Traces of Culture:

The Feedback Loop Between Behavior, Brain, and Disorder

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Abstract

Culture is part of an extensive feedback loop, which simultaneously influences and is influenced by many organismic levels including cultural context, neural events, and behavior, among others. Aside from behavioral variations, however, the influence cultural contexts have on the form and expression of psychiatric disorders has not been widely studied. Studying additional parts of this feedback loop, such as differences in neural processes, may yield new insights into these disorders. Recent studies in neuroscience show that culturally contingent social pressures shape some neural pathways but not others in non-patient participants. Presumably patient studies would reveal equally diverse findings. In which case, methodologies in the neurosciences potentially offer additional ways to assess the impact of culture on psychiatric health and symptomatology. However, implementing these methodologies raises important theoretical and ethical concerns, which must be resolved to maintain patient individuality and to acknowledge the complexity of cultural diversity. This paper discusses cultural context as a major influence on and byproduct of human neural plasticity and advocates a Culture-Brain-Behavior (CBB) interaction model for conceptualizing the relationship between culture, brain, and disorder. Recommendations are made for responsibly integrating neuroscientific techniques into transcultural psychiatric research by taking a systems approach to evaluating disorders.

Keywords: transcultural psychiatry, cultural neuroscience, fMRI, neural plasticity, CBB model, Culture-Brain-Behavior interaction model

Culture describes powerful and dynamic social phenomena that influence most psychiatric disorders. Culture is probably best understood as a process of converging social and contextual elements, which people within a defined demographic largely choose whether or not they subscribe to (Kemmelmeier & Kühnen, 2012; Markus & Kitayama, 2010; Hong et al., 2000). Many disorders, such as schizophrenia, depression, and anxiety, exhibit cross-cultural variations in reported symptoms and presentation (Kalra, Bhugra, Shah, 2012; Bhugra, 2006; Kirmayer, 2001; Kirmayer & Groleau, 2001). Their fundamental nature and etiology also vary across cultures. However, culture is neither simple nor a discrete influence leading to the emergence of psychopathology – and it is certainly not the only systemic pressure playing a prominent role. Instead, psychopathology is a maladjusted byproduct of a multi-level and dynamic feedback system between culture, 'mind,' brain (Ryder, Ban, Chentsova-Dutton, 2011), and perhaps most notably behaviors.

Most transcultural psychiatric research has centered on behavioral presentation and patient-reported symptoms (for reviews see Agorastos, Haasen, Huber, 2012; Asmal et al., 2011), effectively addressing the roles of culture and 'mind' but widely excluding the roles of the brain. Meanwhile, recent studies primarily of 'Western' populations (i.e., mostly Caucasian participants from Western Europe and North America; see Henrich, Heine, Norenzayan, 2010) have heavily relied upon neuroscientific methods (e.g., electroencephalography and eye tracking). Of these methods, functional magnetic resonance imaging (fMRI) is prominently used to study many disorders. Recent findings from non-patient studies using fMRI suggest that some clinically relevant brain-based differences exist across cultural contexts (e.g., Chiao et al., 2013; Chiao & Blizinsky, 2013; Kirmayer & Ban, 2013; Meyer, Way, Eisenberger, 2013; Severance et al., 2013; Wang, Ma, Han, 2013; Cheon, Marthur, Chiao, 2010). The few neuropsychiatric studies that have been conducted transculturally support this claim (e.g., Koh & Milne, 2012). Considering that both psychiatric

disorders and related neural events vary by culture, 'Western'-dominance in neuropsychiatry may produce a systematic sample bias in the data and under-represent the global population in the current literature (Crafa & Nagel, in press). Since neuropsychiatric literature is used as a basis for medical research, the effects of cultural pressures on neuropsychiatric processes ought to be examined to ensure that diverse patients are receiving adequate care.

Increasing use of fMRI and other neuroscientific methods in transcultural psychiatric research would supplement the existing fMRI literature as well as the findings from studies that used behavioral or self-report measures. Such findings would expand knowledge to diverse patient populations across social and cultural groups, and potentially help identify important similarities and differences that may be relevant to diagnosis or treatment.

Although this article endorses increased integration of fMRI and other neuroscientific methods, their use in transcultural psychiatric research must be conducted with the utmost care. In particular, these methodologies risk reliance on cultural stereotyping to form hypotheses or neuroreductionistic interpretations of findings; thus, they have the potential to accidentally reinforce social stigmas and reify cultural prejudices. Current models describing the culture-brain interaction rely heavily on these studies and share their risks. They are not sufficiently nuanced for transcultural clinical research. Furthermore, these models do not accurately reflect the most relevant issues for the study of psychiatric disorders, e.g., the primacy of individual malleability and diversity or the complexity of the culture-brain interaction (Freeman, in press; Han et al., 2013). Such negligence is not appropriate when studying sensitive cultural and clinical communities, and a new model is needed to address these concerns.

By synthesizing the strengths of cultural neuroscience (CN) methodologies with the priorities and considerations central to transcultural psychiatry (TCP), these pitfalls can be avoided. In the following, the Culture-Brain-Behavior (CBB) interaction model will be

proposed as a theoretical framework that attempts to avoid neuroreductionism and emphasize individual malleability and diversity. First, we will illustrate the potential for fMRI research to identify transcultural variations in the phenotypes of psychiatric disorders by focusing on recent findings in CN. Then, problems with over-reliance on fMRI will be outlined, demonstrating the necessity of a responsible model for implementing fMRI in transcultural studies to achieve a comprehensive understanding of the patient population. The reasons neuroreductionism is problematic for TCP will be specifically addressed in this next section. Finally, the CBB interaction model will be offered as an alternative systems approach to transcultural research.

CURRENT CONTRIBUTIONS OF CULTURAL NEUROSCIENCE AND THEIR POTENTIAL APPLICATIONS FOR PSYCHIATRY

Perhaps more than any other methodology, fMRI research in psychiatry is subject to what is commonly termed *Western bias* (Henrich, et al., 2010), meaning that a disproportionate amount of research comes from North American and Western European countries. Despite important contributions from some 'Eastern' countries, such as Japan, many cultures and minority subcultures are not represented in fMRI studies (Henrich, et al., 2010; Isamah et al., 2010; O'Brien et al., 2006; Gogolin, 2002). Evidence supporting prominent treatments are dominated by a handful of countries, many of which share borders or genetic pools, leaving their findings potentially biased. Findings from fMRI studies often substantiate knowledge about disorder phenotypes and may be used as theoretical background promoting specific medications or therapeutic approaches (e.g., Pliszka, 2012). Resulting treatments and therapies can have as much 'Western' bias as the studies they are based on. At worst, this has the potential to harm patients in underrepresented communities. At best, some treatments may be

sub-optimal. Either way, it is necessary to extend the study of disorders to include cultural variations beyond the behavioral level.

The emergence of CN over the last decade has brought new approaches to studying cultural diversity by using fMRI. Many studies compare groups of people living in 'Eastern' and 'Western' countries while other studies compare recent immigrants or ethnic minorities to dominant native populations. These studies have shown that brain activity differs in key areas when participants are from different cultures (Zhu et al., 2007) or in different sociocultural situations (Sui et al., 2013). Although these studies are conducted using healthy control participants, they have implications for clinical research. In particular, brain activity varying by culture substantially overlaps the with brain regions relevant to psychiatric disorders. For example, culture-based differences have been reported in areas of the prefrontal cortex (Han et al., 2011; Frankel, Gross, & Gabrieli, 2010), cingulate cortex (Harada, Lia, Chiao, 2010; Ray et al., 2010), parietal lobe (Hedden et al., 2008), and amygdala (Derntl et al., 2012). These regions exhibit distinct activity in many disorders, such as schizophrenia (Mukherjee et al., 2013; Pedersen et al., 2012; Pomarol-Clotet et al., 2010; Torrey, 2007), post-traumatic stress disorder (Stevens et al., 2013), autism (Kleinhans et al., 2010; Gilbert et al., 2008), major depression (Korb et al., 2011; Murray, Wise, Drevets, 2011), and general anxiety disorder (Ressler, 2010). Accordingly, the brain activity associated with some psychiatric disorders may also vary across cultural groups (Crafa & Nagel, in press).

Some recent studies already demonstrate how neuropsychiatric research could be informative for transcultural diagnosis and treatment. For example, one study compared visual processing in children with and without autism spectrum disorders in England and Singapore in order to evaluate Central Coherence Theory (CCT) (Koh & Milne, 2012; Milne & Szczerbinski, 2009). This leading theory claims that a certain perceptual-cognitive style universally underlies the disturbances in autism (Happé & Frith, 2006; Frith, 1989). When

researchers tested CCT across cultures, Singaporean children – whether autistic or not – displayed a different processing style than expected. This evidence demonstrates that the trait described by CCT may be culture-specific – and the theory may be too (Koh & Milne, 2012).

Such findings have clinical ramifications for culturally diverse patients. In demonstrating that substantial populations of children with autism exhibit a different perceptual-cognitive style, it shows that some features of autism may be culturally diverse. Considering the characteristic social deficits of autism, it is significant that sociocultural information influences perceptual-cognitive styles even in autistic children. This finding underlines the powerful influence sociocultural experiences can have on biological processes associated with psychiatric disorders. Similar studies could be conducted across a variety of disorders and cultures to improve understanding of fundamental variations in disorder phenotypes.

Additional research can help clarify current issues in TCP. For example, as Seligman & Kirmayer (2008) point out, many neurophysiologic studies of dissociation focus on pathology. Culture-specific neural responses may be conflated in studies of the neurophysiology of dissociation. It would be beneficial to implement fMRI research in cultural contexts where non-pathological dissociations are prevalent, such as those where shamanism is commonly practiced, in order to parse which neural processes specifically correlate with pathological dissociation versus non-pathological dissociation. Moreover, current findings imply relationships between certain neural processes and cognitive events, such as memory suppression and shifts in self-regulatory attention, that appear to have different consequences across cultural contexts (e.g., Euro-American compared with Afro-Brazilian contexts with different interpretations of dissociative experiences, cf. Seligman & Kirmayer, 2008). However, these findings are highly heterogeneous across dissociation types.

Improving understanding of diverse neural processes across these communities will help parse the relationship between cultural context, dissociation, and disorder. Such endeavors

must be performed carefully to avoid oversimplifying the relationship between culture and neural processes. However, if pursued correctly, studies like these have the power to use neuroscientific tools to clarify relationships that are currently confounded or conflated and to extend neuropsychiatry to the global community.

Despite the potential that neuroscience has for TCP, CN is a relatively new field and it is still working out its methodological imperfections. Many studies in CN, for example, broadly define 'culture' according to geographic boarders and contain poorly defined or uncontrolled variables (Kagawa Singer, 2012; Dressler, 2004; Hunt & Bhopal, 2004; Winker, 2004). East/West dichotomies are commonly used in CN in attempt to solve this problem by reducing culture to binary terms that can be operationalized. Other binary contrasts, including collectivist/individualist, interdependent/independent, and holistic/analytic, are also commonly included in these experiments. For example, Koh and Milne's (2012) autism study described above arguably compares individuals from 'Eastern' and 'Western' countries to investigate 'holistic' versus 'analytic' visual processing styles stereotypically ascribed to 'collectivist' versus 'individualist' cultures.

These binary categories are not as useful as more nuanced systems for describing culture, such as ecocultural theories (Georgas, van de Vijver, Berry, 2004) or measurements of individual subscription to cultural domains (Choudhury & Kirmayer, 2009), which are complimentary approaches. While the former describes the diverse social and ecological dynamics within cultural contexts (e.g., the varying degrees of autonomy and relatedness observed in different social situations and cultures, cf. Keller, Demuth, Yovsi, 2008; Keller, 2003), the latter describes individual valuations of the beliefs and practices that are common to a subculture or region.

The persistence of East/West categories in CN underlines the current need for a sensitive model, such as the CBB model, which offers a more nuanced approach to the study of brain-

cultural interactions. Despite these issues, CN has taken important first steps toward integrating the study of neural and cultural phenomena, offering new approaches. Although practices like invoking East/West dichotomies remain problematic, these studies also provide an implementable foundation for more nuanced studies to be built upon. By integrating fMRI research into TCP, knowledge of the patient can be extended to include neurological variations and add dimensions to our understanding of disorders and their cultural variability. Broadening this understanding can lead to more accurate diagnostic criteria and increased resources for underrepresented populations in psychiatric research (Hyman, 2007).

THE IMPERFECT FIT OF CULTURAL NEUROSCIENCE MODELS FOR RESEARCH IN TRANSCULTURAL PSYCHIATRY

Although using fMRI can teach us much about the character of disorders around the world, it is not without risks. While fMRI research is not inherently incompatible with the spirit of TCP, interpretations of fMRI findings can contain theoretical biases that preclude patient individuality, changeability, and perspective. In particular, current models describing the relationship between brain and culture — the neuro-culture interaction (NCI) model being among the most prominent (Kitayama & Uskul, 2011) — treat the relationship between culture and neural events as fixed or immutable.

Within these models, culture is generally defined according to established tradition as collectively shared meanings, beliefs, behaviors, and conventions (Kitayama & Uskul, 2011). Individual psychological processes are influenced by the collective culture that the individual is exposed to, and the act of repeating adopted attitudes and practices directly alters the brain: "the brain acts as a crucial site that accumulates the effects of cultural experience" (*ibid*., p. 422). According to Kitayama and Uskul, after culture-specific attitudes and practices have been adopted, they become 'embrained' and are no longer cognitively mediated. Neural events

in the brain initially reflect cultural learning and subsequently, behavioral practice. Although we initially act according to our values, repeating these actions causes deep neural changes that eventually become automatic.

Although careful to acknowledge individual behavioral diversity, the authors explicitly state, "Culturally shaped activation patterns of the brain, however, would enable the person to perform culturally scripted behaviors ... both automatically and seamlessly" (*ibid.*, p. 424). Statements such as these imply, first, that culturally scripted behaviors have been prescriptively learned and, second, that once learned, the cultural script becomes automated. Although the authors may not intend for this to be a rigid description, the eventual automaticity of these processes nonetheless presumes a degree of stability that seems too inflexible. Current literature calls both claims into question (see e.g., Pecchioni, 2012; Bohn, 2010; Chiu et al., 2010; Li et al., 2010). While the first claim arguably excludes accounts of psychiatric disorders from the model's framework, the second claim runs contrary to what is currently known about neural and cultural change across the lifespan (e.g., Canu et al., 2012). Many psychiatric disorders are characterized by inappropriate social behaviors, indicating that culturally scripted behaviors have been incorrectly learned. Some countries estimate that approximately half of the population will experience a mental disorder during their lifetime (Reeves et al., 2011); the ability to behave according to cultural scripts likely also varies. Additionally, while some automaticity occurs, both cultural and neural events are highly flexible and change dynamically across the lifespan (for reviews see During et al., 2011; Jäncke, 2009; Pascual-Leone, Amedi, Fregni, 2005; Poldrack, 2000; Buonomano, 1998).

In fact, alterability appears to be ubiquitous across organismic levels (Schübeler, 2009; Borrelli et al., 2008; Feinberg, 2007). The human brain exhibits pervasive neural plasticity, which is reflected by sometimes dramatic changes in neural network processes in response to individual situations (Thomas & Baker, 2012; Burke & Barnes, 2006) even late into adulthood

(Thomas & Baker, 2012; Kempermann, 2012; Gould, 2007; Dinse, 2006; Rakic, 2002). Experience-dependent neural plasticity occurs when brain events are changed through practice or observational learning (Yu, Roland, Xu, & Stein, 2013; Kleim, 2008). It has been theorized that personal changes made by self-reflection, such as in the case of talking therapy, may also bring about brain-based changes; however, this research is still in the early stages (Morgiève et al., 2013; Zaman, 2010; Frewen, Dozois, Lanius, 2008; Linden, 2006; Roffman et al., 2005).

Such claims are central to psychiatry, which assumes first and foremost, that therapies can bring about change. Treatments and therapies are designed on the assumptions that people are flexible. Their medicinal efficacy is measured by changes in patients. Current CN models are ostensibly somewhat incompatible with assumptions central to TCP.

Current models also do not fully escape three conceptual risks that frequently emerge when discussing fMRI: neuroreductionism; attempts to 'locate' culture in the brain; and reliance on cultural stereotypes to form hypotheses or interpret results. These risks ought be generally avoided to ensure real-world translatability; however, they are particularly problematic for TCP because they undermine the patient's circumstances. By proposing a nuanced framework describing the relationship between culture and disorder, the CBB model avoids these potential risks.

Neuroreductionism, the primary risk when using fMRI, is the assumption that our brains solely determine our actions, thereby attributing beliefs and behaviors entirely to neural events (Kirmayer & Gold, 2012; Choudhury & Kirmayer, 2009; Choudhury, Nagel, Slaby, 2009; Gold, 2009). Neuroreduction precludes dynamic 'human factors,' such as meaning, experience, and culture, and ignores other organismic levels such as physiology and perception, which may be reflected in neural events but are not necessarily reducible to them. Although fMRI can provide information about changes in individual internal states, the

information is still limited to neurophysiologic changes. Brain processes are only fragments of the larger organism-environment interaction the brain adapts to (Fuchs, 2011), and research on these processes must additionally account for ecological accuracy and clinical applicability.

The second major risk is trying to 'locate' culture in the brain. Brain-based definitions of culture risk ignoring the brain's fluidity, which can be thought of as another level of human changeability and population diversity. Cultures observably change over time, and both CN and, to a lesser extent, TCP, must be careful not to forget that findings from one generation may not be true for the next. Corresponding neural processes may even change within one's lifetime or may exhibit plasticity from one situation to the next (e.g., Chiao et al., 2010; 2009). Although brain-based commonalities may reflect the influence of similar sociocultural experiences, such findings are not identical with 'culture' and are more concisely described as byproducts of sociocultural learning. Moreover, substantial diversity may exist in cultural learning, which may be even more prominent in patient communities.

Reliance on preexisting stereotypes is a third risk. Choudhury & Kirmayer (2009) rightly point to the problem of nationality in CN: Individuals residing within the same national borders are assumed to belong to the same culture. Some studies in CN include recent immigrants (e.g., as an 'East Asian' sample) instead of native residents living in their home countries or without acknowledging that immigrants may be experiencing acculturation (e.g., Gutchess et al., 2010), which can occur rapidly and result in high psychological variability (Yorulmaz & Işık, 2011). Considering that people experience and subscribe to different cultural domains to different degrees, experiments are more accurately designed according to discrete and current cultural variations rather than 'culture' as an abstract ideal (Keller, 2006; Greenfield et al., 2003).

Remembering these issues is essential for the sensitive study of cultural differences, which has a history of marginalizing minority groups and reinforcing racism (Kagawa Singer,

2012; Choudhury & Kirmayer, 2009; Chen, 2008; Schouten & Meeuwesen, 2006). Sensitivity is particularly important for TCP, because ignoring changeability – whether on the levels of culture, the brain, or the individual – compromises the patient and reduces integrity of care (Choudhury & Kirmayer, 2009). In order to appropriately understand and treat diverse psychiatric patients each individual must be conceived of as changeable.

With these caveats in mind, useful insights may be gained from current CN models. In particular, the NCI model describes practiced behaviors as leading to neural changes; although they later may become automatized according to this model and presumably less flexible, these initial neural changes accumulate into sociocultural differences reflected in certain brain events (Kitayama & Uskul, 2011). This order of events agrees with evolutionary perspectives on the human brain, as adapted to the environment, and with studies of children across cultures, showing that cultural behaviors and customs are acquired early during childhood (Kärtner, Keller, Yovsi, 2010). When defining the relationship between culture and the brain, a systems approach must be taken, accounting for behavior as a means of cultural learning. The CBB model, which is described in detail in the next section, proposes such an approach.

THE RELATIONSHIP BETWEEN CULTURAL DEVELOPMENT, PSYCHIATRIC DISORDERS, AND THE BRAIN

The CBB model presented here attempts to avoid the pitfalls of other models through carefully interpreting recent findings to portray the relationship between culture, brain, and disorder. The CBB model incorporates the order of events, as described in the previous paragraph, from the NCI model. However, in contrast with the NCI model, it extends this discussion to cultural learning by applying a systems approach to clinical research. The CBB model diverges from central claims of previous models by rejecting the claims that 1) cultural scripts are performed automatically and seamlessly, and that 2) after culture-specific attitudes

and practices have been adopted, they are no longer cognitively mediated. Instead, the CBB model posits that 1) cultural scripts are not always correctly performed and 2) cognitive mediation is a mechanism for change across the lifespan. In fact, cognitive mediation is integral to clinical therapy and to the rich interplay between culture, 'mind,' and brain. Finally, the CBB model offers statistical definitions of cultural and pathological behaviors that compliment existing descriptive definitions while being more easily operationalized in quantitative research. These definitions are meant to replace binary categories used by previous studies.

This approach agrees with others that present culture, 'mind,' and brain as multiple levels of a single, organic system (e.g., Ryder et al., 2011; Fuchs, 2011). Furthermore, this model extends the endeavor to consider individual behaviors and clinical variations within cultures by integrating neuroscientific tools into the repertoire of methods used to build a comprehensive and globally oriented understanding of the patient. Ultimately, this model hopes to provide a conceptual foundation for neuroscientific research in TCP.

Three central tenets of the CBB model

The central tenets of the CBB model can be summarized as follows: 1) the ability to change at any time during the lifespan is central to all organismic levels; 2) these fluctuating levels create a feedback loop, informing and changing each other; and 3) vast individual variations fall along cultural continua of common behaviors within a defined group. Each of these tenets emphasizes the flux that all organismic levels are constantly undergoing. Although embracing the complexity of human phenomena raises difficult questions, such as how to operationally define culture, it helps avoid the three pitfalls described above and provides alternative paths to answering these difficult questions. Unlike the NCI model's suggestion that culturally scripted behaviors are performed "automatically and seamlessly"

without cognitive mediation (Kitayama & Uskul, 2011, p. 424), the CBB model proposes that many behaviors will change across a person's lifetime, either by becoming more refined or through some fundamental change in nature or intention.

The first tenet of the CBB model proposes that plasticity is prerequisite for all learning. The process of cultural acquisition and individual change may be based on a dynamic interplay between social learning and behavioral observation (Meltzoff, 2007a, 2007b; Gergely & Csibra, 2005). This process can be seen in children as young as 2 years old showing culture-specific behaviors (Kärtner et al., 2010). These behaviors often become more entrenched, but they can also become more diverse as the individual progresses toward adulthood (e.g., Scharf & Mayseless, 2010; Krings et al., 2008; Seiffge-Krenke & Gelhaar, 2008; Nelson & Chen, 2007; Arnett, 2007, 2006; Shanahan, 2000; Côté, 2000).

Self-other mapping, for example, is one potential mechanism underlying cultural differentiation and its diversity (Paulus Hunnius, Bekkering, 2012; Losin, Dapretto, Iacoboni, 2009; Meltzoff, 2007a, 2007b). The process of mapping the actions of the other onto oneself through behaviors, such as mimicking, engages brain regions including the prefrontal cortex (PFC), which exhibits different activity patterns relative to sociocultural identity (Saito et al., 2010; Losin et al., 2009). This self-other mapping helps a person to understand others and acquire new behaviors, and it is hypothesized to be at the heart of learning culture-specific behaviors (e.g., Tomasello et al., 2007; Gergely & Csibra, 2005; Brooks & Meltzoff 2002, 2005; Gallagher & Meltzoff, 1996).

In principle, this mapping is similar to the processes described by other models. Through exposure to cultural scripts and practiced behaviors, social conventions are learned and the brain changes. However, unlike other models, the CBB model emphasizes that individuals alter these scripts as they are integrated through cognitive reinterpretation and through either imperfect behavioral mimicry or refinement of observed behaviors. For example, evidence

suggests that infants generally mimic successful behaviors (Paulus et al., 2011; Hauf & Aschersleben, 2008). On the one hand, when they observe someone failing to complete an attempted task, they frequently attempt more successful behaviors (Meltzoff, 2007a, 2007b). On the other hand, disruptions to motor processes or even failure to pay attention to an observed action can result in imperfect mimicry (Cossu et al., 2012). In both cases, the behavior varies but the intention remains the same. However, the demands of different environments may lead to alterations in behaviors by changing intentions (e.g., Koepke & Denissen, 2012; Hammack, 2008). Through a mechanism like self-other mapping, it seems likely that cultural behaviors are learned and interact with many other organismic levels and ecocultural pressures. However, these learned behaviors are not direct replicas of the original behavior. Instead, they deviate from the observed or even mimicked behaviors through cognitive mediation and circumstance.

In this instance, the order of events may be key to understanding the events themselves. The literature on both neural plasticity and human development indicate that the ability to change is a necessary predecessor for social learning and cultural acquisition (Han et al., 2013; Ambady & Bharucha, 2009; Hari, 2009). Moreover, these studies show that the ability to change continues throughout the human lifespan. It is a prerequisite for *all* learning (Caroni, Danato, Muller, 2012; Pavlowsky, Chelly, Billuart, 2012; Valnegri, Sala, Pasafaro, 2012). Evidence from research on neural plasticity during human development demonstrates this claim by showing that the ability to change also holds for biological change. Once learned, cultural behaviors, like all behaviors, must be maintained through practice (Shors et al., 2012); analogously, new experiences arguably lead to neural changes.

This point can be extended: Even for practiced behaviors, the same behavior is not simply replicated but constantly altered and refined. Corresponding neural circuits are continuously

altered and refined as well. This point is essential to cultural learning and leads to the second tenet of the CBB model: fluctuating organismic levels create a feedback loop.

The nature of this feedback loop is reflective. Subtle changes to our beliefs or behaviors are echoed in equally subtle changes in neural events; likewise, changes in neural events can alter our beliefs and behaviors. With practice and repetition, corresponding behaviors and neural events strengthen over time. Experience can reinforce or alter this relationship. Behaviors may develop or change in response to new experiences, a majority of which will be sociocultural in nature. As this occurs, related processes in our brains and epigenetic backgrounds also develop and change. These changes are not random, but alter specific corresponding properties, which the sciences assume can be measured.

These changes may accumulate or resonate within us, and eventually feed back into our sociocultural environment in subtle ways. Our behaviors and other actions create sociocultural experiences that can reinforce or help alter the behaviors and neural events of others. In essence, we act as carriers of culture. This feedback loop is ongoing with each new experience, and research may discover mutable differences in samples and populations over time.

When considering the integration of fMRI into TCP, cognitive mediation plays a key role in the interplay between culture and brain by acting as an intermediary during sociocultural learning. Both new and repeated experiences initiate learning processes, which are cognitively mediated. Through cognitive mediation, new experiences can lead to the development of new behaviors if the individual subscribes to them. Repeated experiences sometimes reinforce existing behaviors, but they can also shed light on their flaws and potentially reactivate cognitive mediation and lead to behavioral change.

The CBB model breaks from the view that after culture-specific attitudes and practices have been adopted, they become ‘embrained’ and are no longer cognitively mediated (cf.

Kitayama & Uskul, 2011). Instead, it claims that the process of cognitive mediation feeds back into cultural learning, altering both the lessons that have been learned and the corresponding neural events that have been formed. Thus, cultural scripts are not always performed "automatically" or "seamlessly" (*ibid.*). Furthermore, cognitive mediation is a mechanism that can alter performance of cultural scripts. Such alterations feed back to the other organismic levels, and are reflected in behavioral and neural changes. This claim is supported by recent neuroimaging studies of cognitive behavioral therapy (CBT), a technique that assumes cognitive mediation can alter behavior. These studies demonstrate that cognitive mediation also alters neural activity (Frewen, Dozois, Lanius, 2008; Linden, 2006; Roffman et al., 2005). The CBB model offers a paradigm shift away from the traditional reductionisms pervasive in neuroscience. Previous models have failed to truly represent the neurology of cultural behaviors, partly because they neglect plasticity — thus simultaneously neglecting the link between culture, the brain, and behavior.

Similarly, the failure to address the role of individual diversity within previous models is the failure to understand the mechanics of this link. As the third tenet holds, vast individual variations fall along cultural continua of behaviors common to a defined group. In any population, there is a large amount of individual variation. This is particularly true when employing an ill-defined term such as 'culture,' which may interchangeably refer to practices common to a geographic region, an ethnic group, or an entire country. On the one hand, these groupings are too general for research and neglect the substantial individual variability that exists within delineated groups. On the other hand, certain practices clearly vary by culture, making cultural phenomena worth studying. The high cultural variability observed in many psychiatric disorders, and most pronouncedly in culture-bound syndromes, demonstrates that sharing similar sociocultural contexts can lead to a pool of behavioral outcomes shared by

many people. Individual diversity lies in the subscription to cultural beliefs and behaviors and in the recombination of processes and experiences.

Many definitions of culture exist across disciplines, which rely all too frequently on stereotypes to explain cultural diversity. Hypotheses that avoid these pitfalls are usually built upon more nuanced models, such as ecocultural models that co-consider local environmental and social pressures, or by surveying participant values and attitudes to determine variations in cultural domains. The ecocultural model is useful for testing personality traits and values in very specific demographic and geographic areas, while cultural domains are more useful for evaluating common behavioral traits and continua of individual variations. Using both ecocultural models and cultural domains allow for individual diversity while still emphasizing culturally shared traits., Single-subject analyses can further probe diversity within populations. By combining ecocultural frameworks with cultural domains, individual variability can be more sensitively characterized for the study of neurocultural events. This approach is most important when dealing with the psychiatric population, where research outcomes can significantly affect pathways to care.

Practically, it requires taking a mixed methods approach to establish converging evidence of cultural differences (for relevant anthropological discussions, see Weisner, 2012; Lieber & Weisner, 2010). Operationally, a statistical definition of culture may be the most useful for conducting neuroscientific research within TCP. From this perspective, culture can be treated as a set of statistically common beliefs and behaviors within a certain population, region, and time. Neural events regularly co-occurring with these behaviors may also be statistically common.

Statistical commonality within a population can be evaluated in narrower terms, e.g., by neighborhood, family, or self-defined group membership. Regional subcultures can be viewed either as cultural subsets or as distinct groups. However, in theory, the frequency distributions

of common behaviors between the mainstream culture and regional subcultures should be different. Subcultures are influenced by mainstream behaviors common to a region, but may also have a subset of statistically common behaviors that are unique to the specific, and usually self-identified, group (cf. Choudhury & Kirmayer, 2009). For example, Hispanic culture in Southern California differs in many ways from Hispanic culture anywhere else in the world, and the 1960s hippie movement in California was uniquely progressive even for its time. Both examples identify subcultures that are distinct from the dominant culture, but still uniquely situated within it. In theory, observational and self-report measures can be used to isolate statistical commonalities and help describe various sociocultural similarities and differences between groups (*ibid.*). Using a variety of measures as part of a mixed methods approach may help avoid binary East/West dichotomies and allow for a more complex picture of common sociocultural traits within a population.

Psychiatric disorders in the CBB model

In contrast with the NCI model, which implicitly suggests cultural scripts can be 'correctly' learned, the CBB model proposes that cultural scripts are always individually altered, resulting in multiple spectra of culturally-situated practices within any cultural context. Psychiatric disorders can be understood as outliers of these spectra. Most psychiatric disorders are characterized by socially inappropriate behaviors, difficulties with sociocognitive processing, or, as in the case of certain neurogenetic disorders, reduced neural plasticity (Ramakers et al., 2012; Cramer & Galdzicki, 2012; see discussion in, e.g., Gipson & Johnston, 2012).

However, the symptoms and presentations of nearly all psychiatric disorders are influenced by culture, indicating that the processing or developmental pathways giving rise to sociocultural learning occur differently in these populations. These extreme variations exist

within culture and are also part of the cultural feedback loop. Cultural scripts draw attention to certain symptoms, amplifying some experiences while minimizing others (Ryder et al., 2011) and many cultural scripts interplay simultaneously (Ryder et al., 2008). Individual mechanisms involved in this loop hypothetically occur somewhat differently from the 'statistically common' mechanisms observed in the typical population, and an interplay between atypical cognitive processes and these cultural scripts could also contribute to presented symptoms.

This raises the question of whether or not 'abnormal' (or statistically uncommon) neural processes are shared across cultures in common psychiatric diagnoses. For example, compare schizophrenia in Canada with Japan, or contrast hallucinatory experiences of certain culture-bound syndromes with the hallucinations of 'Western' conceptions of psychosis. Shared symptoms may or may not reflect shared events. Disorders are largely influenced by cultural norms and certain symptoms and syndromes appear to develop in response to different cultural and environmental stressors; it follows that neural processes formed *a posteriori* will be unique across diverse psychiatric populations (Escobar & Gureje, 2007). Considering current interest in developing brain-based definitions of various disorders (e.g., Agarwal et al., 2010; Miller, 2010; Hyman, 2007), these are important and timely questions that the CBB model provides a framework for answering.

From a statistical perspective, patients with different psychiatric disorders can be thought of as forming their own subcultures, which are simultaneously culturally contingent and distinct. While certain behaviors associated with individual disorders may be statistically uncommon relative to the general population, they are statistically common among other patients with the same disorder and may also be geographically or temporally unique. These definitions are useful for neuroscientific inquiries into the effects of 'culture,' because they suggest a framework for defining idioms, symptoms, behaviors, or neural events as common

to a certain group within a certain culture and compared to groups across cultures. For example, dissociations are experienced by people across cultures and may have different culture-specific explanations and different associated disorders or symptoms (Seligman & Kirmayer, 2008). By using a statistical framework, we can evaluate the neural events that may be statistically common for one group of patients with dissociations but statistically uncommon for another. This has the potential to lead to a more diverse and nuanced understanding of neural events associated with different conditions.

Testing the CBB Model

These components of the CBB model are supported by current literature discussing culture, neuroscience, and psychiatry, but have not been directly tested using the integrated approach proposed in this paper. This opens the door for a rich array of studies investigating claims supporting each of the three central tenets. For example, different cultures are known to have different cultural learning pathways, which are often studied by comparing mother-infant dyads across cultures (Graf et al., 2013; Bornstein et al., 2012; Keller et al., 2011; Enquist et al., 2010). Self-other mapping based on imitation is hypothesized to make these interactions effective for cultural learning (Shimpi, Akhtar, Moore, 2013; Gergely & Csibra, 2005) and some corresponding neural events have already been identified (Paulus, Hunnius, Bekkering, 2012). Complementary studies could investigate the neural events that underlie self-other mapping or alternate theories, to determine whether they are active during these cultural exchanges. Such studies could also assess whether different social cues produce this neural activity, identifying 1) neural correlates of different cultural pathways and 2) whether cultural learning can cause certain neural changes. This second outcome is particularly salient, because it would help characterize the role of sociocultural events in shaping the brain. Such studies would support the framework for cultural learning proposed in the first tenet of the CBB

model. They could be further extended to include children who are at-risk for certain disorders, by identifying difference in sociocultural pathways, neural events, or execution of cultural scripts. For example, mothers across cultures teach behaviors that they want their children to learn, such as saying "thank you" when someone gives them a gift. Children with learning or developmental disabilities may learn different lessons from this maternal modeling than children without disabilities do (Tronick & Beeghly, 2011), e.g., they may over- or undergeneralize when to say "thank you" or they may not learn from the interaction at all. Divergences in lessons and learning processes can lead to different behavioral phenotypes emerging across cultures (e.g., Keller et al., 2011; Tronick & Beeghly, 2011). This type of research would be informative for understanding formative mechanisms that contribute to the development of disorders, and may help early diagnosis and intervention techniques to reach the global community.

The role of cognitive mediation in the feedback loop could be tested directly by studying the efficacy of CBT or similar therapies in patients globally. Studies could investigate long-term neural and behavioral changes corresponding with CBT, using a mixed methods approach. By testing the ability of cognitively mediated change to feedback to multiple organismic levels, they would also test the second tenet of the CBB model. The third tenet of the CBB model can be tested by statistically visualizing culturally common and uncommon behaviors and neural events within defined groups, using ecocultural frameworks and cultural domains as guides for the construction of both the studied samples and behaviors.

THE CBB MODEL AS A SYSTEMS APPROACH TO TRANSCULTURAL NEUROPSYCHIATRY

The CBB interaction model proposed in this paper resolves many of the incompatibilities between CN and TCP. Through this systems approach, behavior, brain, and culture become

three levels of a vast and ubiquitously flexible feedback loop. The CBB model maintains that utilizing neuroscience in TCP research must be grounded in pervasive changeability and in the equal influence and flexibility of each organismic level. Accordingly, it endorses a statistical definition of culture that simultaneously considers individual and circumstantial variability while also allowing for regional or ethnic generalities to be made.

While the CBB and NCI models agree that practiced behaviors can lead to neural changes, the models diverge in most other ways. These divergences are reflected in the CBB model's three central tenets. By taking a systems approach, the CBB model also avoids the three main theoretical pitfalls discussed earlier. First, neural events play key roles in the model, but the individual is never reducible to neural events. Instead, the CBB model acknowledges the individual's capacity to change, thus altering their behaviors and neural events. Secondly, it does not view culture as 'locatable' in the brain. Although culturally common neural events may be statistically observable on the group level, they cannot be located within individuals and are assumed to change across situations and lifetimes. Thirdly, the CBB model proposes nuanced alternatives to avoid reliance on cultural stereotypes. Some 'Western' cultures may share certain cultural domains with some 'Eastern' cultures, while other cultures located within the same hemisphere do not. Additionally, subcultures may have notable differences in cultural domains when compared to the surrounding dominant culture. People within the subculture may respond or self-identify differently depending on whom they are interacting with (Matsunaga et al., 2010).

In resolving the incompatibilities of contemporary models with TCP, we propose a few additional points. 1) Taking a systems approach to the study of TCP avoids overemphasizing one organismic level, and views the whole patient as a single individual with multilevel organismic pressures. Within such an approach, culture is mediated by behavior, the brain, genes, experience, etc. and is not 'unmediated' as other models have proposed. 2) Grounding

such an approach in the phenomenon of plasticity acknowledges the patient's individuality without ignoring related neural events. 3) In line with Choudhury & Kirmayer's (2009) proposal, culture is not a single entity defined by geographical or political boundaries. Instead, it is composed of sets of cultural domains, which are behaviors and beliefs that are common within a specific historical time and ecocultural group. This conceptualization replaces binary categories like 'collectivist cultures,' which are used synonymously with 'Eastern' cultures, with more nuanced categories. These categories are based on empirically measured participant-reported values rather than stereotypes and are observable in cultures across hemispheres.

NEUROSCIENCE AND THE BENEFITS OF A SYSTEMS APPROACH TO TRANSCULTURAL PSYCHIATRY

In conclusion, the current dearths of neuroscience in TCP research and of cultural diversity in traditional neuropsychiatry leave a majority of the global population underrepresented in biomedical research. Extending TCP research to include neuroscientific techniques could benefit patients who have immigrated into countries where biomedicine is practiced or who are receiving treatments through global mental health outreach efforts. Despite underlying theoretical conflicts, many current studies in CN are directly applicable to the patient population (Crafa & Nagel, in press). They can be modified to provide new insights into disorders and have the potential to better represent diverse patient populations – a task that TCP is uniquely positioned to tackle.

TCP provides a conversational space that is uniquely suited to debate difficult theoretical questions, such as what it means to say that culture is "stored in people's brains" (Ames and Fiske, 2010, p. 72) and what the role of the PFC is in storing or producing "the shared webs of

signification that make up culture" (Domínguez et al., 2009, p. 60)•. Evaluating these questions through the lens of TCP provides a unique framework for identifying answers and developing a richer understanding of neurocultural events.

The overarching conclusion of studies from CN is that culture and neural events are "inextricably linked" (Zhou & Cacioppo, 2010). Although this conclusion is not surprising, it highlights the potential fMRI has for shedding new light on the relationship between culture and disorder. By applying the CBB model, CN paradigms could be carefully adapted to investigate cultural variations in the psychiatric community. For example, numerous studies have found differences in neural activity across cultural backgrounds (e.g., Goh et al., Leshikar, Sutton, 2010; Gutchess et al., 2010; Kitayama & Park, 2010; Chiao et al., 2008; Hedden et al., 2008). Many of these studies have focused on differences in neural pathways used for language or self-knowledge processes, while others show differential activity in regions like the hippocampus and amygdala that are associated with memory and emotion. Each of these brain processes are commonly associated with features of psychiatric disorders (Carmichael et al., 2012; Liemburg et al., 2012; Lombardo et al., 2010). For example, the high variability of amygdalar responses to certain events or stimuli may have implications for anxiety patients with diverse backgrounds (Sotres-Bayon et al., 2008).

Schizophrenia provides a second example. Although schizophrenia is globally ubiquitous, its symptoms and outcomes are highly heterogeneous (Kalra et al., 2012; Suhail & Cochrane, 2002). Higher rates of schizophrenia are associated with immigration, social inequality, and racial discrimination (Kirkbride et al., 2013; Kirkbride et al., 2012; Smith et al., 2006; Jarvis, 1998). Subcortical variations in neural network activity have been observed in individuals with schizophrenia (for review see Shenton et al., 2001), as has abnormal PFC volume (Wible, Anderson, Shenton, 2001) as well as PFC connectivity and processes (Tan, Sust, Buckholtz,

• Many thanks to an anonymous reviewer for directing us to these considerations.

2006; Hill et al., 2004; Callicott, 2003). Abnormalities in the PFC predict individual affect and may additionally relate to pathological dissociations (Steiner & Coan, 2011; Seligman & Kirmayer, 2008). The PFC also seems to be closely tied to sociocultural self-identity (e.g., Ma et al., 2012; Sul, Choi, & Kang, 2012). Studying the role of the PFC in schizophrenia across cultural contexts may help disentangle some of the cross-cultural heterogeneity observed in this disorder.

CN paradigms may also be used to investigate fundamental controversies, such as the theory of mind debate (Wilkinson & Ball, 2012), and may yield new insights into non-verbal patients or patients with impaired ability to self-report. For example, many disorders (e.g., schizophrenia, autism) have disruptions to 'self' processes (Lombardo et al., 2010; Stephan, Friston, Frith, 2009), impairing the ability to self-report and limiting the therapist's access to the patient. Some fMRI studies have identified disruptions in the networks of neural processes that are active when thinking about oneself (Lombardo et al., 2010). Complimentary studies in CN have shown that neural 'self' processes exhibit some flexibility across social situations (Ng et al., 2010; Chiao et al., 2010; 2009)., raising the question of whether the same degree of flexibility exists in these disorders (Meyer-Lindenberg & Tost, 2012; Lazar et al., 2011; Dawson, 2008). Modifying paradigms used by cultural neuroscientists to study neural flexibility may help assess key aspects of clinical phenomena.

A final benefit that fMRI research may have for TCP is the ability to learn more about biomedical norms through identifying similarities across cultures (Ryder et al., 2011). Identification of similar neuroanatomical features or neural processes across cultures may help illuminate neurobiological variations that are closely tied to shared symptoms. Identifying these commonalities in disorders like autism, for example, may help identify early biomarkers and facilitate early intervention. Determining similar neurological traits between common disorders (e.g., schizophrenia) and culture-bound syndromes could allow analogies to be

drawn, improving understanding and, potentially, treatment options for these disorders (Crafa & Nagel, in press).

The research questions and methods advocated in this paper aim to enrich 'Western' biomedicine by promoting the inclusion of diverse patient populations in research. Although this perspective should in theory help improve the treatment options available for patients globally, 'Western' biomedicine is not the only mental health system and it is not always the most appropriate treatment framework (Kirmayer, 2012). The focus on biomedical research in this article is due to the authors' expertise, and different types of research questions may need to be asked to accommodate other medical systems. The CBB model and its central tenets emphasize systemic fluidity and are general enough to be extended and adapted to fit different medical systems.

In order to more thoroughly integrate neuroscience and its methods into cross-cultural psychiatric research, the CBB model proposed in this paper offers an alternative to other contemporary models. Through applying the CBB model, TCP would be uniquely positioned to study the relationship between culture and the brain by making observations on three levels: culturally common behaviors and neural processes, individual variations within those behaviors and neural processes, and circumstances in which the individual may behave more or less according to social convention. All three levels are clinically interesting, because they address degrees of normalcy and divergence. Although culture and brain are closely interrelated levels, their relationship within psychiatry has not been widely explored. fMRI provides an additional way to examine common cultural elements that may contribute to global symptomatic representations and variations, providing new insights for therapies that counterbalance these stressors. Developments in this field hold promise for better representing underserved populations in psychiatric research and may lead to new understandings of the relationship between culture and disorder.

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