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Review Article

Neuroplasticity, cultural evolution and cultural difference

Bruce E. Wexler

Abstract. *The most fundamental difference between the human brain and those of other mammals is the extent to which development of structure and function is influenced by sensory input. Evolutionary changes led to a marked increase in the number of neurons in the human brain and in the length of time after birth during which interconnections among neurons are easily shaped by environmental input. The importance of these changes is amplified by the fact that humans alone shape the environments that shape their brains. This cultural evolution creates adaptive population variability, cumulative intergenerational change, and cross-cultural differences in brain and mind. A homology is created between internal neurocognitive structures and features of the environment by the developing brain shaping itself to the environment, and then is maintained in adulthood by people acting on the environment to keep and make it consistent with established internal structures. Marked changes in the environment like bereavement, immigration and incorporation of one culture into another create disjunctions between internal and external structures that are of clinical and public health significance.*

Keywords: nature; nurture; endophenotypes; gene environment interaction

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INTRODUCTION The most fundamental difference between the human brain and those of other mammals is the extent to which development of structure and function is influenced by sensory input. Brain cells require sensory input to maintain vitality and functionality. This input forges connections among cells that create functioning cell ensembles and neural functional systems; "neurons that fire together wire together." Psychological processes and cognitive operations are properties of these ensembles and systems, not of individual cells. Evolutionary changes in two parameter settings in pre and post natal neurodevelopment make this brain-environment interaction particularly powerful in human beings. First is a marked increase in the number of neurons in the human brain, particularly in the cortex. Second is increased length of time after birth during which interconnections among neurons are easily shaped by environmental input. These changes make it possible for environmental input to create more elaborate and powerful neural functional structures in humans than in any other animal.

The importance of these changes is amplified by another critical process: humans alone shape and reshape the environments that shape their brains. This cultural evolution differs from Darwinian biological evolution in important ways. Firstly, it creates more rapid, incremental, and widespread population variability. Second, it uses different processes to store the information that influences the development of brain structure and function. In biological evolution, information is stored in the largely stable base sequence of DNA molecules. In cultural evolution, the information is stored in all aspect of cultural artifacts and practice. In biological evolution the information is stored in identical

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and complete form in many individuals. In cultural evolution, the information is distributed in different and incomplete form across many individuals and artifacts.

Processes of cultural evolution are relevant to psychiatry for several reasons. First, they constitute aspects of brain development and function that are unique to human beings. Like other brain processes, they must be subject to disease and therefore be the basis of diseases unique to human beings and without animal models. Moreover, the pathophysiological and behavioral elaboration in human beings of disease processes potentially shared with other animals can only be understood by reference to these processes. Secondly, cultural evolution leads to cross-cultural differences in brain and mind function, which in turn can potentially lead to cross-cultural differences in manifestations of a shared disease process. Third, the relationship of the individual to his or her particular environment defined by these processes, and their changes across the life span, are directly relevant to understanding two important clinical observations; the higher incidence of mental disorders among immigrants who relocate to a cultural environment different from the one that shaped their brains during development, and the increased incidence of depression and other disorders associated with bereavement.

In this paper I will review evidence demonstrating the processes and extent of environmental shaping of brain structure and function, and discuss the implications of changes in these processes across the lifespan. Children have limited ability to act on the environment but are profoundly affected by it. A homology is created between the external environment and internal structures because the brain shapes itself to the recurring features of the specific rearing environment in which it develops. By young adulthood, however, the powerful neuroplastic processes in the developing brain are replaced by the less powerful ones of adulthood, and now established internal structures are self maintaining. Individuals are now able to act on the general environment and do so largely to make the environment match the internal structures established by the mix of elements in their rearing environment. Since their rearing experiences and associated internal structures are different from those of their parents' generation, they act to change the general environment from one that matched the internal structures of their elders to one that matches their own internal structures. Competition among individuals and between communities to shape the environment ways most consistent with their own internal structures can be fierce. These actions on the environment by one generation create new rearing environments for the next. Each new generation thus differs from the one before, and when each gains the ability to alter the environment, it changes it to be consistent with its own internal structures and sensibilities. In the process, each generation creates a new rearing environment for the next, which leads to the development of a new generation with different internal structures and sensibilities which they in turn seek to impose on the environment.

A CONTEMPORARY NEURAL SYSTEMS VIEWS OF HUMAN BRAIN FUNCTION

There are 100 billion neurons in the human brain each directly connected to over 1,000 other neurons. Neuronal activity changes in multiple brain areas when people perform simple cognitive operations (e.g., D'Esposito, 2007). When tasks are repeated within minutes or hours, there are different patterns of task-related regional activation changes associated with the task (Poldrack *et al*, 1999; Kelly *et al*, 2006; Loubinoux *et al*, 2001). Brain activation patterns associated with the same task change as people get older indicating that the same tasks are done by different combinations of brain areas at different ages (e.g., Gaillard *et al*, 2000; Stebbins *et al*, 2002). Furthermore, if the same component cognitive operation is performed as part of different overall cognitive functions, the pattern of regional brain activation associated with that component operation is different (e.g., Friston *et al*, 1996; Wexler, 2004).

These observations of functional brain imaging are consistent with the notion of cerebral functional systems described by Luria (Luria, 1973; see also Vygotsky, 1978). Luria noted that localized injuries usually affected multiple cognitive operations and that individual cognitive operations were affected by injuries in multiple different areas of the brain. Luria concluded that while groups of cells in a specific anatomic location might collectively have some elementary tissue function, such functions do not correspond to mental functions like perception, memory or cognition. Mental operations are instead properties of functional systems that perform the same function through different means or components in different circumstances and at different times. The mental operations are properties of the system, not of specific anatomic locations. They emerge from combinations of different local units just as words emerge from combinations of letters (Wexler, 2004).

Sensory stimulation and neural viability and growt: neurons that fire together wire together

Information processing structures along pathways from peripheral sensory receptors to cortical processing centers atrophy without sensory input. Rod and cone photoreceptor cells in the eyes are morphologically abnormal (Liang *et al*, 1995); ganglion cells in the retina which carry excitation from photoreceptor cells are smaller and reduced in number (Rasch *et al*, 1961); and the number and size of cells are reduced in the lateral geniculate (e.g., Hubel, 1988; Hubel & Wiesel, 1970; Wiesel & Hubel, 1963; Kupfer & Palmer, 1964; Sherman *et al*, 1972; Sherman & Sanderson, 1972; Tigges & Tigges, 1993) and visual cortex (e.g., Aghajanian & Bloom, 1967; Cragg, 1970; Fifková, 1970; Kumar & Schliebs, 1992; 1993; Rakic *et al*, 1991; Robner *et al*, 1993). Studies of olfactory deprivation have yielded a similar picture (e.g., Benson *et al*, 1984; Najbauer & Leon, 1995; Skeen *et al*, 1986).

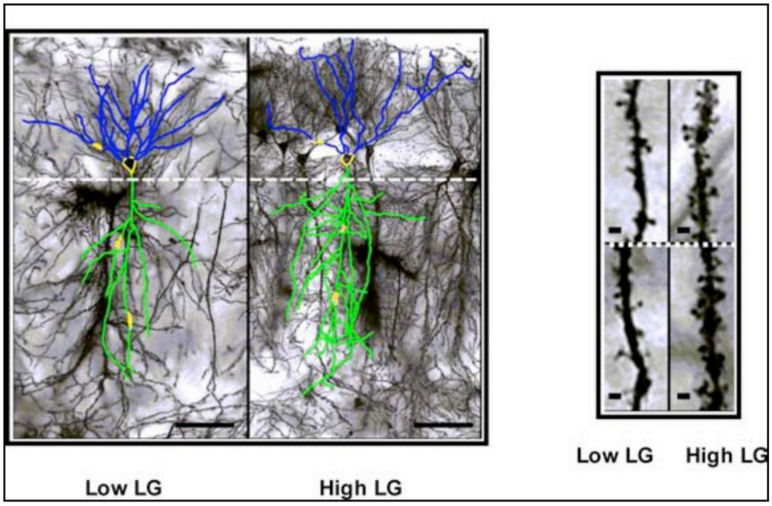
Neurons compete for connections with other neurons following the principle that "neurons that fire together wire together". In their Nobel prize winning work, Hubel and Wiesel showed that when a kitten's eye was sutured closed shortly after birth and reopened 10 weeks later, 85% or more of cells responded preferentially to the previously non-deprived eye, and few if any cells responded exclusively to the previously deprived eye (Hubel, 1988). Similarly, kittens raised in strobe light that prevents appreciation of movement have decreased numbers of motion sensitive cells (Cynader *et al*, 1973; Cynader & Chernenko, 1976). Kittens raised in dark except for exposure to stripes moving from left to right have a marked increase in the proportion of cells selectively responsive to left/right rather than right/left movement (Tretter *et al*, 1975). Kittens exposed to vertical black and white stripes for a few hours each day, but otherwise reared in darkness, have only cortical cells with vertical line orientation preferences (Blakemore & Cooper, 1970). Kittens raised wearing goggles that allowed them to see only vertical lines in one eye and horizontal lines in the other, have fewer than the normal number of cells that respond to oblique lines. Moreover, cells responsive to vertical lines are active only with stimulation of the eye that had been exposed to vertical lines, and cells responsive to horizontal lines are active only with stimulation of the eye that had been exposed to horizontal lines (Hirsch & Spinelli, 1970). In a dramatic demonstration of this sensory driven plasticity, the optic nerve in one-day-old ferrets was rerouted to provide visual rather than auditory input to what is normally the auditory cortex. The auditory cortex developed a functional organization of ocular dominance columns highly similar to the normal visual cortex rather than its usual tonotopic structure, and the ferrets saw with what would normally have been the auditory regions of the brain (Sharma *et al*, 2000).

These studies provide evidence that mammalian brains (and minds) develop concrete perceptual structures, capabilities, and sensitivities based on prominent features of the rearing environment, and then are more able and more likely to see those features in the world around them. Turning it around, mammals have limited ability to see even prominent features of a new environment if those features were absent from their rearing environment. Two additional observations made by Hubel and Wiesel are also of particular relevance to cultural evolution. When visual input to the deprived eye is restored, the altered pattern of cortical cell sensitivities persists despite the fact that both eyes are now receiving unobstructed visual input. As long as neurons from the previously non-deprived eye remain active, they are able to maintain their abnormally acquired hegemony. However, if the previously non-deprived eye is occluded while the animal is still young enough, the abnormal response pattern can be normalized or reversed in favor of the previously deprived eye (Hubel, 1988). The first point of interest is that socially generated activity can create unusual structures that alter the interaction with the environment so as to maintain themselves. In this case, when the eye was occluded, cortical structure changed so as to be unusually responsive to input from only one eye. When the occlusion was removed and input was available to both eyes, the brain still registered input almost exclusively from only one eye. The neural resources necessary to process input now available from the previously occluded eye had been appropriated by the active eye during the period of unilateral occlusion, and the active eye maintained the extra resources as long as it kept those resources actively engaged in processing input within the systems that had appropriated them. This situation could be reversed by occluding the previously open eye, demonstrating that the plastic potential remained, that the brain could be shaped or normalized by corrective intervention, but active intervention was necessary for the "normal pattern" to reassert itself even in a new or normal situation. The second conclusion of interest was that such active intervention to reverse the effects of the initial unilateral occlusion was only effective in young animals. After a certain stage in development there is a higher degree of stability in established neural structures, in part because neurochemical mechanisms that support neuroplasticity are less powerful in older individuals.

Social interactions: an important source of early environmental stimulation

The work of Harlow and Mears, and later of Meaney and colleagues, places neuroplasticity and the "fire-together wire-together" principle squarely in the domain of conspecific social stimulation. Infant monkeys were separated from their mothers and raised with access to both a wire mesh and a cloth surrogate mother. Half of the monkeys received milk via the wire mesh mother and half via the cloth mother. Both groups spent much more time on the cloth than the wire mesh mother and this preference became greater over time, the opposite of what would be expected from a classical conditioning model if the most important thing to the infants was getting milk. Harlow and Mears (1979, p. 108) concluded that 'the disparity [in favor of selecting the cloth mother independent of which mother provides milk] is so great as to suggest that the primary function of nursing as an affectional variable is that of ensuring frequent and intimate body contact of the infant with the mother.' Instead of the provision of milk being the end goal of mother infant interaction, it is a means of ensuring contact between the mother and the infant because this contact is essential for provision of sensory stimulation necessary for brain development, and for production of population variability through variability in that stimulation. Meaney and colleagues demonstrated that naturally occurring differences in stimulation of rat pups by their mothers have life long and specific effects on the brains and behavior of the offspring, and that these changes are mediated by changes in DNA structure (Weaver *et al*, 2004a; 2004b). Adult rats that have been licked more as pups have decreased behavioral and hormonal responses to stress, and greater spatial learning abilities – a capacity in which areas of the hippocampus play an important role (Weaver *et al*, 2004b). Examination of their brains found greater levels of two specific types of messenger RNA. One carries the information from the DNA to parts of the cells that synthesize the glucocorticoid receptors important in regulating stress responses. The other carries information necessary for building the NMDA receptors important in promoting neuroplasticity. Anatomic examination of the hippocampus revealed that offspring of high licking mothers had longer neurons with more of the branches and interconnections so important in brain function (**Figure 1**, Champagne *et al*, 2008). Examination of the DNA identified selective demethylation of genes that produce the glucocorticoid receptors in the hippocampus and frontal lobes that regulate the stress response. Such demethylation makes the genes more active. Adoption studies demonstrated that these changes in genes and behavior were due to the differences in maternal behavior and not to genes that high licking mothers passed on to their offspring (Weaver *et al*, 2004a; 2004b).

Figure 1



Apical (blue) and basal (green) dendritic branching in adult rats who received lower (left) or higher (right) amounts of licking and grooming as infants. Stained neurons are pyramidal cells from the hippocampus. The study found significantly more branching in the rats who had received more licking and grooming. This is also visible in the photographs of branching points along the axonal spine shown on the right. (from: Champagne *et al*, 2008)

Two more findings from these important studies are also of relevance to cultural evolution. First, there were some advantages to having been raised by low licking mothers; when given learning tests in high stress environments, adult rats raised by low licking mothers outperformed rats raised by high licking mothers. The adaptive value of the population variability induced by cultural evolution is thus evident. Second, some of the persistent neurochemical and behavioral effects of maternal care of female infants affect the way the infant functions as a mother herself when she becomes an adult. Females that had been separated from their mothers when they were infants, showed lower than normal gene expression in areas of the brain associated with maternal behaviors when they themselves became mothers (Fleming *et al*, 2002). They also licked and crouched over their pups less often than other mothers (Gonzalez *et al*, 2001), and their generally decreased ability to maintain attention and increased response to stress have been hypothesized to further compromise their maternal competence (Fleming *et al*, 2002). Such intergenerational effects are potentially self-propagating and even self-amplifying. Moreover, since litter size (Fleming *et al*, 2002; Jans & Woodside, 1987) and food availability (Lyons *et al*, 2002) can influence the amount of licking and other behavioral interactions between mother and infant, a variety of environmental factors can influence maternal behaviors and their impact, across generations, on a range of individual and group behaviors. All this depends on the post-natal sensitivity of the mammalian brain to sensory stimulation, and the proximity of mammalian infants and mothers ensured by nursing.

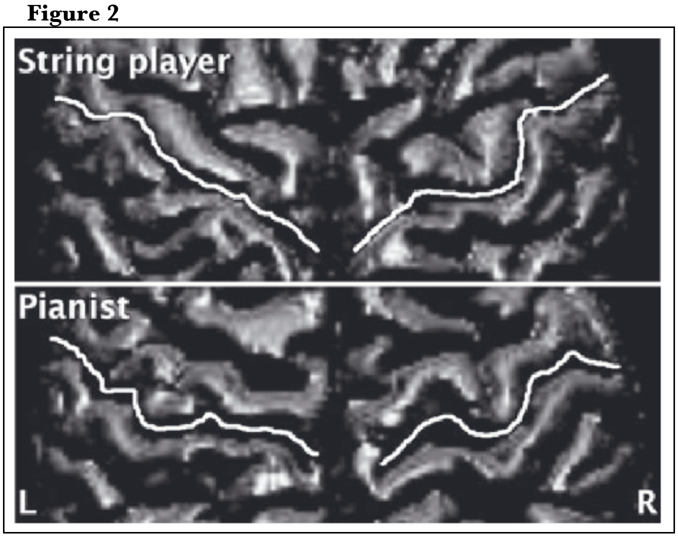
The human rearing environment

Human rearing behaviors include massive social components and influences from extended families, communities, and nation states. Influences beyond the family include schools, mass media, arts, laws and customs. Social and economic factors affect the states of mind, time, and energy of the parents, thus affecting their interactions with their offspring in a manner analogous to the effects of food supply on rat maternal behavior. Language - spoken and written - facilitates the influence of the human-made and extended social environment on the development of children, and the latter is itself clearly a product of cultural evolution and it seems increasingly probable that the former is in large part as well. Human infants can distinguish their mother's language from other languages at birth, based on stimulation received in utero (Mehler *et al*, 1988). They show a selective interest in looking at the human face within hours of birth, with the interest greatest for the full face as experienced in social interactions rather than for the face in profile. Within days they prefer their mother's face and voice to those of others (Carpenter, 1974; Fifer & Moon, 1994; Goren *et al*, 1975; MacFarlane, 1978; Mehler *et al*, 1988; Mills & Melhursh, 1974; Spitz & Wolf, 1946). Within the context, parents provide objects of play and structure interactions and activities. As Kenneth Kaye (1982a, p. 193) remarked, 'social interference in the object-directed activities of babies is such a commonplace occurrence that few authors have remarked on its absolute uniqueness to our own species.' Through nearly all aspects of the child's experiences, the characteristics of the adults shape the stimulation that shapes the child's growing brain. Input comes from wider and wider circles of direct interaction, beginning with primary care givers and growing to include extended family members and then members of the community and society more broadly. While some of the social input is actively shaped and provided by others, much is absorbed through constant imitation beginning within days of birth (Meltzoff & Moore, 1977; 1989). From infancy on, children learn how to do things simply by watching them done (Kaye, 1982b; Klinnet *et al*, 1986). Mirror neurons fire when people watch an act being done, and are then active when the individual performs the action previously observed (Iacoboni *et al*, 1999; Rizzolatti *et al*, 1996; Umiltà *et al*, 2001). Similarly, looking at someone else in pain activates the same regions of the brain as are active when the observer experiences pain him or herself (Gu & Han, 2007; Jackson *et al*, 2005; Singer *et al*, 2004). This environment-induced neural activation shapes brain development to be consistent with the largely human-made rearing environment.

Psychologists noted the role of the social environment in shaping mental development well before the neuroscience research added further support to their observations. Fenichel (p. 57) stated in 1926 that 'changes in the ego, in which characteristics which were previously perceived in an object are acquired by the perceiver of them, have long since been familiar to psychoanalysis.' Freud (1933, p. 47) described identification as 'the assimilation of one ego to another one, as a result of which the first ego behaves like the second in certain respects, imitates it and in a sense takes it up into itself.' Greenson (1954, pp. 160-161) stated that 'identification with an object means that … a transformation of the self has occurred whereby the self has become similar to the external object […] one can observe behavior, attitudes, feelings, posture, etc., which are now identical to those characteristics belonging to the external object', and that at early stages of development 'perception implies transformation of the self.' Reich (1954, p. 180) explained that 'the child simply imitates whatever attracts his attention momentarily in the object […] normally these passing identifications develop slowly into permanent ones, into real assimilation of the object's qualities.'

With new brain imaging methods it is now possible to see changes in brain structure and function resulting from motor activity or sensory input during childhood. For example, intensive practice of string instruments leads to selective increase in volume of the right somatosensory and motor areas associated with the rapid, fine motor movements of the fingers of the left hand that provide intricate and fast moving sequences of pressure to the strings. The changes in the brain are greater in adults who practiced more hours and began practicing at younger ages (Schlaug, 2001). **Figure 2** shows the "highly muscled" motor cortex in the right hemisphere of string players (the increase in volume is actually visible to the naked eye!) and bilaterally in piano players who practice with both hands (Bangert & Schlaug, 2006).

Figure 2

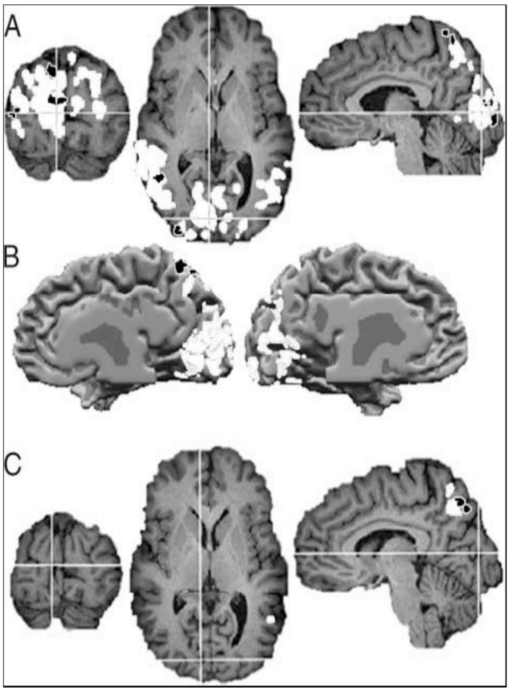


Expansion of sensori-motor cortex unilaterally (right side) in long time players of string instruments and bilaterally in long time piano players. These changes in brain structure result from many hours of music practice during childhood and are evident to the naked eye. Only the left sensori-motor cortex in string players is not affected by the practice since it controls the bowing (right) hand which makes many fewer and simpler movements than does the left hand. Thus, the left sensori-motor cortex in the string players serves as a reference that demonstrates the increase in size of the other sensori-motor cortexes. (From: Bangert & Schlaug, 2006).

Another set of studies looked at brain activations in areas of the brain usually responsive to visual and auditory stimulation in individuals who were blind or deaf at birth or shortly thereafter. Both these "experiments of nature" and the findings are directly analogous to the earlier cited work of Hubel and Wiesel in animals. In early blind subjects, the area of the brain that is normally the site of early visual processing is activated instead by auditory and tactile stimulation (**Figure 3**, Weaver & Stevens, 2007). It is also more active during language processing tasks than is the case in sighted people (Amedi *et al*, 2003). As in the animal studies, when the normal sensory input to an area was absent, other sensory input and cognitive operations moved into the territory. Moreover, among the blind individuals, memory performance was higher in the individuals who made more use of the "visual" areas during the memory task.

These neuroplastic processes provide a foundation for potentially extensive shaping of the particulars of brain functional organization by culturally specific features of the environment. Such effects have now been demonstrated in a large and expanding body of empirical research. Other papers in this issue provide examples of this research. Other examples can be found in the work of Richard Nisbett and Shinobu Kityama on cross cultural differences in cognition (e.g.,) and the work of Shihui Han and colleagues looking more directly at characteristics of brain function through ERP and fMRI (e.g.,).

Figure 3



Areas of the cortex that usually respond to visual sensory input are shown here to respond to auditory stimulation (white) and tactile stimulation (black) in individuals who were blind at birth or became so shortly after. (From: Weaver & Stevens, 2007).

NEUROPLASTICITY, CULTURAL EVOLUTION AND PSYCHIATRY

By young adulthood there is a fundamental change in the relationship between the individual and the environment. In the first decades of life a homology is established between the major features of the environment and major internal neurocognitive structures because the brain shapes itself to the environment. Once established, however, internal neurocognitive structures then affect the individual's interaction with the environment so as to maintain themselves, as demonstrated in the early work of Hubel and Wiesel (Hubel, 1998). Moreover, neurochemistry itself changes and the powerful processes of developmental neuroplasticity are replaced with the less powerful processes of adult learning. As a result, adults act to maintain or change the environment as circumstances require to make it match the less flexible internal neurocognitive structures. Nearly a century of psychological research has documented such activity: we affiliate with like minded people; have higher perceptual threshold for information with which we disagree or are unfamiliar; ignore, discredit and forget information that does not match experience-based internal structures; and like things simply because they are familiar (see Wexler, 2006, for detailed review). There are, however, times when environmental changes are too large for these processes to preserve a fit between established internal structures and the external environment.

One such time is bereavement when a very prominent feature of the external environment and internal structures has disappeared from the external world. It takes human beings a full year to painfully and laboriously restructure their internal worlds so that the missing person is no longer so pervasively present internally. During this year, the bereaved function less well in multiple domains and have higher medical morbidity and mortality. Fully 25% of people meet criteria for pathological grief syndrome, reporting symptom such as feeling that part of themselves has died, that they hear the dead person talking or feel the dead person touching them (Jacobs & Douglas, 1979). Psychiatrists maybe called upon to help people understand and move beyond such experiences.

Another situation in which external changes are so great that the significantly disrupt the internal/external homology despite then repertoire of usual repair processes is immigration. Here individuals find themselves in a milieu that differs in numerous ways from the one that shaped them. Immigrants usually attempt to create a microcopy of their original cultural environments in their new setting. They live in communities with compatriots, speak their mother tongues and cook their native foods in their homes, and furnish and decorate their homes in ways similar to how they would have in their countries of origin. A multitude of special challenges face the immigrant in the work place, many, for example, related to cultural variations in ways of doing and expressing things and cultural differences in negotiating hierarchical relationships. Many immigrants do not achieve the same levels of status and responsibility they would have had in their countries of origin, altering family dynamics. Family relationships are further strained by the greater ease with which children incorporate the customs of the new culture. As with bereavement, the disjunctions between internal and external occasioned by immigration are associated with psychiatric morbidity, but in this case it is multigenerational.

Finally mention should be made of contact and clashes between cultures. Because of the neurobiological importance of the homology between internal structures and the external environment, people do not like living inside someone else's symbol system, and since our images of our children are so richly represented within us we do not like our children turning into "foreigners." A United Nations report suggests that are 5,000 small, "indigenous" communities around the earth today that are threatened with likely loss of their culture, language, ecosystem, means of production and ways of life by larger expanding cultures (Davis, 1999). Children in these disappearing cultures face the difficult challenges of learning new ways of life, dealing with dislike and distrust by members of the dominant culture in which they will live, and negotiating these, as well as the more ordinary life challenges, without the usual support and guidance of parents and other older family members. Experience indicates that many will succumb to substance abuse problems, and many others will have only limited opportunities for self-development and personal satisfaction. More tragic still is the plight of the adults in these disappearing cultures. Their worlds are being pulled from under them and most are unable to learn and adjust to the ways of a new culture. Their neurobiological development is out of synchrony with the opportunities for skill and role development in the new culture. There are often limited matches in their new environments for the knowledge and skills they developed in their original environments. Happiness, peace and satisfaction in realizing childhood goals, contributing to and receiving the approval of a vital community to which they belong, and assuming the roles of the parents and other community elders they had admired are not available to them. We are in the midst of an unprecedented global cultural transformation that is cutting 100's of millions of human beings adrift from the essential sources of peace, happiness and security, and denying them the opportunities to live their adult lives as fully functioning human beings. The mental health consequences of these social/historical processes often escape attention. Attending to them from a psychiatric perspective might lead to social interventions that reduce psychological morbidity and new insights on cultural and individual variance in resiliency.

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