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Retraction

Culture as a variable in neuroscience and clinical neuropsychology

A comprehensive review

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Culture as a variable in neuroscience and clinical neuropsychology

A comprehensive review

José Roberto Wajman[1,2,3], Paulo Henrique Ferreira Bertolucci[2], Letícia Lessa Mansur[3,4], Serge Gauthier[1]

ABSTRACT. Culture is a dynamic system of bidirectional influences among individuals and their environment, including psychological and biological processes, which facilitate adaptation and social interaction. One of the main challenges in clinical neuropsychology involves cognitive, behavioral and functional assessment of people with different sociocultural backgrounds. In this review essay, examining culture from a historical perspective to ethical issues in cross-cultural research, including the latest significant and publications, the authors sought to explore the main features related to cultural variables in neuropsychological practice and to debate the challenges found regarding the operational methods currently in use. Literature findings suggest a more comprehensive approach in cognitive and behavioral neuroscience, including an interface between elementary disciplines and applied neuropsychology. Thus, as a basis for discussion on this issue, the authors analyzed key-topics related to the study of new trends in sociocultural neuroscience and the application of their concepts from a clinical perspective.

Key words: neuroscience, neuropsychology, cross-cultural comparison, epigenetic processes.

CULTURA COMO VARIÁVEL NA NEUROCIÊNCIA E CLÍNICA NEUROPSICOLÓGICA: ENSAIO ABRANGENTE PARA REVISÃO

RESUMO. Cultura é um sistema dinâmico de influências bidirecionais entre indivíduos e seus ambientes, incluindo processos biológicos e psicológicos que facilitam na adaptação e interação social. Um dos maiores desafíos da clínica neuropsicológica se refere à avaliação cognitiva, comportamental e funcional de pessoas com diferentes contextos socioculturais. Neste ensaio para revisão, traçando uma trajetória partindo de perspectivas históricas até temas éticos em pesquisa transcultural, os autores procuraram explorar os principais achados relacionados a variáveis culturais na prática neuropsicológica, além de debater os desafíos encontrados que estão relacionados com métodos operacionais atualmente utilizados até as mais importantes e atuais publicações sobre o assunto. Achados da literatura sugerem uma abordagem mais apropriada da neurociência cognitiva e comportamental, incluindo a relação entre disciplinas elementares para seu entendimento com a clínica neuropsicológica. Assim, a fim de propor uma discussão sobre este tema, os autores analisaram neste artigo tópicos-chave relacionados ao estudo de novas tendências em neurociência sociocultural e a aplicação de seus conceitos através de uma perspectiva clínica.

Palavras-chave: neurociência, neuropsicologia, equiparação transcultural, processos epigenéticos.

INTRODUCTION

Sociocultural neuroscience is an emerging subdiscipline in the neurosciences and, although brain-behavior relations in a sociocultural context have been of long-standing interest to neuropsychologists, there is still a lack of research in this complex area. This may, among other reasons, be due to the scarcity of available knowledge on aspects such as concepts and definitions. The question of

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how mental processes can be shaped by sociocultural influences poses a tremendous challenge for cognitive researchers in the twenty-first century because how current models of brain-behavior interaction fit into different cultural contexts, and likewise into social situations in the same culture, remains unknown. Given this "Ebbinghausian paradox" of cross-cultural neuropsychology (statements about psychology as a scientific discipline) it becomes clear that, in fact, application in this area has a long past but a short history.

Are humans all the same in terms of cerebral organization of perception, language, memory and cognition, or does culture affect patterns of higher cortical function? Is the way in which people perceive and solve problems determined by interaction of their genetic endowment and the culture in which they mature, or is the mind universal? Following this line of questioning we could wonder that, if mind like brain is one and therefore unitary in all humans, then neuropsychological assessment founded on human universals will work equally well in Montreal, Guangzhou or the subsistence farming villages of South Africa and Brazil. If mind is many, however, then identical tests may make geniuses of average people in one culture and imbeciles of equally average people in another.[1]

Another important question is the contemporary neuropsychology subject *per se*. Indeed, is this measured by clinical neuropsychological instruments in which neuropsychologists believe? Does brain dysfunction affect performance on a given task or could it be a lack of patient familiarity with the cultural norms and attitudes that are being measured? What would be the ecological validity of the results without elementary cultural contextualization? Biology, culture, and individuals are three interacting complex organisms of the same system; hence, as perceptively noted, one of these should not be studied without considering the others.[2]

It has been argued that the development of new cross-cultural normative databases stratified by salient sociodemographic factors calls for an "anthropological neuropsychology" viewpoint.[3] Race, ethnicity, and native language significantly influence neuropsychological test performance.[4] Given the current situation in which neuropsychologists recognize the need to include issues of diversity in ongoing research and practice, the matter of how to best operationalize this objective is under discussion.

In an age highly influenced by postmodern thought,[5-7] one might wonder if each culture is as particular and persuasive as to invalidate the possibility of meaningful cross-cultural assessment of neuropsychological functioning. This line of reasoning has been supportive of calls for the development of indigenous neuropsychological and cognitive assessment instruments, particularly in Asian settings.[8-10] While popular, this perspective suffers from a number of limitations. As researchers have pointed out,[11] care must be taken to avoid the intrusion of political ideology into research concerning the validity of cross-cultural measurements.

In principle, the specific cultural milieu in which an assessment instrument was originally conceived does not preclude its valid use in different societies and ethnic groups.[12] Likewise, if exclusionary emic canons guide cross-cultural assessment questions, it will be very difficult for communities of scholars to develop an integrative understanding of the comparative abilities of distinct populations (i.e., test and measurements will be unique for each cultural group). A balanced appreciation of the influence of individual differences, group specificity factors, and the uniformity of human functioning across cultures is, of course, the desired goal for anthropologically informed neuropsychology.

For this semi-systematic review, article quality index was determined considering aspects of methodology, selection of samples, comparability of populations, diagnostic criteria adopted, and clinical instruments used. From July 2014 through May 2015 a search of Medical Literature Analysis and Retrieval System (MEDLINE), Excerpta Medica Database (EMBASE), PubMed, Cochrane database, Lilacs, Scielo, and Cumulative Index to Nursing and Allied Health Literature (CINAHL) was conducted based on the key terms "Sociocultural Neurosciences", "Transcultural Psychiatry", "Translational Psychiatry", "Bio psychosocial Neuropsychology", "Cultural-historical Psychology" in addition to their derivations and combinations. Given the exploratory nature of this essay, it is worth mentioning that most of the studies analyzed were reviews and meta-analyses, with inclusion of some experiments in addition to literary works and book passages. Due to the native tongue of the authors, references were sought mostly in the English language with a small proportion in Spanish, and Brazilian Portuguese. For this research, articles written in other languages were not assessed in full text. Papers which met the eligibility criteria were descriptively analyzed as regards to their importance to the topic, main results, and final discussion.

IN SEARCH OF A DEFINITION FOR "CULTURE"

The concepts of culture and ethnicity are difficult to define. In cultural studies and cultural anthropology,

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ethnicity is determined as the classification of humans into groups based on a large range of criteria: language spoken; cultural identity; physical traits, etc. Cultural anthropologists, considering ethnicity and the people within these ethnic groups, have only the capacity to define the specific social setting of these groups. For the purposes pursued here, culture is a symbolic form, a category of relations composed of reciprocal representatives and social rules.[13] The development of attitudes towards contextual and global knowledge is becoming increasingly imperative and this produces the emergence of the ecological mentality that situates every event, item of information or piece of knowledge in an inseparable relationship with its environment, be it in cultural, social, economic, political or natural terms.

Culture is a broad concept that is not easily defined. The study of culture as a unique phenomenon can be traced back to Greek historian and philosopher Herodotus and currently several definitions of culture are in use. Generally, culture refers to a body of customary beliefs and social norms that are shared by a particular group of people.[14]

The first step in discussing cultural concepts defining culture itself. Culture can be defined as the system of shared beliefs, values, customs, behaviours, and artifacts that members of a community use to cope with their world and with one another, and which are transmitted from generation to generation through learning.[15] This definition highlights a critical point: culture is not merely the sum of cultural products. Beliefs, behaviours, and artifacts are created through the transmission and modification of these products within and between generations by means of cultural learning.

An eminent researcher describes cultural learning as a form of social learning in which perspective-taking plays a critical role in both the transmission of information and the resulting cognitive product.[16] During cultural learning, information, in addition to modeled behaviors such as the inferred intentions and emotional states of the model, are encoded and retained, along with the contextual meaning of behavior. The cited author proposed that cultural learning includes imitative learning, instructed learning, and collaborative learning, all of them successive stages of development.

More recently, advances in the study of human behavior have led to the emergence of cultural psychology, which examines human behavioral diversity, and human neuroscience, which has been largely influenced by conventional biological notions of natural selection.[17] According to this perspective, culture neurosciences were motivated by neuroscientific investigation of aging and culture. Thus, culture serves an important role later in life as a compensatory mechanism for the decline in cognitive abilities due to neural changes in cellular and structural organization of the brain.

Imitation and social learning are also the propellant that drives cultural evolution; the basic process by which ideas, thoughts, knowledge and beliefs spread and change over time.[18] In the mid-20th century, social sciences started to study how and why various ideas spread in a population. Research concerning the diffusion of innovations was pioneered by Everett Rogers, who examined attributes of innovations and adaptation, categories of adopters, diffusion networks and the consequences of innovations.[19] Further, a distinguished biologist, Richard Dawkins, coined the term "meme" to describe a cultural information unit (or cultural gene) that replicates and propagates from one mind to another.[20] The concept of memes as evolutionary replicators was further promoted and the founding of memetics, a new scientific discipline that studies evolutionary models of information transmission.[21,22]

In fact, cultures never stand still but evolve showing many similarities to biological evolutionary processes. Ideas (or memes for that matter), percolate as units of cultural information, which is analogous in many ways to the spreading of genes, the units of genetic information. Concepts of natural selection and mutation can also be applied to the study of cultural evolution to explain why one idea becomes extinct while other ideas survive, spread and change over time.[23,24] These similarities led to the formation of various mathematical frameworks (mostly originating from classical population biology theory) that study cultural transmission and its interaction with the evolutionary process.[25-27] These frameworks allow social scientists to model cultural transmission and evolution using a well-established, quantitative, and rigorous toolbox.[28]

Given these findings, cultural neuroscience sustenance was introduced to explain how theoretical and empirical approaches across different fields within the social and natural sciences may further understanding on how ecological and genetic factors influence the human mind, brain, and behavior not only during the life span but also within situations and across evolutionary timescales.[29] Discovery of cultural influences on neural representations of self and identity led to the notion that culture is a dynamic system of bidirectional influences with the individual, including psychological and biological processes that facilitate social interaction.[30] The goal of cultural neuroscience is to facilitate an understanding of both environmental influences and

biological constraints to cognitive functioning throughout development and in late adulthood.

CULTURAL-HISTORICAL PERSPECTIVE IN PSYCHOLOGY

Among the first attempts to bring cultural issues into scientific psychology was the theory of cultural-historical psychology, which is associated with the Russian psychology school, with the prominent scholars Lev Vygotsky and Aleksandr Romanovich Luria. Vygotsky's fundamental hypothesis was that the higher mental functions are socially formed and culturally transmitted. His theory has three major postulates. First, evolution resulted in the capability of human beings to change their environment. Second, as a consequence, human beings have learned to operate with their own consciousness. This led to development of voluntary forms of action, and in turn, to the emergence of higher mental functions.

Additionally, these two processes are tool-mediated, that is, while mechanical tools are applied to operate with nature, psychological tools – symbols – are used to operate with one's behavior. The third part of Vygotsky's concept is what he referred to as "interiorization" that is the reorganization of external psychological tools (e.g., symbols, words said out loud) into internal concepts and images. Thus, higher psychological functions are based on the usage of inner, usually verbal, sources originally acquired in communication with others. Vygotsky pointed out that functional systems are characterized by a new integration and co-relation of their parts. The whole and its parts develop in parallel to each other and concomitantly. Thus, higher psychological (or neuropsychological) functions are voluntary, tool-mediated and social in their origin.

Cultural-historical psychologists hold that historical change in human thought arises in two interrelated ways. First, there is the shift from natural and unmediated to cultural and mediated thought. Second, there is development in the complexity and sophistication of mediational means that entails a corresponding development of thinking.[31] This view was largely based on the ideas of late nineteenth (and early twentieth) century social anthropological research.

Another source of cross-cultural neuropsychological concepts can be traced back to the 1930s when the young soviet neuropsychologist A. R. Luria, conducted a set of studies in the former Soviet Republics of Uzbekistan and Kirgizia. The purpose of the research was to determine whether introduction of modern culture and public education, which accompanied collectivization occurring in the former Soviet Union at the time, affected performance on simple cognitive tasks in native Uzbek people, compared to those who had no formal education and were not exposed to "western" sociocultural norms. Luria implied that people on a different level of modernization would perform differently on given cognitive tasks. The results of the experiments showed that illiterate subjects were unable to form categories according to abstract characteristics.

Luria concluded that introduction of formal schooling and new models of socioeconomic life promoted a qualitative shift in the processes of perception, categorization, imagination, and self-analysis.[32] Luria emphasized the importance of the environment in the development and maturation of functional systems and the importance of the roles different brain areas play in a given task. The more complex the behavior, the more variable its underlying functional system can be among different cultures; the more basic the behavior, the more likely the systems are universal. According to this Lurian scheme of neuropsychological investigation, functions are evaluated from a variety of perspectives to ensure that a deficit is consistently present regardless of the way it is evaluated.

A "neuro-culture" interaction model was then developed to suggest a causal trajectory whereby cultural practices reinforce values and tasks that become "culturally patterned neural activities" due to neuroplasticity or neural change, which then facilitate social survival via biological adaptation and reproductive success.[33]

A FRAMEWORK OF CULTURAL NEUROSCIENCE: INTRODUCTION TO THEORY, MODELS AND METHODS

Cultural neuroscience bridges theories from distinct fields, including anthropology, cultural psychology, neuroscience/neurogenetics, and population genetics.[34-36] In the past four decades or so, researchers in sociocultural science have developed new theories to explain dimensions along which nations and cultures may vary, such as individualism-collectivism, power distance, short-term-long-term orientation, uncertainty avoidance, and masculinity-femininity.[37] Cultural constructs such as analytic-holistic cognition,[38] socioeconomic status[39] and tightness-looseness[40] further describe how a person may think, feel, and behave differently across geographic and cultural circumstances.

To illustrate some of the models mentioned above, authors state that East Asians are more likely to engage in holistic cognition, specifically attending to the entire field of a scene and relying on dialectical reasoning; on

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the other hand, Westerns are more likely to show analytic cognition, attending to objects rather than their context and using rules to reason.[41] Tightness-looseness refers to the cultural spectrum that affects how sensitive people are to social norm compliance and violations. For instance, individuals who live in tight cultures are more likely to be socially sensitive to social rules, whereas people who live in loose cultures are more likely to be tolerant to social deviances.[42]

In the last two decades, approximately, the relationship between brain structure and function as predictors of behavior has been the main focus of neuroscience. Theories such as modularity of mind indicate that the mind and brain comprise modules that are information-encapsulated engrams, that from the outset, rapidly and automatically process different kinds of specialized information, and are found across different species.[43] Major advances within human neuroscience research have led to the notion of modules within the human brain for processing specific kinds of information, such as faces, objects, scenes, and people.[44]

Methods in cultural neuroscience vary across levels of analysis that include behavioral surveys in order to explore cultural values, practices, and beliefs. However, most studies in the cultural neuroscience field rely on qualitative measurement (or a combination of quantitative and qualitative methods).[45,46] Open-ended interviews and ethnography are another important kind of approach that cultural scientists use to study the behavior of individuals. Studies within cross-cultural neuropsychology have shown that racial/ethnic variation in performance on cognitive tasks are sometimes due to cultural factors, such as language abilities, acculturation (a term often used referring to Western culture or isolated villages), and level of formal education.[47]

Also on the subject of cultural neuroscience techniques and procedures, behavioral genetics studies rely on integrating genetic information with behavioral data. This line of investigation examines gene-behavior and gene-neural-behavior associations with a given culture or population. Recent advances in population genetics indicate significant variation in allele frequencies across the globe as a function of population structure due to multiple evolutionary factors, including natural selection, genetic drift, mutation in gene expression, and gene flow.[48]

The culture-gene coevolutionary construct asserts that adaptive behaviors are the product of at least two interacting yet complementary evolutionary processes, more specifically: cultural and genetic selection.[49,50] Cultural traits are adaptive and emerge due to environmental and ecological pressures that vary across geography under which genetic selection occurs. Therefore, a key goal in cultural neuroscience research is to understand how both cultural and genetic selection further shape neural and psychological architecture.[51] A prominent example of culture-gene coevolution is lactose tolerance. Regions within northern Europe with a higher prevalence of people who can digest milk also had a higher number of milk cattle, indicating a culture-gene coevolution between cattle milk protein genes and human lactase genes.[52]

One of the most important aspects of social interaction is the capacity to have knowledge and awareness of oneself and others. Cross-cultural and cultural psychology research has shown that two primary dimensions exist for how people define themselves and their relationship to others, a mechanism referred to as individualism and collectivism.Individualism refers to the self-defined as autonomous from others, whereas collectivism refers to the self as connected to or defined by others or the social situation.[53,54] According the aforementioned premise, people living in the United States and Japan who endorse individualistic cultural values are more likely to show increased neural response within Medial Prefrontal Cortex (MPFC) to general (e.g., "I am humble") compared to contextual self-statements (e.g., "When talking to my mother, I am humble"); by contrast, people who endorse collectivistic cultural values are more likely to show greater MPFC response to contextual compared to general self-statements.[55]

These findings indicate that cultural values, rather than nationality or race modulate neural response during self-processing. Furthermore, cultural influences on neural bases of the self may reflect not only different kinds of stable knowledge but also transient and dynamic representations of self and others. Recognizing the feelings or phenomenological experiences of others serves an adaptive function, allowing one to know about whether environmental or ecological pressures, such as danger or reward, are present as well as what kinds of behaviors may be adaptive in a given situation.

Also concerning the line of research on American and Japanese people, it has been assumed that culture affects not only the neural process associated with self-processing but also affective processing, such as perceiving emotional expressions in the environment. Researchers have proposed that people living in the United States and Japan show increased amygdala response to their own-culture compared to other-culture fear faces, even in the absence of behavioral differences in the ability to recognize emotion.[56] Consistent

with a culture-gene coevolutionary theory of emotion, it is likely that both cultural selection of individualism-collectivism and genetic selection produce heightened amygdala reactivity to affective cues in response to environmental or ecological pressures.

Socioeconomic Status (SES) is often measured as a combination of education, income, and occupation. It is commonly conceptualized as the social standing or class of an individual or group. When viewed from a social class perspective, privilege, power, and control are emphasized. Furthermore, an examination of SES as a gradient or continuous variable reveals inequities in access to and distribution of resources. SES is relevant to all realms of behavioral and social science, including research, practice, and education. Human brain development occurs within a socioeconomic context and childhood socioeconomic status (SES) influences neural development — particularly of the systems underlying language and executive functions. Research in humans and in animal models has implicated prenatal factors, parent–child interactions and cognitive stimulation in the home environment in the effects of SES on neural development. These findings provide a unique opportunity for understanding how environmental factors can lead to individual differences in brain development and toward improving the programmes and policies that are designed to alleviate SES-related disparities in mental health and academic achievement.

COGNITIVE NEUROSCIENCE OF HUMAN SOCIAL BEHAVIOUR: PRESENTING THE SOCIAL COGNITION CONCEPT AND THEORY OF MIND

While some aspects of cognition (such as language, for example) contribute substantially to the regulation of social behavior, the intuition has been that emotion plays a prominent role. Social brain science has indeed ruled out a restricted domain of cognition, and the majority of studies emphasize emotional and motivational factors. This intuition has a functional explanation: emotions can be thought of as states that coordinate homeostasis in a complex and dynamic environment regulating social behaviours. In fact, a class of emotions called moral emotions serves specifically in this capacity and probably guides altruistic helping and punishment.[57,58]

From a functional anatomy standpoint, certain structures have been shown to be important in processing emotions and therefore also imperative for social behavior. These structures include specific regions in higher-order sensory cortices, amygdala, the ventral striatum and orbitofrontal cortex, cortical regions such as left prefrontal, right parietal, and also anterior/posterior cingulate cortices. It is possible to relate these groups of regions to different groups of processes. The amygdala, striatum, and orbitofrontal cortex mediate an association of this perceptual representation with emotional response, cognitive processing, and behavioral motivation. Thus, higher cortical areas are involved in the construction of an internal model of the social environment, involving representation of others, their social relationships with oneself, and contexts of social groups.

According to these investigations, social visual signals include information about the face (expression and gaze direction) and about body posture and movement. Although prototypical facial expressions reliably signal basic emotions such as fear or happiness, human viewers are also surprisingly adept at making reliable judgments about social information from impoverished stimuli, such as weak changes in facial expression or a few seconds of body interactions.[59] Likewise, humans are probably exceedingly sensitive to the social signals themselves and also to the details of the context in which they occur.[60]

Social psychologists first showed our propensity to make social inferences from visual motion of abstract shapes in the 1940s[61,62] and recent studies indicate that specific movement cues might generate attributions of animacy, intentionality, and agency.[63,64] Briefly, visual motion stimuli elicit attributions of intentionality and animacy in infant and robustly elicit intentional, emotional, and personality attributions in adults, even when only static depictions of their trajectories are shown. Besides more anterior and dorsal temporal lobe regions (such as the superior temporal gyrus and sulcus), the fusiform gyrus, and other less well specified regions of the occipitotemporal cortex, and therefore be thought of as an interconnected system of brain areas that construct a spatially distributed perceptual representation of different aspects of faces.

It is important to mention that findings urge caution in the rigid assignment of cognitive processes to neural structures because it is possible that a given structure participates in several different processes, depending on the exact moment at which its activity is sampled and on the specifics of the given task and context. For instance, it is conceivable that the amygdala participates both in the initial, rapid evaluation of the emotional significance and in a latter assessment within a given context goal. Beyond this, the amygdala is involved in more complex social judgments. It shows differential habituation on activation to faces of people of other

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ethnicities,[65] and its activation to faces has been found to correlate with race stereotypes of which the viewer might be unaware.[66] However, other brain regions in the extrastriate visual cortex are also differentially activated as a function of race where amygdala lesions do not seem to impair race judgments.[67]

Higher-level manipulation of social information involves more than perception and primates, specifically humans, stand out in their ability to take into account what others are thinking. This ability requires the representation of what might be going on in other people's minds. Competences known as "theory of mind"[68] allow us to attribute mental states to other people.[69] Attributions of beliefs, specifically false beliefs, to other subjects have been particularly studied. These abilities may be unique to some primates and humans, and might comprise a set of more basic skills by which animacy, actions, goals, and intentions to stimuli are assigned.

Although there are indications that theory of mind capacities emerge during development, so far there is only preliminary evidence showing it to a neuroanatomical package. Rather than attempting to assign the whole set of theory of mind abilities to a particular neural structure or system, it might be more promising to explore the dependency of specific components of this ability on specific neural structures. During the late 1990s, researchers have found that damage to orbitofrontal cortex impaired the ability to detect gaffe (or *faux pas*), perhaps indicating that this brain region contributes to our understanding of other people, in part by engaging the emotions and feelings that accompany social interaction.[70] Supporting this idea, investigators discovered that appreciation of humor, social-norm transgression resulting in embarrassment, viewing of erotic stimuli, and elicitation of other moral emotions, all activate the MPFC.[71] Findings could be interpreted as the specialization of prefrontal cortices for aspects of social cognition or the reliance of social cognition on more general resources provided by this region of the brain.

More concisely, it seems that humans can figure out how others are feeling, intending, or planning to act. In part, this is related to our ability to put ourselves in others´ shoes (as a figure of speech). The fact is that this process could be entirely automatic and covert, but it seems likely that there are considerable differences in how skilled different people are at employing it. These differences would be expected to correlate with differences in empathy, emotional awareness, or their dysfunction (sociopathy and alexithymia, respectively).

In studies of relationships between specific brain structures and moral behavior, authors use some dilemmas that produce choice options and thus possible conflicts.[72] These conflicts can arise from short-term versus long-term goals or from those advantageous for others or for society as a whole. It is therefore closely related to altruistic behaviour, social cooperativity and cognitive processes that guide behavior in fields as diverse as politics and economics. In the "prisoner's dilemma", players can choose to give or keep money, which determines how much they are paid in turn. If only you keep the money and the other player give it away, you make the most money and the other player loses the most. If both of you give it away, you both make a moderate amount of money. Thus, there is a conflict between the selfish strategy of keeping money and the cooperative strategy. When playing multiple times, various kinds of patterns in social behavior can emerge.

An evident progress in understanding of the neural basis of social behaviour has occurred. Further progress crucially depends on advances in the development of new experimental methods of the current theories. As mentioned, although the future technology shows more clearly how neural events co-vary with stimuli and behaviour, how to interpret such data will remain a major theoretical challenge.[73] This raises the question of whether social cognition is reducible to emotional or motivational processing. For instance, when we find a face attractive or trustworthy, do we engage the same mechanisms as when our behaviour is reinforced by food? Or does the way in which social stimuli are processed differ fundamentally from reward and punishment for non-social stimuli? There are strong indications that the orbitofrontal cortex might be more specialized for social and moral judgments, whereas the amygdala might play a broader role in emotional processing that includes basic emotions.[74,75]

WHEN SOCIOCULTURAL NEUROSCIENCE FINDS ITS ROOTS: THE EPIGENETIC CONCEPTION AND ITS CONTRIBUTION TO NEUROPSYCHOLOGY

From a historical perspective, the word epigenetic was first used by William Harvey, known for the expression "ovo omnia" (all animals come from eggs), who described the complexity of how form gradually emerges during embryogenesis.[71] In this context, the English physician used the following words to explain his idea about this process: "*the addition of parts budding out from one another*." About 300 years later, the developmental biologist Conrad Waddington applied the epigenetic term to specify how genes interact with their surroundings to produce a phenotype (the effects a gene has on the

outside world that may influence its chances of being replicated). He illustrated the concept explaining how external events, some random, combine with inherited information coded in the genes to produce members of a species that, although recognizably related, have individual characteristics.[77]

Briefly, in a broad sense, epigenetics works as a link between genotype and phenotype (a phenomenon that changes the final outcome of a locus or chromosome without changing the underlying DNA - Deoxyribonucleic Acid, sequence), as once proposed. Thus, epigenetics may be defined as the study of any potentially stable and, ideally, heritable change in gene expression or cellular phenotype that occurs without changes in the Watson-Crick base-pairing of DNA. By the end of the 20th century, epigenetics has grown to become a widely recognized subdiscipline of biology and an interface with numerous other disciplines. Epigenetic today has taken on a very different meaning to Waddington's epigenetics, but the same can be said for many other terms in biological sciences. A valuable aspect of the term is that it has commonly been associated with the interactions of genes, their products, and the internal and external environment.

Related to the neurosciences, the term epigenesis (also called epigenetics) refers to the selection and stabilization of synaptic connections in the Central Nervous System (CNS) by activity, through which the animal learns to adapt to its environment.[78,79] Social and cultural evolution is associated with variable synaptic efficacy and the establishment of "outside brain" memories in the form of spoken, written, and pictorial material. Spoken language and, perhaps even more significantly, writing, are seminal innovations that distinguish humans from other primates; they drove the development of modern civilization and have probably also been central to the expansion of human mental capacities.

The aforementioned researcher first introduced the theory of the epigenesis of neuronal networks by "selective stabilization" of synapses to account for the interactions that take place between the brain and its physical, social, and cultural environment in the course of development. This theory, therefore, accounts for the variability in the brain's connectivity associated with the variability of the environment. Such an epigenetic variability of brain anatomy would be superimposed on that created by the variability of the genome. According to his idea, the same learning input may not establish the same connective patterns in different individuals, but will result in the same behavior.

The maintenance of gene expression behind the epigenetics mechanism allows genotypically identical cells to be phenotypically distinct (for instance, brain and liver cells). Taking the liver as an example, once an embryonic cell is triggered to differentiate into some singular cell type (i. e., a liver cell), that cell and its subsequent daughter cells might be required to undergo thousands of cell divisions over the lifetime of the organism. Heritable epigenetic mechanisms that allow the cell's identity to manifest as the subset of genomic DNA that it expresses, also allows any cell to "remember" that it is (once again), for instance a liver cell, over the course of cell division.

Epigenetic mechanisms such as DNA methylation and histone acetylation acquired as part of the differentiation process but self-perpetuating during DNA replication and cell division, mark the genome.[80] Moreover, changes in histone acetylation (developmentally-induced) are stably propagated from mother to daughter cells in mammals,[81] so some cell may perpetuate its specific pattern through these heritable epigenetic marks as an example of lasting memory at the cellular level. The formation of epigenetic memories is not limited to animal or mammalian cells. Plants are induced to flower by a process known as vernalization.[82] In this way, plant cells "remember" their exposure experience to the winter cold (between its first and second years of existence) and are then prepared for the plant to flower during the next spring. This process results from the activation mechanism that involves DNA methylation and acetylation of histones (basic proteins).

Neurons express a complement of proteins that are important for their function, but would adversely affect physiological function in other cell types, including proteins involved in excitability, transmitter release, and the maintenance of transmembrane potential.[83] Genes that are to be expressed in neurons, but not in any other cell types, carry the "Neuron-Restrictive Silencer Element" known as NRSE. This regulatory element, which is approximately 21-24 base pairs long, can completely silence a gene in non-neuronal cells.[84]

Concerning memory formation and taking into account the psychological point of view, memory describes the processes that are used for long-term storage of information (also referred to as knowledge). Studies have shown that the formation of long-term memories is a complex process that involves, among others, signaling pathways and the regulation of different genes.[85,86] An interesting study has shown that the same process leading to the formation of long-term behavioural memories also leads to epigenetic marking of the genome.[87] This data was the first to indicate that

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epigenetic tagging of the genome occurs during consolidation of long-term memories, and also suggests that there might be a histone code for memory formation, whereby specific types of memory are associated with specific patterns of histone modification.

In addition, the activity-dependent changes in synaptic strength (called synaptic plasticity) is widely believed to underlie the formation of long-term memories. Mechanisms responsible for the induction, expression, and maintenance of synaptic plasticity are similar to those involved in memory formation. Thus, induction of synaptic plasticity might involve epigenetic mechanisms like those involved in long-term memory. Several disorders of human cognition can be attributed to dysfunction in the mechanisms that underlie epigenetic marking of the genome. When considering these attributions, it is imperative to distinguish between a developmental need for epigenetic mechanisms to allow formation of a normal nervous system, versus an ongoing need for these mechanisms as part of cognitive processing *per se* in the adult.[88]

There are different instances in which epigenetic mechanisms meet clinical neuroscience as a causal basis for cognitive disorders. Notable among these are: Rubinstein-Taybi Syndrome (RTS), an autosomal dominant disease;[89] Rett Syndrome (RS), an X-linked disease; fragile X syndrome, one of the most common forms of mental retardation;[91] schizophrenia, in which evidence indicates deficiencies in the extracellular matrix protein reelin,[92] while finally and probably the most widespread form of dementia, Alzheimer's disease (AD). AD seems to be, at least in part, due to an increase in soluble β-amyloid peptides in the brain, suggesting that some of the pathology of AD is due to misregulation of histone acetylation.[93]

In conclusion, epigenetics is emerging as a new frontier to be transposed in the scientific area. One of the biggest challenges is elucidating the mechanisms involved in the silencing and activation of genes that predict some of the most common neuropsychiatric diseases. Upon review, the epigenetic field presents a large body of evidence on the relationship between biological markers and their modification by exposure to environmental factors and should be one of the main lines of research adopted in comparative research across different cultures in modern neuroscience.

CULTURALLY SENSITIVE NEUROPSYCHOLOGY ACROSS THE CONTINENTS AND REQUIREMENTS FOR VALIDATION

Levels of education have proven to have an important role in the cerebral development and organization of cognitive skills and consequently on performance on neuropsychological tests.[94-104] According to the cited authors and maintaining a Lurian perspective, it has been suggested that illiterate individuals solve cognitive problems functionally and specifically, and respond better to the perceptual and functional attributes of stimuli, whereas educated participants respond to abstract concepts and to logic relations between stimuli.

A challenge that presents itself entails dissociation between concepts. Although educational level has a significant influence on the nature of performance on traditional neuropsychological measures of verbal and nonverbal skills, it is often difficult to distinguish between education and culture. A prominent psychologist hasemphasized that the differences found in performance on tests between Anglo-Americans and Anglo-Hispanics are frequently attributed to cultural variables, without taking into account that a large proportion of these differences are simply the result of different social inclusion and educational levels.[105] The fact is that, culture includes not only the knowledge of skills to survive physically or socially, but also how to express emotions, appreciate music, or to experience pain.[106] Although it is recognized that culture is an important variable involved in the development and use of specific cognitive and behavioral skills, to date very few studies have analyzed how culture influences neuropsychological test performance.[107]

Among the few examples of cross-cultural studies in South America is an evaluation of Auca Indians from the Ecuadorian basin conducted by Anneliese Alma Pontius. Pontius administered a four-colored Kohs Block Design test and found deficits in block design, particularly related to representations and construction of certain spatial relations and graphic-representational skills.[108] The author also conducted another neuropsychological evaluation in members of a hunter-gatherer society from Indonesia. In this case, it was found that due to hunter-gatherer's survival dependence on prompt assessment of the salient shape of prey and attacker, their basic cognitive process (i.e., visual-spatial pattern matching, representation, and construction) differed from those of Western urban societies. Similarly, because time restrictions are meaningless in the Arauco culture, performance on the tests was extremely slow according to Western standards.[109]

In Colombia, a group of Arauco Indians was evaluated using a neuropsychological test battery.[110] Twenty participants were selected: 12 men and 8 women. The age range was between 8 and 30 and education level

between 0 and 6 years. The adults were monolingual (indigenous language) and illiterate; the minors were bilingual and educated. The battery with which they were assessed included copying a cube, copying and recalling the Rey-Osterrieth figure, the Spanish version of the Wechsler Intelligence Scale for Children-Revised block design, identification of overlapped figures, identification of multiple choice figures, ideomotor praxis, drawing a map, spatial memory, verbal fluency, modified Wisconsin Card Sorting Test, and a laterality questionnaire. The authors reported that on some of the tests, the performance of the indigenous group was almost perfect (identification of overlapped figures and ideomotor praxis skills), whereas on other tests was almost impossible (cubes, a map, Rey's figure, spatial memory and Wisconsin). They concluded that three variables affected the performance of participants: (a) educational level, for which a significant correlation was found with test performance; (b) cultural relevance, in which some tests were significant and important whereas others made no sense and were impossible to understand, and finally; (c) age, for which a significant association was found with test performance.

Additional cross-cultural research was conducted founding that Chinese students outperformed their Canadian peers on given tasks.Results showed that differences in performance are not related to formal education but are dependent on extracurricular, culture-specific factors. They suggested that the wide-spread extensive use of calculators in early education in the Western world might restrict the level of expertise achieved in working memory skills for arithmetic.[111]

Development of instruments appropriate for different cultural contexts represents a challenge for neuropsychologists and cognitive researchers. When reviewing records, researchers should be aware of the fact that some variables which seem equivalent at first sight hold different meanings across cultures.[112] For example, 10 years of formal education in Russia results in a high school diploma, whereas in the United States it takes 12 years to complete the program, and in Germany high school programs are based on 13 years of attendance and yet diplomas may be comparable. College degrees from some European countries are equivalent to a Master's degree in the United States. Likewise, during interviews, the researcher should consider the native culture of the individual, the value and significance of specific cultural concepts, model of knowledge, and model of communication.[113] Prior testing background, level of education, and acculturation also need to be taken into account.

When selecting assessment methods, researchers should address the variable that needs to be measured and then select the test that measures those variables; select measures that have been accurately translated according to cognitive rather than linguistic equivalence; whenever possible, use tests that have appropriate norms accompanied by specific instructions and protocols; select tests that reflect the language ability and culture of the patient, and if available, use ecologically validated tests of functionality.

In the same vein, authors recommended that when translating the tests to apply to different cultures, researchers should choose the items that are relatively simple and include words with roughly the same frequency as the original. Each test item must be reviewed for appropriate cultural content with regard to the intentions of the item.[114] They emphasized that while arithmetic and memory scales translate reasonably well, intelligence scales pose the greatest challenge in cross-cultural adaptation. Thus, the following criteria for test selection were suggested: short and easy to administer; adapted to the living conditions of the cultural group being tested, and sampling a wide range of cognitive abilities (i.e., language, memory, spatial, constructive, perceptual, praxis, and conceptual abilities). With regard to testing, preferably, native and well-trained members of other cultures should be consulted when carrying out cross-cultural analysis.[115] Furthermore, for language scales, including writing and reading, it is not always enough to translate accurately when applying the scales to another cultural group. It is more important to maintain the original intent (i.e., cognitive equivalence) of the item, than to word it exactly. Where the repetition of basic phonemes is necessary, items must be modified to include frequent sounds in a given language. One of the most important considerations in an assessment is to place the client in his or her own bio psychological context and not the psychologist's context.[116]

When developing tests to be used across cultures, the researcher has to know what is relevant and what is being measured in a particular neuropsychological domain, for example, while spelling is a significant task in English, it is not as relevant in Spanish, and nonexistent in Chinese. Overall, some types of equivalence ought to be considered in test development to control for cultural bias: (1) Functional Equivalence, in which the test scores have the same meaning in different cultural groups and measure the same psychological construct; (2) Conceptual Equivalence, in which groups have the same level of familiarity with the test items; (3) Linguistic Equivalence, in which the language used in

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the tests has equivalent meaning across cultural groups; (4) Psychometric Equivalence, the extent to which tests measure the same thing at the same level across cultural groups; (5) Testing Condition Equivalence, the idea that testing and the procedures are equally familiar and accessible across groups; (6) Contextual Equivalence, evidence that the cognitive ability being assessed is comparable across environments and; (7) Sampling Equivalence, in which subjects representing cultural groups are comparable.[117]

ETHICAL ISSUES IN CROSS-CULTURAL NEUROPSYCHOLOGY

Race is a classification system used to categorize humans into large and distinct populations or groups by anatomical, cultural, ethnic, genetic, geographical, historical, linguistic, religious, or social affiliation. First used to denote national affiliations, the term began to be used for physical traits in the 17th century. In the early 20th century the term was often used, in a taxonomic sense, to denote genetically differentiated human populations defined by phenotype. Since the second half of the 20th century, the associations of race with the ideologies and theories that grew out of the work of 19th-century anthropologists and physiologists have led to the use of the word race itself becoming problematic. Although still used in general contexts, it is now often replaced by other words which are less ambiguous and emotionally charged, such as populations, ethnic groups, or communities, depending on context.

Despite the difficulty in adequately conceptualizing the term, what we have gleaned from a global overview, whether in first world countries or developing countries is the fact that the population is fast becoming more heterogeneous and referrals for neuropsychological evaluation among ethnic minorities are growing commensurately,particularly among older adults.[118] Thus, this raises the following central question; should culture or race be considered in neuropsychological testing? In the ensuing paragraphs, an attempt will be made to justify why the answer to this question is yes, however cautiously.

Because of this increased diversity, recent efforts have focused on the examination of cross-cultural differences in neuropsychological test performance among both clinical and neurologically healthy adults. Studies, in general, have reliably demonstrated poorer performance on tasks of visual confrontation naming among ethnic minorities compared to "Whites".[119-121] Continuing this trend, other researchers have reported significantly lower performance in ethnic minorities compared to Whites on tasks of nonverbal abilities.[122-125] Regarding discrepancies, differences often persist despite statistically controlling or matching for highest level of educational attainment.[126,127]

Although not absolutely conclusive, the number of studies that have reported differences among ethnic groups leads to the obvious question of what factors account for the discrepancies in cognitive scores. If the overarching null hypothesis of these studies is that no true differences in neuropsychological functioning exist among ethnic groups, and assuming that neuropsychological evaluation assesses underlying brain functioning, these replicated findings would initially suggest that the null hypothesis should be rejected and there are true neurobiological differences between ethnic minorities and White Americans. Regardless of these differences, however, and central to the question of whether race or ethnicity should be considered in clinical evaluation, is the definition of race or ethnicity.

Despite all the neurobiological findings, researchers now agree that racial characterization itself is socially or politically determined and has insufficient basis in genetic or true biology.[128,129] Scientists, as a result, have begun to identify relevant factors that may help account for these discrepancies among ethnic groups in the field of neuropsychological assessment. What is beginning to emerge from this literature is that differences among groups do in fact exist, but they can be explained by a number of variables. These variables or factors include, among others, quality of education,[130] acculturation,[131-133] literacy,[134] test-wiseness,[135,136] and racial socialization.[137,138]

Therefore, following the line adopted here, another rhetorical question which arises is what ethical learning can be drawn from studies of neuropsychological test performance among ethnic groups? Despite findings, it would inaccurate to attribute score to race or ethnicity. Ethnicity and race do not cause variability in cognitive test performance but rather are markers for a number of contributory factors that do impact performance. For clinical neuropsychologists, a primary responsibility is to consider the potential influence of these factors on test performance when conducting simple evaluation or a broader neuropsychological investigation. The clinical team therefore must have some familiarity with a patient's specific cultural, educational, and linguistic background so that they can assess how these factors might be uniquely operative within the group and contribute to the individual presentation.

Adequate normative data maximize the diagnostic utility of neuropsychological assessment. Any neuro-

psychologist who compares a patient's test performance to a normative data set should question whether the norms used are appropriate for the patient interests. Criteria for this determination might include consideration of the time in history the norms were created and developed; whether an adequate number of subjects was included; and, most importantly, that the normative data are appropriately stratified in ways that best capture demographic factors that contribute to performance on a given measure. In recent years, race-specific normative data sets have been created.[139-144] The fact is that, in a relatively obvious but not always respected manner, the accuracy of diagnosis is best when the patient is demographically similar to those individuals included in the normative data.

Systematic examination of the race term in neuropsychology is considered to be a sensitive topic that requires a careful approach to social and political motivations. Race-based normative studies, in some circumstances, have been used to base irresponsible biological and genetic conclusions.[145-146] Proponents of the utilization of race-based norms need to explicitly highlight that those norms are not created as a claim of biological differences among groups; instead, race, like other demographic variables such as age or gender, is a strong correlate of other factors that impact performance but not an inherent cause of cognitive performance. Until race and ethnicity can be deconstructed into the component parts that account for between-group differences and then reconstructed, utilization of race-based norms nonetheless may represent a step toward fair assessment of ethnic minorities.[147]

Sociocultural expertise at the individual level is essential for the clinician who is working with cross-cultural populations. One central ethical issue involves the method by which tasks are developed in new languages from existing English-language measures, and another involves the evaluation of patients whose first language is different from that of the clinician. Guidelines have been established to aid development and translation of tests into different languages.[148-151] In terms of development and evaluation of cognitive tools in cross-cultural populations, researchers with competence in psychometric construction, as well as a deep appreciation and understanding of ethnicity-related variables that impact performance, are best poised to develop tests for specific cultural groups.

Educating future clinical neuropsychologists in cross-cultural issues involves incorporating multicultural theory and philosophy into existing courses as well as providing specific coursework on the topic. Indeed, since programs have begun emphasizing cultural diversity, there is a general consensus that this has improved clinical abilities specifically and produced more competent psychologists in general.[152] Studies also collected survey data about cross-cultural education on all accredited clinical training programs in the United States at the time, and compared the data to those obtained from a survey conducted a decade earlier. Results from these surveys suggest that clinicians in general were inadequately educated on cross-cultural psychology, although it is clear that cross-cultural issues are gradually being integrated into the education of future clinicians.[153]

Due to the importance of this formal education in cross-cultural psychology, neuropsychology and neuroscience have only become appreciated in recent years, and problems of inadequate cross-cultural training stem from the fact that clinical supervisors have not themselves been formally trained in this area.

CHALLENGES, PROMISES, AND ASPIRATIONS FOR THE NEAR FUTURE

One of the most important contributions of cultural neuroscience to science as a whole, and to public policy, is the capacity to enhance understanding of the etiology of population disparities in health. Population health disparities (a social reality clearly observed in underdeveloped countries) arise from cultural and genetic variation in psychological and neural processes that emerge due to environmental and ecological pressures.[154-156] For instance, Ashkenazi Jews are more likely to develop Tay-Sachs disease, whereas people from Northern Europe are more likely to develop cystic fibrosis.[157] In addition, prevalence of substance abuse, such as nicotine addiction, varies across racial and ethnic groups, due to, at least in part, to allelic frequency of the *CYP2A6* gene. Protective forms of the *CYP2A6* gene are very rare in Europeans and Africans but more prevalent in Japanese and Koreans.

Future cross-cultural, behavioral, and genetic research may be able to further demonstrate the extent to which the interaction of genetic and environmental factors in the production of intergroup relations varies as a function of cultural values, practices, and beliefs. Cultural selection may occur not only for traits, such as religiosity, but also for social attitudes, such as feelings toward people of different groups, which are typically acquired or transmitted through social interactions with others or with the environment.[158] Another curiosity is that social scientists recently discovered that the psychological ability to acquire negative or positive feelings toward other people varies as a function of genes,

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specifically the serotonin transporter polymorphism (*5-HTTLPR*).[159]

Studies in cultural neuroscience show that key environmental features, including cultural, geographic and socioeconomic factors, modulate genetic, neural, and behavioral mechanisms underlying mental health.[160,161] One of the main challenges is improving research capacity and ownership of theory and methods in cultural neuroscience. Due to the limitations in access to and maintenance of necessary laboratory settings and equipment within Low-to-Middle Income Countries (LMIC), researchers seeking to elucidate cultural and biological factors that contribute to health in the developing world remain constrained. For instance, the appropriateness of the kinds of theories or empirical paradigms developed in LMIC compared to High-Income Country (HIC) countries may vary; however without adequate resources to develop novel scientific knowledge, there will continue to exist a significant need for research that effectively addresses health problems within the developing world.

Collaborating together with students and researchers from both the developed and developing world in large multi and interdisciplinary research teams may provide an effective solution to expanding the breadth and sophistication of theory and evidence of cultural neuroscience research in the future.

CONCLUSION

This essay aimed to demonstrate that cultural and ethnical experiences are essential influences on behavior, yet detailed research explaining the role of these variables in neuropsychological testing as well as cognitive and functional aspects, is incipient. Continued empirical research in this area will provide clearer guidance to trainees, test publishers, researchers, and clinicians about neuropsychological evaluation of ethnically and linguistically different people. Promoting the scientific study of sociocultural neuroscience, including the development of interdisciplinary educational infrastructure and research capacity for studying human diversity across multiple levels of analysis, is key to closing gaps in population health disparities in the near and far future.[162]

Paradoxically, findings confirm that scientific approaches to culture are clearly shaped by culture at large, and have in the past depended on ideological and practical motivations. A critical, meaning reflexive, cultural neuroscience must acknowledge and examine the links between the cultural context in which neuroscience is practiced and the object of neuroscientific inquiry,.[163]

Science philosophers discuss objectifying an identity, stage of life, culture or behaviour in terms of the brain interacting with the experience (and likely, the neural correlates) of that which is classified. This statement largely corroborates this kind of interaction between classification of people and their ways of being the "looping effect of human kinds".[164] Here, this idea of looping by no means aims to pit a constructivist argument against a realist science. Rather, it holds that while neuroscience reveals real phenomena about behaviour and its instantiation in the brain, the cultural context of neuroscience interacts with scientific knowledge claims and influences the experience of the people to which they pertain.[165]

In conclusion, the following question may be raised: how can cultural neuroscience work within a framework that does not give primacy to either the brain or culture? One possible way is to blur the common contrast between "nature and culture" or the "brain and culture" and integrate an understanding of the neurocognitive mechanism with the social and cultural practices in which they are embedded. In other words, this essay ultimately sought to argue that if the brain is in constant interaction with its context, then such dichotomies are untenable in terms of future directions in neurosciences and clinical neuropsychology.[166]

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