genomic, neurobiological and psychological processes over time and how such effects, in turn, facilitate complex social experience and even broader behavioral processes, such as perception and cognition.

THEORY AND METHODS IN CULTURAL NEUROSCIENCE

We now have the tools necessary to discover cultural variation across multiple levels in ways previously unimagined, due in large part, to fortuitous theoretical and

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methodological advances in three distinct fields: cultural psychology, neuroscience and molecular genetics. In recent years, cultural psychology has made major advances in identifying cultural traits that characterize the diversity in social groups around the world as well as articulating the criteria for creating culturally appropriate behavioral measures that ensure the psychological phenomena of interest is tractable in people of all cultures (Norenzayan and Heine, 2005; Kitayama and Cohen, 2007). Human neuroscience, including cognitive, social and affective neuroscience, has revolutionized the study of the mind and brain by developing an arsenal of techniques for mapping neural processes to psychological processes at varying degrees of spatial and temporal resolution (Gazzaniga *et al.*, 2002; Heeger and Rees, 2002; Handy, 2005). Molecular genetics has witnessed major transformations in the scope of data and techniques now available for understanding the functional impact of inter-individual variability in the structure of the human genome. From techniques for studying the association between variability in single genes and behavior to genome-wide maps that assess the association between variation across the entire genome and a given behavior, the development of molecular genetics techniques has led to an explosion of possible ways for mapping genes to neural, mental and cultural processes. Taken together, the convergence of these tools enables unprecedented ability to investigate the mutual constitution of genes, brain, mind and culture.

KEY CHALLENGES IN CONDUCTING CULTURAL NEUROSCIENCE RESEARCH

A number of key challenges arise when conducting cultural neuroscience research. Here, we highlight a set of core challenges and offer strategies for addressing them. Given that the majority of cultural neuroscience conducted to date has utilized functional neuroimaging (fMRI) for measuring neural activity, below we focus specifically on the methodological issues that arise when conducting cross-cultural fMRI.

Studying culture, not cultural stereotypes

Culture refers to the shared values, practices and beliefs of a group of people. Culture is often defined by or inferred from nationality and race, but such overgeneralizations often fail to capture the rich complexity of cultural systems and milieus. Directly measuring cultural values of participants via standardized behavioral surveys or cultural priming methods, respectively, enables researchers to reliably determine the cultural values, practices and beliefs of their study populations, rather than stereotyping them by virtue of their nationality or race alone. Over 30 years of elegant cultural psychological research has produced several measures of key cultural dimensions that characterize the majority of the world's cultures.

For instance, Hofstede (2001) proposed that cultures could be distinguished according to five cultural dimensions: *individualism–collectivism, uncertainty avoidance, power distance, long-term/short-term orientation and masculinity/femininity*. The cultural dimension of *individualism–collectivism*, in particular, has been shown to reliably affect a wide variety of mental processes at a behavioral level, including self-concept, motivation, perception, emotion and cognition (Markus and Kitayama, 1991; Triandis, 1995). Individualism refers to when individuals construe themselves as separate and autonomous from each other, whereas collectivism refers to when individuals construe themselves as highly interconnected and defined by their relations and social context. Another potent cultural construct is *holistic vs analytic cognition,* a dimension thought to characterize differences in thinking styles between Westerners and East Asians. East Asians are thought to primarily engage in holistic cognition, attending to the entire field of a scene and relying on dialectical reasoning, whereas Westerners have been shown to primarily exhibit analytic cognition, attending to objects more than their context and using rules, such as formal logic, to understand reason about themselves and the world (Nisbett *et al.*, 2001). Finally, *socioeconomic status or social class* has been shown to serve as an important cultural lens shaping one's sense of free will, choice and related behaviors (Snibbe and Markus, 2005; Savani *et al.*, 2008). These cultural dimensions provide a core theoretical foundation from which cultural neuroscientists can formulate novel hypotheses about how and why culture may influence brain functioning. Formulating sound hypotheses about how cultural traits modulate neural mechanisms *a priori* is critical to building better theories about how culture may shape neural systems and why as well as ensuring that evidence of cultural variation in neural systems is not misinterpreted as evidence for essentialist theories of race, which are typically based on oversimplified generalizations or stereotypes (Tate and Audette, 2001). Incorporating measures of cultural values, practices and beliefs into neuroscientific studies of culture is critical to ensuring that cultural processes, rather than cultural stereotypes, are being studied and related to neurobiological processes.

Culture is a dynamic process

Often cross-cultural psychologists conceptualize nation or race as a proxy for culture; however, such gross characterizations of culture are impoverished as they fail to capture the individual variability within cultures, the dynamic nature of culture and the fact that an individual can possess awareness of and appreciation for more than one cultural system simultaneously. To address these important issues, cultural psychologists (Hong *et al.*, 2000; Oyserman and Lee, 2008) have developed *cultural priming* techniques to directly manipulate cultural value systems within mono- and multicultural individuals to examine how cultural values dynamically shape behavior. Cultural priming involves temporarily

heightening individuals' awareness of a given cultural value system through either explicit (e.g. writing an essay about individualism) or implicit means (e.g. search for synonyms of individualism in a word search). A number of different types of cultural priming techniques have been successfully used to elicit cultural variation in a range of behavioral (Oyserman and Lee, 2008) and neural (Chiao *et al.*, 2010; Ng *et al.*, in press) processes. Notably, prior research has revealed that not all cultural priming techniques have equivalent influence across domains; that is, some cultural priming methods are more likely to trigger cultural variation in social relative to cognitive processes and vice versa (Oyserman and Lee, 2008). Hence, when adopting cultural priming to study the direct influence of cultural values on neural mechanisms, it is important to select a cultural priming technique that is task-appropriate.

In addition to examining the effects of cultural priming at the neural level, conducting cross-cultural comparisons of neural structure and function across the lifespan provide novel insight to the varying influence of culture and life experiences on the maturation process at neural and behavioral levels of analysis (Park and Gutchess, 2006). The developing brain exhibits tremendous plasticity early in life, from infancy through adolescence, and then continuously changes and adapts albeit with relatively diminished efficiency from young and late adulthood. Cultural variation observed in older relative to younger brains provides evidence for what kinds of neural structures and functions are susceptible to cultural influence during specific developmental windows, whereas cultural invariance in neural processes in older relative to younger brains provides evidence for universal processes that occur across development (Park and Gutchess, 2006). Hence, cultural comparisons in neural processes across the lifespan provide an important and compelling window into the dynamic influence of culture at multiple time points.

Culturally appropriate experimental tasks

In addition to theoretical frameworks, cultural psychologists have developed a number of novel behavioral methods for investigating cultural influences on behavior. First, a popular and effective way of measuring cultural traits is via *behavioral surveys*. Indeed, a lion's share of prior cultural psychological research has been focused on creation and validation of cultural value surveys, such as those used to measure individualism and collectivism (Singelis, 1994). Importantly, cultural psychologists have discovered that people living in diverse cultural value systems demonstrate different types of response biases when completing behavioral surveys. For instance, collectivists tend to show moderacy biases, such that they respond to items using the midpoint of Likert scales, whereas individualists tend to show extremity biases, such that they typically respond to items using the endpoints of Likert scales (Heine, 2008). Understanding when and how these response biases may emerge is critical for cultural neuroscientists wishing to map cultural variation in behavior to cultural variation in neural functioning.

Another important cultural psychological method is *situational sampling*. One of the hardest challenges in designing cross-cultural experiments is in ensuring that one's experimental stimuli have the intended meaning across cultures. Situational sampling refers to a technique for generating experimental stimuli that are optimized to reveal cultural variation in behavior. In experiments utilizing situational sampling, researchers ask participants from two or more cultures of interest to generate examples of the phenomena of interest (e.g. what is your idea of success or failure?). Then, these examples are used as stimuli in a subsequent experiment to test cultural variation in responses to the culturally specific stimuli (Heine, 2008). At a minimum, ensuring that stimuli used across cultural contexts carry similar meaning to both populations is critical for ensuring that the psychological and neural processes that one wishes to study are indeed received by the subject properly.

Defining culturally appropriate brain templates

When comparing behaviorally relevant neural mechanisms from diverse populations, one important consideration that arises is whether to normalize all the brains to a common brain template or make them population specific. During the analysis of neuroimaging data, spatial normalization is a key step for matching an individual's brain to a common neuroanatomical template allowing for comparison across individuals. Nevertheless, brain templates currently available from widely used neuroimaging statistical analysis packages, such as SPM, as well as standard brain atlases, such as Talairach (Talairach and Tournoux, 1988), are based on Caucasian individuals. Given the variability in brain structures across diverse populations, such as Westerners and East Asians (Chee *et al.*, 2010), it is likely that the development of culturally appropriate brain templates will be necessary for accurate comparison of brain structure and function across cultures. Furthermore, mapping between these culturally specific templates will be critical for making population based comparisons.

Cross-site MRI scanner comparison

Studying culture at the level of neural mechanisms often involves testing across two or more experimental sites. Some cultural neuroscience studies have been conducted at only one site by either recruiting diverse cultural samples from within a given population (Zhu *et al.*, 2007) or from nearby populations and then transporting participants to one experimental site (Ng *et al.*, in press). However, this is not always possible given the potentially high costs of transporting participants to a single testing site. Moreover, it is not always possible to safely assume cultural values of individual participants on the basis of geography, nationality or race per se (Oyserman *et al.*, 2009; Chiao *et al.*, 2009).

Several prior neuroimaging studies have demonstrated approaches for ascertaining and minimizing cross-site variation in fMRI data (Parrish *et al.*, 2000; Friedman and Glover, 2006; Friedman *et al.*, 2008). The probability of systematic, site-dependent effects in fMRI sensitivity between the scanner facilities can be reduced in four ways. First, neuroimaging data should be collected with nearly identical protocols, but optimized for the vendor's instrumentation. This is true for both functional (e.g. activation and rest) and structural (e.g. volumetric and diffusion tensor) imaging. Second, conducting an interscanner reliability test by scanning a separate cohort of participants or phantom data at each scanner facility enables one to quantify and statistically compare signal-to-noise ratio (SNR) across scanner sites (Parrish *et al.*, 2000). Conducting a cross-site scanner comparison is necessary to ensure that any group differences observed in neural activity are due to functional differences between participants groups rather than between instrumentation. Third, the presentation software and hardware should be identical, calibrated and tested at each session, a critical step for experiments involving the presentation of visual stimuli and auditory stimuli. Systematic variations can be introduced by differences in stimulus delivery devices and later misinterpreted as cultural effects by experimenters. The environment of the scanning and training should be made to match as best possible so that any lingering anxiety or stress felt by participants will be equivalent. Scripts should be written and implemented across the sites in a culturally appropriate manner to ensure proper training of the participants. Fourth, all imaging data should be inspected on site and run through a series of quality assurance tests to eliminate data being thrown out due to protocol violations, faulty equipment at all levels, environmental issues, or data loss due to a corrupt archive.

Identifying functional genetic polymorphisms of interest

The human genome is incredibly conserved with only ~0.2–0.4% of the genome varying across individuals (Tishkoff and Kidd, 2004). Nevertheless, cultural variation is evident in the observed frequencies of many common variants or polymorphisms across the human genome. Cultural variation in allelic (or copy) frequencies of a given polymorphism may occur due to number of evolutionary processes, such as natural selection and genetic drift. Natural selection may lead to differential frequency of genetic variants when certain alleles confer reproductive advantages over another. Genetic drift may also changes allele frequencies within populations over time, but in a random manner. For instance, founder effects, a type of genetic drift, can lead to a loss of genetic variation when a new population is established by a very small number of genetically similar individuals from a larger population.

Identifying functional polymorphisms that may have co-evolved with specific cultural customs is key for building a culture–gene co-evolutionary (CGC) theory of the human brain and behavior, which posits that cultural traits are adaptive, evolve and influence the neural, behavioral, social and physical environments under which genetic selection operates (Boyd and Richerson, 1985). A central claim of CGC theory is that once cultural traits are adaptive, it is likely that genetic selection causes refinement of the cognitive and neural architecture responsible for the storage and transmission of those cultural capacities (Boyd and Richerson, 1985).

A prominent example of dual inheritance theory across species is the CGC between the cattle milk sugar genes, especially for lactose, and the human lactase gene, which encodes the enzyme necessary for digesting lactose in cattle milk (Beja-Pereira *et al.*, 2003). The cultural propensity for milk consumption in humans has led to culturally specific genetic selection for genetic variants that increase milk sugar in cattle and genetic variants that produce more effective lactase in humans.

Similar phenomena have been observed in behaviorally relevant phenotypes. For example, Chen and colleagues (1999) discovered that relative to non-migratory populations individuals from migratory populations possess a disproportionately higher frequency of a common functional polymorphism influencing dopamine signaling in brain circuits supporting novelty and sensation seeking. Presumably, this bias reflects selection for underlying traits adaptive for the challenges of migration. Additionally, Chiao and Blizinsky (2010) recently reported evidence for CGC of individualism–collectivism and a common functional polymorphism impacting brain serotonin signaling. Specifically, they found that cultural values of individualism and collectivism are associated with the frequency of alleles conferring relatively increased or decreased serotonin signaling (5-HTTLPR short and long alleles, respectively) across nations. Collectivistic cultures were significantly more likely to be comprised of individuals carrying the short allele of the 5-HTTLPR across 29 nations. Additionally, cultural values and frequency of short allele carriers negatively predict global prevalence of anxiety and mood disorder. That is, increased frequency of short allele carriers predicted decreased anxiety and mood disorder prevalence owing to increased collectivistic cultural values. These findings support the notion that cultural values have adaptive value, buffering genetically susceptible populations from increased prevalence of affective disorders.

Molecular biologists have designed online databases (e.g. ALFRED) to facilitate public dissemination of catalogues documenting variation in frequencies of genome-wide polymorphisms for populations around the world (Osier *et al.*, 2002). In addition to studies that examine the relation between allelic frequencies of various functional polymorphisms and cultural values across nations (Chiao and Blizinsky, 2010; Way and Lieberman, in press), cross-cultural neurogenetic (Hariri, 2009) and behavioral studies (Kim *et al.*, in

press; Nikolaidis and Gray, in press) are needed to determine the direct and indirect effects of culture–gene interactions on brain and behavior. Another potentially important future research direction will be to determine whether or not cultural variability in copy number variation (CNV) of DNA sequences are similarly related to culturally relevant phenotypes (Redon *et al.*, 2006).

Notably, behavioral genetic and neurogenetic associations observed in one given population may not be meaningful in another population, due to cultural and environmental differences that interact with genes in the complex cascade of events underlying biobehavioral processes. For instance, a recent meta-analysis found that a robust association between amygdala activation and the serotonin transporter gene linked polymorphic region (5-HTTLPR) exists within Caucasian populations, but not East Asian populations (Munafo *et al.*, 2008). These findings demonstrate the importance of investigating gene–behavior and gene–brain–behavior relations cross-culturally, given the distinct role that cultural values, beliefs and practices play as environmental variables that interact with genetic variables in regulating human brain and behavior. An important theoretical puzzle for future cultural neuroscience research is to understand how CGC may have shaped mechanisms in the mind and brain differently across cultural contexts, due to the diversity of selection pressures across geographical regions.

CONCLUSION

Research in cultural neuroscience has the potential to address research biases in the human neuroscience literature as well as provide novel insight into gene-by-environment models of complex phenomena (Caspi et al., 2010), including population health disparities (Williams *et al.*, 2010). Similar to research biases in the behavioral sciences (Henrich *et al.*, in press), within the field of human neuroimaging, over 90% of peer-reviewed neuroimaging studies come from Western, industrialized nations (Chiao, 2009b) and most do not consider the impact of environmental factors, such as cultural values, practices and beliefs, on the relation between human brain function and behavior.

Such research biases in the behavioral and brain sciences are particularly worrisome given the important interplay of culture and genes in the study of population health (Shields *et al.*, 2005; Wang and Sue, 2005). For instance, whereas Ashkenazi Jews have a greater likelihood of Tay-Sachs disease, people from Northern Europe are more likely to develop cystic fibrosis (Exner *et al.*, 2001; Wang and Sue, 2005). Another example of population differences in health as a function of variability in allelic frequency at a specific genetic locus stems from research on the gene *CYP2A6*, which encodes an enzyme involved in the peripheral metabolism, and nicotine addiction (Shields *et al.*, 2005). Protective alleles of the *CYP2A6* gene, which are associated with less metabolism of nicotine, are very rare in Europeans and Africans (~3%), but more prevalent in Japanese and Koreans (~24%) who exhibit reduced levels of nicotine addiction (Shields *et al.*, 2005). Importantly, numerous population health disparities in prevalence of mental disorders exist between different socioeconomic status groups, races and minority populations, for which the relative contributions of culture and biological factors still remain unknown (Miranda *et al.*, 2008).

How do differences rooted in functional genetic polymorphisms affect brain systems and behavior underlying physical and mental health conditions? How do cultural factors influence the relative frequencies of these functional polymorphisms and their regulatory effects on brain and behavior? The answers to these and other intriguing questions are finally within our empirical grasp. By integrating theory and methods from cultural psychology, human neuroscience and molecular genetics, we will be able to successfully identify and investigate candidate phenomena using the cultural neuroscience approach and ultimately, enhance our understanding how sociocultural and biological forces interact and shape each other across multiple time points.

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