

Group differences in mental health: A role for culture in neuropsychiatry

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Abstract. *There is a need to diversify mental health research that uses brain imaging. Currently, this research almost exclusively includes participants from the 'Western' world, a majority of whom are Caucasian (Henrich et al, 2010a; 2010b). In light of studies from cultural neuroscience, which use brain imaging to demonstrate that people from different countries exhibit different neural activity, the lack of diversity in contemporary mental health research may pose a systematic bias of the data and interpretation. Considering that disorders are highly diverse between patients and across cultural groups, brain-based characteristics of disorders may vary across populations, making aberrant neural signatures difficult to identify if they exist at all. Further research could expand clinical understanding of diverse disorder phenotypes for globally shared disorders (e.g., schizophrenia) as well as generating new knowledge about culture-bound syndromes. This paper begins by demonstrating the underrepresentation of diverse populations in neuropsychiatry and then systematically discusses problems that increasing representation may solve, as well as research opportunities and implications for mental health practice, particularly for fields like transcultural psychiatry and global mental health.*

Keywords: neural diversity, cultural neuroscience, heterogeneity, transcultural psychiatry, diagnosis, neuropsychiatry, culture, mental health

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INTRODUCTION Mental health research is currently undergoing a challenge of diversity. On the one hand, diagnosis is not always clear-cut due to the inhomogeneity of disorder symptoms and presentations across individuals (American Psychiatric Association, 2013; Kraemer *et al*, 2012). On the other, external factors, such as differing environmental and social environments appear to play roles in shaping symptom distributions and idioms of distress across cultures and patient groups (Kohrt *et al*, 2014; Escobar & Gureje, 2007; e.g., Grover & Ghosh, 2014; Keys *et al*, 2012). Globalization has increased immigration and diversification across the 'Western' world, and mental health clinicians are treating patients from diverse cultural backgrounds more frequently now than in the past. Many patients bring different customs and cultural expectations with them. These differences can lead to clinical misunderstandings, such as over-diagnosis or misdiagnosis (Adeponle *et al*, 2012; e.g., Fountain *et al*, 2011; Mandell *et al*, 2009; Raghavan, 2009), which have been well-documented and are increasingly addressed through cultural competence trainings and targeted research studies.

However, neuropsychiatric research is one area of psychiatry that remains grossly negligent of cultural differences. Currently, very few studies have used neuroscientific methods, such as eye tracking or

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fMRI, to investigate clinically relevant differences in patient populations. Surprisingly, this neglect continues in the face of findings from cultural neuroscience (CN) that robustly demonstrate the influence culture can have on clinically-relevant neurobehavioral processes: multiple culture-based differences have been reported in brain regions that exhibit distinct activity in many disorders, such as the prefrontal cortex, cingulate cortex, parietal lobe, and amygdala, which show different processes in disorders like schizophrenia, post-traumatic stress disorder, autism, major depression, and general anxiety disorder (Crafa & Nagel, in press). The absence of cultural neuropsychiatric literature creates a two-fold problem: First, only a small portion of the global population is represented in this research. A majority of neuroscience research comes from Caucasian populations in Western Europe and North America (Henrich *et al*, 2010a; 2010b). Considering that neural activity varies across cultures, at least some brain processes relating to mental health likely do as well. Therefore, medical advancements that are based on neuropsychiatric research may thus be suboptimal for patients from underrepresented cultural groups. Second, it may feed into a larger problem psychiatry faces in understanding brain-based characteristics of disorders. Over the past fifteen years psychiatric research has been using neuroscience, especially fMRI, to attempt to characterize ‘dysfunctional neural pathways’ of clinical disorders. Perhaps the most salient example of this attempt is the development of the DSM-5 in North America, which explicitly aimed to produce a diagnostic manual that widely included neuroscientific differences in disorders (e.g., Charney *et al*, 2002) but could not satisfyingly do so after over a decade of concentrated efforts (Kapur *et al*, 2012; Hyman, 2007) and was ultimately criticized by Thomas Insel, the director of the U.S. National Institute of Mental Health (Insel, 2013).

The reasons for this apparent failure are multifold (for discussion see Kapur *et al*, 2012; Frances, 2009; Hyman, 2007). One possible explanation is that the inhomogeneity of psychiatric symptoms and presentations confound the data. Recent studies demonstrate that patients show different neural networks activity when contrasted with controls, while family members of the patients shared activity patterns that overlapped with both the patient and control groups (e.g., Khadka *et al*, 2013). Such findings show inhomogeneity within single demographic groups (in the case of the example, control participants were mainly non-Hispanic Caucasian and African American adult residents of Hartford, Connecticut; Tamminga *et al*, 2013). This paper proposes that these brain-based continua may be multidimensional, varying across demographics and cultural groups as well, just as behavioral symptoms and presentations do.

KNOWN PSYCHIATRIC VARIATIONS ACROSS PATIENT GROUPS

Psychiatric research across cultures has identified differences in the appearance of symptoms, or idioms of distress, of common disorders across cultures. These differences may emerge as qualitative differences. For example, somatic symptoms of anxiety are more likely to appear as stomach problems in North America but as burning sensations in regions of Africa (Escobar & Gureje, 2007). Hallucinatory voices associated with disorders like schizophrenia are frequently threatening or scary in North America but more good-natured or even playful in Ghana and India (Luhmann *et al*, 2014). Symptoms and disorders are also conceived of differently across cultures. Hallucinations, for example, are seen as spiritual in some cultures and disturbed in others (Johnson & Friedman, 2008). Their sources are also subject to interpretation – while some cultures may attribute hallucinations to biomedical causes, others may see them as signs of possession, revelation, or guilt (McCarthy-Jones, 2012). These difference in the conceptualization of ‘symptoms’ and ‘disorders’ influence how socially acceptable these experiences are, the degree of stigma associated with them, and, most importantly, whether they are culturally understood as problems that require treatment.

Across cultures, people who are stigmatized or recipients of discrimination tend have higher rates of diagnoses and greater severity of symptoms (Chou *et al*, 2012; Luhmann *et al*, 2014; Thornicroft *et al*, 2010; Teachman *et al*, 2006). Such findings elucidate one way the social world interacts with biological predisposition to shape the appearance and experience of having a psychiatric disorder. These differences may impact the brain (and possibly even epigenetic) processes associated with individual

psychiatric disorders. They may partially explain the reasons neuropsychiatry has failed to develop clinical definitions of specific brain processes as signature characteristics of specific psychiatric disorders.

CLINICALLY-RELEVANT BRAIN-BASED VARIATIONS ACROSS PATIENT GROUPS

Evidence from CN, which primarily studies non-clinical differences in brain-based processes, has recorded diverse neural responses across and within populations. Although CN paradigms have not widely been applied to psychiatric research, they point to substantial variations in brain activity that are contingent on personal values as well as social context (e.g., Chiao *et al*, 2010). For example, bicultural individuals who have been raised around both individualist and collectivist values exhibit flexibility of neural activity depending on whether individualist or collectivist values are more appropriate in a given context (*ibid.*). Such variations are also likely to be observable in patient groups, although they may look different. For example, patients who struggle with social interaction might not exhibit the same neural flexibility across contexts compared to more adaptable controls (cf. Uddin *et al*, 2014). Moreover, such findings from CN reflect mutable differences that are value- or cognition-based but change across contexts. The ability of bicultural individuals to adopt values appropriate to a context reflects the influence of their phenomenological experience on their neural activity (i.e., Chiao *et al*, 2010) – which go beyond culture ‘in the brain’ but rather reflect thoughts or interpretations of the surrounding environment. In patient groups, differences in neural activity in comparison with controls may be contingent on differences between phenomenological experiences as opposed to brain states (Fuchs, 2011). In other words, cognitive and perceptual interpretations of context (which may also be brain-based) may sometimes be the origin of the disruption while the ‘disrupted’ brain state may be a secondary reaction to the original processing error. In the case of people with schizophrenia across cultures, for example, different neural processes are likely active if the voices inspire fear than if they are benevolent. This stands to reason because, at very least, areas of the brain such as the amygdala and regions of the prefrontal cortex and frontal gyrus that are associated with fear are much more likely to show heightened activity in the first group (e.g., Mak *et al*, 2009; Fossati *et al*, 2003; Northoff *et al*, 2000).

Other recent studies demonstrate that, even within patient groups, differences in brain activity compared with controls may only be a matter of degree, as in the case of the previously discussed study demonstrating that the neural processes of families of patients with bipolar activity did not resemble the patients or the controls, but had features of both (Khadka *et al*, 2013). Such findings suggest that the natural diversity of neural responses exists on a continuum of qualitative factors. Considering that disorders are highly diverse between patients and across cultural groups, such brain-based continua of disorders may vary across populations, making the neural signatures of disorders difficult to identify if they truly exist at all.

PROPOSED MULTI-DIMENSIONALITY OF PSYCHIATRIC VARIATIONS

In mainstream psychological research, experimental findings are commonly assumed to be representative of patients with the studied disorder, both within the country of study and globally. However, this assumption may be erroneous. Considering the heterogeneity of data within psychiatric research as well as the brain variations in non-patients across cultures, cultural background may be a confounding dimension that neuropsychiatry has not widely considered to-date. This paper proposes that brain-based continua of disorders may be multidimensional, varying across cultural (or even sub-cultural) groups, just as behavioral symptoms and presentations do.

This proposal mirrors the recent paradigm shift in the way disorders are thought about by North American psychiatrists, who define disorders along continua or spectra as opposed to lists of symptoms (American Psychiatric Association, 2013; cf. American Psychiatric Association, 2000; e.g., Graf *et al*, 2014). However, it adds that these continua are couched within a sociocultural background and may

vary across backgrounds. Culture simultaneously shapes the brain and behavior, and disorders emerge from this interaction, resulting in a complex feedback loop between the external environment and internal biological processes (Crafa & Nagel, in press; Fuchs, 2011).

Moreover, disorders may emerge from a conflict between neural circuitry and culture (Kirmayer & Crafa, 2014). Society may exasperate social deviations (e.g., stigmatizing hallucinations) or shape them (e.g., causing threatening hallucinations rather than playful ones). Both stigmatization and threatening experiences can intensify symptoms of a disorder while social acceptance and benign experiences can facilitate high functioning, which changes the face of the disorder. When negative emotions are greater, the effects of stress on brain processing likely also takes a greater toll. After time and repetition, an association may be formed between these neural processes and certain symptoms (e.g., coupling of neural connections).

Additionally, other culturally-shaped features of a disorder, such as its idioms of distress and symptom frequency, may also influence brain processes or reflect neural differences. As mentioned for example, in some societies the sensation of burning is a common somatic expression of anxiety while stomach problems are in other societies (Escobar & Gureje, 2007). These idioms may initially vary because the social meaning of each behavior is culturally different. However, repetition of these somatic experiences may develop relationships between neural processes associated with anxiety and those necessary for performing the somatic expression. On the other hand, these cultural associates may emerge as an offshoot of the neurobiology of the disorder. For example, idioms of anxiety may vary across cultures in part as a byproduct of different cross-cultural neural processes underlying anxiety. Better understanding the relationship between culture and the brain may help evaluate the complex interplay between psychological, biological, and cultural influence on symptoms and benefit assessments of treatment options.

Possible practical outcomes of a multi-dimensional perspective The possibility that brain-based continua of disorders may differ across cultures suggests that, at very least, neuropsychiatric research should report country of study and scrutinize whether research findings outside their own country could have cultural variations. However, more research into the influence of culture on the brain and disorders could also have many benefits for patients globally. This research could expand understanding of diverse disorder phenotypes for globally shared disorders (e.g., schizophrenia) as well as generating new information about culture-bound syndromes. This may be especially beneficial for immigrant groups and cultural subgroups already living within a population, which have higher rates of disorders compared to the general population in many countries (Crafa & Warfa, in press).

RESEARCH CHALLENGES AND PROSPECTS Several challenges are faced when undertaking research investigating the influence of culture on the brain and disorders. For one, psychiatry is an imperfect science: 1) ‘Culture’ is also an ill-defined term that requires researchers to develop an *a priori* operational definition. Such definitions may be created by identifying statistically common behaviors within a given geographical area (Crafa & Nagel, in press), and questionnaires or ethnographies may be used to determine what these behaviors are; 2) Disorders are constructs that refer to sets of symptoms, which vary widely across individuals (Kendler *et al*, 2011; Gone & Kirmayer, 2010; Hyman, 2010). In some cases, studying individual symptoms may be more valid than studying the disorders themselves; 3) Neuroscience methods, especially functional magnetic resonance imaging (fMRI), can yield findings that are difficult to interpret or easy to manipulate. Researchers also must be careful to avoid reporting brain data as causal or reducing the patient to their neural processes in order to properly represent the complex interactions at play that may be influencing observed neurobiological processes.

Provided that these precautions are taken, neuropsychiatric research that co-considers social and cultural contexts has the potential to provide new perspectives on old problems. First, although disorders appear to arise from a complex interaction between the patient’s individual circumstances

and their biological makeup, the specifics of this relationship are only partially known. Studies from social neuroscience have identified relationships between the social world and neural processes, and cultural neuroscience has extended such studies to include cross-cultural populations. Much of this research still comes from Western Europe and North America, although there are prestigious labs in other countries, including Russia, China, and Japan. As a result, the pool of research themes is still fairly focused. To date, few studies have investigated common psychiatric disorders across cultures, and very few studies have investigated global mental health issues, such as possession epidemics, which are relatively common in the developing world (Tseng & Zhong, 2012). These are broad paths with countless opportunities for new research ventures. Second, the existing body of literature demonstrates that neural processes vary across contexts (e.g., Brodeur *et al.*, 2011; de Loye *et al.*, 2013) and cultures (for review see Rule *et al.*, 2013). Studying disorders across cultural contexts provides a means of investigating the diversity of neuronal responses to social stimuli.

CONCLUSION As the world continues to globalize and migration rates continue to rise, understanding individual variations becomes increasingly important. Moreover, these differences appear to be intimately related to variations in culture, contexts, neurobiology, and psychology and the complex interrelationship therein. Combined, these broadly defined sources of patient diversity may partially explain the failure of neuroscience to identify brain-based patterns of disorders. This failure may have emerged because populations are more complex than originally assumed and brains are less uniform. Understanding the effects of culture on the brain and mental health can provide deeper insight into this diversity and may help to better characterize neural processing patterns in a way that is useful to mental health.

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