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The Neurobiological Toll of Early Human Deprivation

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Abstract

Children raised in institutions frequently suffer from a variety of behavioral, emotional, and neuropsychological sequelae, including deficits in attention, executive functions, disorders of attachment and in some cases a syndrome that mimics autism. The extent and severity of these disorders appears to be mediated, in part, by the age at which the child entered and, in some cases, left the institution. Here we review the neurobiological literature on early institutionalization that may account for the psychological and neurological sequelae discussed in other chapters in this volume.

There are millions of children throughout the world who have lost one or both parents to death, severe impairment, ill health, or abandonment. Care for such children varies from country to country. For example, when such children cannot be cared for by relatives, in some countries most are placed in foster care while in others they reside in institutions. Estimates of how many orphaned or abandoned children reside in institutions are difficult to obtain, but by some estimates the number is thought to be in the vicinity of 8,000,000 (Human Rights Watch, 1999).

The question we seek to address in this chapter concerns the neurobiological toll of early deprivation. Specifically, what are the neurobiological sequelae that may possibly account for the behavioral phenotype of the previously institutionalized child?

The Effects of Early Institutionalization on Brain Development

Before reviewing the literature on the neurobiological sequelae of early institutionalization, it is important to preface our remarks by providing some background to brain development in general.

As reviewed extensively by a number of authors (e.g., Fox, Levitt, & Nelson, 2010; Nelson & Jeste, 2008), brain development begins just a few weeks after conception, starting with the construction of the neural tube. This is followed by the generation of neurons and glia, with the former then beginning their migratory phase to build the cerebral cortex; as a rule, much of cell migration is done by the end of the second trimester of pregnancy. Once cells have migrated to their target destination they can differentiate, that is, they develop cell bodies and processes (axons and dendrites). Following this the connections between neurons can commence – a process referred to as synaptogenesis. The synapse, of course, is the *sine qua non* of brain function because it permits one neuron to communicate with another, and

eventually, entire circuits to be built in an organized fashion. Finally, some axons in the brain develop a coating that speeds information along the length of the axon – a process known as myelination.

Prenatally, these events are largely under genetic control (although experience can affect some of them – prenatal exposure to alcohol is but one example). However, postnatally the scenario changes. Now experience begins to “get under the skin.” This is a process generally referred to by some as neural plasticity. For example, although the generation of synapses – which are massively overproduced early in development – is largely under genetic control, the pruning of synapses – which occurs primarily after birth – is largely under experiential control. For example, the prefrontal cortex of the one-year-old child has many more synapses than the adult brain, but over the next one to two decades, these synapses will be pruned back to adult numbers, based largely on experience.

Not surprisingly, neural plasticity is a two-edged sword. In theory, if the child is exposed to “good” experiences, then the brain benefits; however, if the brain is exposed to “bad” experiences, including deprivation of the types and amount of stimulation the brain needs to organize its pathways, then the brain may suffer. Perhaps most importantly, it is often the timing of the experience (be it good or bad) that is crucial to developmental outcome. The concept of sensitive or critical period is often used to capture the issue of timing (Chapter 6). For example, for binocular vision to develop normally the child’s eyes must be able to converge on a distant object and the child must have access to a normal visual world. If this is not possible – for example, the child has strabismus – then the child’s vision must be corrected before the end of the sensitive period. In this example the sensitive period refers to the point in time when synapses in the visual cortex have been pruned back to adult numbers, most likely the end of the preschool period. If the child’s vision is not corrected by this time, then vision will never be normal because the brain has lost its plasticity (for elaboration on the concept of sensitive periods, see Fox et al., 2010).

Before turning our attention to how early deprivation impacts brain development, there is one additional related concept we wish to discuss. This has to do with what William Greenough refers to as experience-expectant and experience-dependent development (e.g., Greenough, Black, & Wallace, 1987). *Experience-expectant* development refers to the construction of neural circuits that are driven by experiences common to all members of the species and that occur during a sensitive period of development. For example, the development of normal pattern recognition abilities is predicated on the child having access to a normal visual world – one full of patterned light – that occurs during the first few years of life. If the child’s visual system is corrupted somehow (e.g., the child is born with a cataract) or if the visual world is corrupted (e.g., the child is brought up in a dark room), then the child’s vision will suffer. The beauty of experience-expectant development is the efficient use of genes. Thus, rather than having to code for all manner of functions in the brain, the brain instead is built in such a way that its further elaboration and refinement will be driven by experience – experience that throughout human evolution typically has been present and available to members of the species. In contrast, *experience-dependent* development is unique to the individual. Learning and memory are classic examples of this,

because they occur throughout the lifespan and vary from individual to individual. As a rule, there are no sensitive periods associated with experience-dependent development.

It is important to stress that the differences between experience-expectant and experience-dependent development are not always crystal clear. For example, one dilemma we face pertains to how one defines the normal or expectable environment. The developmental psychologist may view this through the lens of what elements of the environment may facilitate typical development, whereas the evolutionary biologist may view this through the lens of what optimizes reproductive fitness. A second consideration has to do with both expectant and dependent processes playing a role in the same domain of development. For example, developing language likely depends on experience-expectant processes (hearing language, being spoken to), while which language one develops depends on the language one is exposed to.

Similarly, it may well be that the formation of an attachment relationship reflects an experience-expectant process. Thus, because our species' young cannot take care of themselves, an assumption is made that there will be a caregiver to take care of the offspring, and once infants are of an age typically associated with mobility, they will organize their behavior around seeking and maintaining proximity to their caregiver. However, as we are well aware, there are enormous individual differences in quality of caregiving which is related to ways that infants pattern proximity seeking and maintenance. Thus, the way that attachment is organized (e.g., secure, avoidant, resistant, disorganized) may reflect an experience-dependent processes.

Why are these concepts important given our charge to describe the neurobiological toll of early deprivation? Because children who are raised in institutions may well be deprived of the kinds of experiences that are needed to optimize development. This may be particularly true for infants who spend the early part of their lives in institutions; it may not be true (or certainly, it may be less true) for children who spent the first years of their lives in families and were then placed in institutions. In this latter example, we assume that the child's brain was normally constructed; in the former example, the risk of abnormal brain development is considerable because the experiences the brain "expected" to receive may not have existed. Thus, the risk of circuits either not being formed to begin with or being abnormally formed is far greater in the case of children institutionalized early in life vs. children institutionalized later in life.

With these constructs in hand, let us now turn our attention to the literature on the effects of early institutionalization on brain development.

Malnutrition and Brain Growth

There is extensive literature documenting that institutional care is associated with significant delays in physical growth, including head circumference which, in infants, is associated with brain growth (Chapter 4). Deficiencies in the diet as well as infections, parasites, and stress can all interfere with absorption and use of nutrients and likely contribute to poor growth in institutionalized children. Although whether weight at adoption (as a marker for sub-nutrition) predicts post-adoption outcomes is discussed elsewhere (Chapter 4), it is

important to note that caloric restrictions are not the only nutrient issues relevant to brain development in institutionalized and post-institutionalized children. Micronutrients, such as iron, are also critical for normal brain development (Chapter 4). Recent evidence indicates that many (e.g. 25%) children adopted from institutions are iron deficient (ID) at adoption. Despite sufficient dietary iron in the months post-adoption, ID persists, and in those children who grow the most rapidly after adoption, ID may increase (Fuglestad et al., 2008). Furthermore, ID is not strongly correlated with weight at adoption. Thus, in considering factors threatening healthy brain development in institutionalized children, we should consider more than weight as an index of the nutrient environment of the institutionalized child's developing nervous system.

The relation between early institutional deprivation and brain growth stunting has been studied in detail in the English Romanian Adoptees Study (ERA; Sonuga-Barke et al., 2008; Sonuga-Barke, Schlotz, & Kreppner, 2010). Initial effects were dramatic with many of the Romanian adoptees measuring over three SDs below the developmental norms on head circumference (a measure closely associated with brain size) at their time of entry to the UK. These effects were strongest in those who experienced the longest periods of deprivation. By adolescence there was considerable catch-up, especially in those most affected. By age 15, head size was nearly normal in the group with less than six months deprivation; but in those experiencing longer periods of deprivation, head circumferences were still substantially below developmental norms.

The effects of sub-nutrition as indexed by weight at the time of entry into institutions (which typically occurred very soon after departure from the institutions) were investigated. Sub-nutrition was defined as being 1.5 or more SDs below the UK norms and therefore indexed deprivation in terms of caloric intake rather than more subtle differences in micronutrients. Many institutionalized children (although not all) fell below this figure. While sub-nutrition was associated with head circumference and IQ effects, other outcomes were not significantly affected (e.g., inattention/over activity, disinhibited attachment) when duration of deprivation was accounted for. Although weight at adoption can only be considered a rough proxy for sub-nutrition in the institution, these results suggest that psycho-social aspects of deprivation alter neuro-biology even when nutrition is adequate. One cannot rule out the possibility that even those children with deprivation-related difficulties whose growth was normal (i.e., they were not sub-nourished in the authors' terms) were subject to deficiencies in iron and other micronutrients. Although head circumference was associated with a range of deprivation-related problems, statistical analysis did not support the hypothesis that the pathway between deprivation and outcomes was strongly mediated by gross brain size effects.

The implication of this is that more subtle neuro-chemical and neuro-anatomical effects may mediate the effects of institutional deprivation on development (Mehta et al., 2009; Mehta et al., 2010). The effects are currently being investigated in more detail with data to age 15 now available.

Positron Emission Tomography (PET)

In one of the first studies to examine the effects of early institutionalization on brain development, Chugani and colleagues (2001) used Positron Emission Tomography (PET) to study 10 children who had been adopted from a Romanian institution. PET involves the injection of a radioactive isotope (e.g., oxygen, glucose) that decays over time (generally, minutes). When the isotope decays, it emits positrons that can be detected in a PET scanner. PET imaging essentially involves identifying the neural source of these positrons, and in so doing, provides the investigator with a reasonable estimate of which regions of the brain are making the most use of the isotope (for example, are some regions using too little glucose or oxygen?). The average age at study was eight years, and nearly all children had been placed in the institution before age 18 months and had lived in the institution an average of 38 months before being adopted. These children were compared to a group of healthy adults and a group of 10-year-old children with medically refractory epilepsy. The authors reported that the adoptees showed significantly reduced brain metabolism in select regions of the prefrontal cortex (e.g., orbitofrontal cortex) and the temporal lobe (e.g., amygdala). These, of course, are regions typically associated with higher cognitive functions, memory, and emotion. Neuropsychological testing revealed that the adopted children suffered from mild cognitive impairments, including impulsivity, attention, and social deficits.

Magnetic Resonance Imaging (MRI)

Magnetic Resonance Imaging (MRI) is a non-invasive imaging technique that does not expose participants to radiation. The MRI consists of one large electromagnet and several smaller electromagnets. When MRI is used to assess the structure of the brain, participants lie in the center of the electromagnetic coil so that their brain is in isocenter, the part of the magnet for which the magnetic field is most homogeneous. If tissue is placed in a strong magnetic field a small fraction of the protons that make up this tissue align themselves with the field (called B0). Next, smaller electromagnets near the center of the magnet are turned on locally changing the magnetic field. This causes a small fraction of the protons aligned with B0 to orient to this new magnetic field. When the local field is turned off, these protons decay back to the original direction of alignment (B0). The rate of decay differs for protons in different contexts. That is, in the context of fatty cells (e.g. myelin) the rate of decay is different than in the context of water (e.g. cerebral spinal fluid). A radio frequency coil (placed around the head) is used to detect this rate of decay and a picture is constructed of where specific cell types are. The result is a high-resolution picture of what the brain looks like.

Eluvathingal et al. (2006) conducted a follow up study of their original sample of children, this time examining white matter connectivity using MRI. The authors found that white matter connectivity was diminished in the uncinate fasciculus region of the brain in the early deprivation group compared with controls. The uncinate fasciculus provides a major pathway of communication between brain areas involved in higher cognitive and emotional function (e.g., amygdala and frontal lobe), leading the authors to conclude that connectivity between brain regions is negatively affected by early institutionalization. This, in turn, may

lead to deficits/delays in inhibitory control, emotion regulation, and other functions that are overseen by the connections between these brain areas.

In yet a third study by Chugani and colleagues (Govidan et al., 2010), a new, highly sensitive neuroimaging analysis technique, Tract Based Spatial Statistics (TBSS), was employed to evaluate further white matter changes in children with a history of early deprivation. Seventeen children with a history of institutional care since birth and subsequent adoption were compared to 15 typically developing non-adopted children. The adopted children were found to have reduced organization of portions of the bilateral uncinate and superior longitudinal fasciculi, with the magnitude of white matter disorganization significantly associated with duration of time spent in institutional care. These findings are consistent with the previous studies in identifying both functional and structural abnormalities in relevant brain pathways for children who have experienced early severe deprivation. Presumably such children would suffer from deficits/delays similar to those speculated by Eluvanthinal et al. (2006).

Collectively, work by Chugani and colleagues suggests that children who experienced early institutionalization suffer from metabolic and connectivity deficits in the areas of the brain believed to be involved in higher cognition, emotion, and emotion regulation. Two shortcomings of this work must be noted, however. First, the sample was small and not representative of children adopted out of Romanian institutions (e.g., most of the study children had spent several years in an institution) and thus, these findings may not easily generalize to other previously institutionalized children. Second, PET is an unusual imaging tool for use in children because it involves the injection of a radioactive isotope. As a result, it will be very difficult to replicate the original PET study.

A recent addition to our knowledge of the neurobiological sequelae of early institutionalization comes from the English Romanian Adoptees Study (ERAS; Rutter et al., 2007), in which a cohort of Romanian children institutionalized at birth and then adopted into homes in the UK has been studied. Mehta and colleagues (2009) used structural MRI to explore the influence of early institutional care on the hippocampus, amygdala, and corpus callosum, three key brain structures that previous research has identified as sensitive to early adverse experiences. Study participants were adolescents and included 14 Romanian adoptees, all with a history of severe early institutional deprivation, and 11 non-institutionalized, healthy controls. The authors found that the adoptees had significantly reduced total grey and white matter volumes compared to the control group. After correcting for brain volume, the adoptees had enlarged relative amygdala volumes compared to the control group, particularly in the right hemisphere. However, further analyses found that the left amygdala volume correlated significantly with the duration of institutional care, with longer stays in an institution correlated with a smaller left amygdala volume. One possibility is that this apparently contradictory finding is due to the nature of the control group who were neither adopted nor institutionally deprived. This opens up the possibility that differences between the groups (larger amygdala) are due to adoption effects – perhaps linked neural compensation on the part of the adopted children following the severe early deprivation, while the differences within the group associated with duration in the institution (smaller amygdala) are effects of deprivation. This small pilot study highlights the need for

additional research into the volumetric changes in brain structure associated with early deprivation, particularly in the amygdala.

Finally, Tottenham and colleagues (Tottenham et al., 2009) also used MRI to examine the effects of early institutional care on the volumes of whole brain and limbic structures. Imaging was done on 34 previously institutionalized children and 28 comparison, never-institutionalized children. Of note, 79% of the previously institutionalized children had been adopted from Asia (mostly China); hence this is one of the only imaging studies so far that has not relied solely on Russian/Eastern European children. Late adoption (classified as after 15 months) was associated with significantly larger adjusted amygdala volumes than early adoption or the control group.

Taken together, these two MRI studies provide additional evidence that early institutional care is associated with long-lasting effects on neuroanatomical development. These studies also underscore the importance of further work to clarify the association between amygdala volume and early deprivation, as well as to understand the functional significance of the enlarged amygdala. At this stage we can only speculate on the specifics of the causes and effects of these alterations in relation to early institutional care. In previous research using both pre-clinical and clinical models, the amygdala has been identified as a key brain structure sensitive to negative and/or stressful experience during childhood (Teicher et al., 2003; Sanchez et al., 1998; Suomi, 1997), such as those associated with neglect and physical/sexual abuse (e.g. Tupler & De Bellis, 2006; Teicher et al., 2004). The results here suggest that these effects may extend to adversity related to institutional care. Furthermore, work reviewed earlier in this chapter has focused on the period after three or four years. The data here suggest that effects are also seen following very early exposure. Indeed, the period before age three years is a phase of dramatic growth in the amygdala and related structures (e.g., hippocampus & corpus callosum; Hayakawa et al., 1989; Nishida et al., 2006; Pfluger et al., 1999).

The amygdala plays a role in the processing of emotionally salient information both in terms of the formation of emotional memories and the guiding behavior based on emotional/threat-related stimuli through the attentional modulation of other areas of the cortex (Gosselin, 2007; Spezio et al., 2006). While in general terms a dysfunction of the amygdala would be predicted to lead to deficits in the socio-emotional domain of functioning, it is currently impossible to specify these more precisely. For example, would we expect a blunted emotional response, sometimes associated with psychopathic traits, or a more pronounced response to threat as seen in the case of anxiety? Furthermore, it is unclear how alterations in amygdala-based emotional processing are linked to the disinhibited social approach so typical of children experiencing institutional deprivation (Chapter 3). Future studies also need to explore the direction of effects, specifically, whether changes in amygdala volume are the result of deficits in socio-cognitive and emotional processing or the reverse, that children with atypical amygdalae respond differently than those with typical amygdalae to being in an institution, which in turn impacts social-cognitive and emotional processing.

A recent study by Mehta et al. (2010) with the ERA sample highlights the potential role of another sub-cortical region – the ventral striatum – in the neuro-biological effects of early

deprivation. This region plays a key role in processing reward signals (Knutson et al., 2001), and functional alternations have been linked to a number of psychiatric disorders (Juckel et al., 2006; Scheres et al., 2007; Wrase et al., 2007). The authors used a task designed to measure the brain response to the anticipation of monetary reward so that they could examine the functional integrity of brain regions previously shown to be implicated in reward processing. Adolescents (N = 12) who had experienced early deprivation were compared with 11 controls. The results were very striking in showing that, in contrast to a non-adopted comparison group, the Romanian adoptees did not recruit the ventral striatum during reward anticipation despite comparable performance accuracy and latency on the task. This study provides the first evidence for reward-related brain dysfunction following early deprivation which may help explain some of the behavioral deficits found in early deprived children including ADHD type problems and depression (e.g., a child may develop difficulties in maintaining attention or act impulsively because they may fail to fail to associate either paying attention or being thoughtful and reflective with external rewards, such as good grades, positive attention, etc.)

Neurochemical Findings

To gain an understanding of the neurochemical sequelae of early institutionalization, Pollak and colleagues (in Wismer Fries et al., 2005) examined the effects of early institutionalization on oxytocin and vasopressin, two hormones associated with affiliative and positive social behavior. The previously institutionalized children showed lower overall levels of vasopressin than controls, along with lower levels of oxytocin after interacting with their caregiver compared with controls. Unfortunately, because these data were collected several years after adoption and because no current data on children's social behavior (such as attachment) were reported, it is difficult to draw a causal link between early experience per se and the observed changes in hormones.

Turning our attention now to cortisol, animal models of early deprivation reveal marked effects on stress-responsive neuroendocrine systems, particularly the hypothalamic-pituitary-adrenocortical (HPA) system. The end product of this system, cortisol (CORT) in humans, and its central releasing hormone, corticotrophin-releasing hormone, operate in many of the neural systems which in animal models and in the studies reviewed above are affected by early deprivation. In animal models, CRH and CORT have been shown to mediate some of the impact of early deprivation on the development of the hippocampus. CRH has also been shown to increase the permeability of the blood-brain-barrier, increasing the passage of inflammatory factors and mast cells into the brain, which challenge the integrity of developing white matter systems. CRH and CORT also interact with major transmitter systems (serotonin, dopamine, norepinephrine), affecting the development of their receptors and uptake of these transmitters. It is believed that these processes underlie the relation between early deprivation and later susceptibility to drug and alcohol self-administration in animal models.

While the invasiveness of procedures needed to examine these mechanisms precludes their direct study in children, there is evidence that institutionally-reared children show marked alterations in the normal functioning of the HPA system while they are still in institutional

care (Carlson & Earls, 1997), and children from extremely deprived institutional settings may exhibit elevated CORT levels years following adoption if they are removed from institutional care beyond 4–6 months of age (Gunnar, Bruce, & Grotevant, 2000). Consistent with research showing that elevated CRH and CORT affect growth hormone production and sensitivity of the liver to growth hormone, both resulting in reduced development of the long bones (i.e., height), there is also evidence that extremely short stature in institutionally-reared children and rapid catch-up growth post-adoption is associated with abnormalities in HPA functioning that persist years following removal from institutional care (Kertes et al., 2009).

Recently Pollak and colleagues (Fries, Shirtcliff, & Pollak, 2008) extended their earlier study of oxytocin to cortisol. A group of post-institutionalized children and never institutionalized children were studied at baseline (no psychosocial manipulation), when in contact with the mother and when in contact with an unfamiliar adult. The authors report that greater dysregulation of the HPA axis was observed when the child interacted with his/her mother vs. an unfamiliar adult, and that the more severe the early neglect, the greater the dysregulation. Length of institutionalization was unrelated to dysregulation; however, as all of the post-institutionalized children had been in institutional care for the first 7 to 8 months of life, we can only conclude that institutional care beyond that period was uncorrelated with dysregulation in this study.

Neuropsychological Evaluation

Neuropsychological testing provides an approach to help us identify which domains of cognitive development may be particularly affected by institutional neglect. Pollak and colleagues (Pollak et al., 2010) assessed memory, attention, and executive function using two well-validated test batteries, the Cambridge neuropsychological test automated battery (CANTAB, a computerized series of neuropsychological tests) and the NEPSY developmental neuropsychological assessment. Internationally-adopted children between the ages of 8 and 10 years with a history of prolonged institutionalization (adoption > 12 mos.; 75% institutional care prior to adoption) performed worse on tests of memory, visual attention, and learning than early adopted (< 8 mos.) or non-adopted control children who did not differ on any task. More time spent in an institution was associated with poorer performance on tests of inhibitory control, visual attention, and visual memory/learning (all of which are consistent with the neural circuitry identified by the authors of the PET and MRI data reviewed earlier). These findings clarify some of the specific neurodevelopmental sequelae of early deprivation and support the hypothesis that children who experience significant periods of early institutional care show impairment patterns in domains of functioning associated with later-developing neural structures such as the prefrontal cortex.

In the ERA study, the link between institutional deprivation and Theory of Mind (ToM; Strange stories; Happé, 1994) and Executive Function (EF; Stroop; Stroop, 1935) was explored (Colvert et al., 2008) in a group of 165 Romanian adoptees and a group of 52 domestic-UK adoptees. The Romanian adoptees displayed deficits on both measures, with the effects strongest among those who had experienced more than six months of institutional deprivation. Deficits in both domains (ToM and EF) were associated with quasi-autism,

disinhibited attachment, and inattention/over activity. Both ToM and EF mediated quasi-autism, although mediating effects of EF for inattention/over activity were less marked. However, neither ToM nor EF accounts fully for the overall pattern of deprivation-related difficulties. It is interesting to speculate about how these neuropsychological effects might be related to the alterations within brain structure and function.

Inhibitory-based executive function deficits such as those implicated in performance on the tasks reported in these studies are well established in the case of ADHD (Sonuga-Barke et al., 2008). Functional imaging studies suggest these are underpinned by altered patterns of activation in fronto-striatal brain circuits with reciprocated projections from the right dorso-lateral prefrontal cortex to the head of the caudate (Milham et al., 2005). These are also related to patterns of disrupted cortical growth and connectivity (e.g., Ashtari et al., 2005). Theory of mind, on the other hand, has been isolated to a network of brain regions thought to play a similar role in a number of mental functions that have as a common element the ability to project oneself into other situations or occasions. Other functions thought to be co-mediated by this network include remembering, prospection, and spatial navigation. A recent activation likelihood estimation (ALE) analysis suggested that the network activated during these processes shared much in common with the so called default mode network (Broyd et al., 2009). The key areas of interest in this widely distributed network are the medial prefrontal cortex, posterior cingulate/precuneus, and lateral parietal cortex. Frontostriatal and default mode networks constitute important targets for future imaging studies. Given alterations within the amygdala in those suffering institutional deprivation reported above, it also seems important to examine the extent to which limbic structures might play a role in dysfunction within these two networks and the processes they underpin.

The Bucharest Early Intervention Project (BEIP; see Zeanah et al., 2003, for elaboration) is a randomized clinical trial of foster care as an alternative to early institutionalization. Participants include institutionalized children, children with a history of institutionalization who were assigned to a foster care intervention, and community children in Bucharest, Romania. Memory and executive function were assessed for all participants at the age of eight years using the CANTAB. As in the Pollak study, children with a history of early institutional care (care as usual group; CAUG) performed worse on measures of both visual memory and executive functioning compared to their peers without a history of institutional care (Bos, Zeanah, & Nelson, 2009). In comparing children randomly assigned to the foster care intervention with their peers who had continued care in the institution, there were by and large no group differences on any of the memory or executive function outcomes. However, children in this study were placed into foster care at a relatively late age (mean age of placement, 23.6 months, youngest age 8 months) and thus the findings do not rule out the possibility of significant effects in these domains for children placed earlier into a foster care placement. When taken together with the results of the Pollak study and the ERAS study, this proposition may underscore the importance of family placement at a very young age rather than institutional care for abandoned children (Bos et al., 2009).

Electrophysiological Findings

The BEIP study of foster care described above also included two measures of brain activity, the EEG and the event-related potential (ERP). The EEG reflects the electrical activity of large populations of neurons distributed throughout the brain, whereas the ERP reflects the synchronous neuronal activity involved in performing a sensory, perceptual, motor, or cognitive task. ERPs are used most often to examine perceptual or cognitive functioning.

EEG findings

Marshall et al. (2004) reported that at baseline, the institutional Care As Usual Group (CAUG) had increased levels of low-frequency power and decreased levels of high-frequency power in the EEG compared with the Never-Institutionalized Group (NIG). In other words, the CAUG had less cortical brain activity than the control group. Notably, very similar findings were obtained for children adopted largely from institutions in Asia between the ages of 10 and 16 months and examined at 18 months relative to non-adopted children (Tarullo, Garvin, & Gunnar, under review). In the BEIP study at the 42 month follow up, Marshall et al. (2008) reported that the Foster Care Group (FCG) as a whole did not differ from the CAUG; however, upon closer inspection, the children placed in foster care before two years did show EEG activity that more closely resembled the NIG than the CAUG. Overall, institutionalization led to dramatic reductions in brain activity (as reflected in the EEG), whereas placement in foster care before two years of age led to a more normal pattern of EEG activity several years later. Finally, at 8 years the authors reported that, for high frequency alpha power, the FCG was comparable to the NIG, particularly for children placed in foster care before 24 months; those placed after 24 months more closely resembled the CAUG (Vanderwert et al., 2010).

ERP findings

Parker et al. (2005a, b) reported two studies involving cognitive testing of BEIP children while recording ERPs. In one, researchers presented children with images of different facial expressions; in the other, they alternated images of the caregiver's face and the face of a stranger. In both cases, the CAUG showed reduced amplitude in several ERP components compared with the NIG.

These same two tasks were performed again when the children were 42 months of age (Moulson et al., 2009). For both the facial expressions and the face recognition tasks, the FCG showed ERP amplitudes and latencies intermediate between the CAUG and the NIG. These results demonstrate that the ERP results previously observed in young children exposed to deprivation persist to at least 42 months. In addition, these findings suggest that placement in high-quality foster care may be somewhat effective in remediating this deficit in face processing. However, in contrast to the EEG data, there was no relation between the age at which children were placed into foster care and ERP outcomes.

In summary, brain development is impacted by the early institutionalization of young children in a variety of ways. First, it appears to reduce and/or alter metabolic, physiological, and neurochemical activity. Second, it leads to changes in the size of select

areas, such as the amygdala. Finally, white matter tracts in select areas are also compromised, which may underlie a connectivity problem. How these changes in the structure of the brain relate to changes in behavior is unclear, although the BEIP group has shown associations among reduced EEG activity, head circumference, and IQ. Moreover, the general pattern of findings obtained in the imaging studies collectively suggests that children who have experienced institutionalization in the early years are likely to develop deficits in emotion regulation, executive control, and possibly memory. Clearly, more research is needed to examine function/structure relations.

Why is Institutional Rearing Bad for the Brain?

Early institutionalization (when characterized by profound sensory, cognitive, linguistic, and psychosocial deprivation) has a negative impact on behavioral and brain development. The question we address in this final section is why?

As discussed earlier, Greenough and colleagues have argued that brain development reflects a combination of experience-expectant and experience-dependent mechanisms (Greenough et al., 1987). A short list of experience-expectant features of the environment might include access to a caregiver, adequate nutrition, sensory (e.g., visual, auditory, tactile) and cognitive stimulation, and linguistic input¹. This list is far from exhaustive, but by inference, it illustrates a key point: many forms of institutional life lack most elements of an “expectable” environment. As a result, the immature nervous system, which actively awaits and seeks out environmental input and does so during sensitive periods of development, is deprived of such input. This lack of input may lead to underspecification and miswiring of circuits (see Nelson et al., 2007; Nelson et al., 2009).

Furthermore, some domains of function are more experience-dependent than others, and domains vary in when experience is required to facilitate a typical developmental trajectory. With regards to data on brain development reviewed in this chapter, both cross-sectional and longitudinal studies suggest that removing children from institutional care in the first 6 months of life is the most likely to result in functioning comparable to family-reared children. Unfortunately, very few studies have been able to examine children placed in families this early; thus we need to be tentative about this conclusion. Alternatively, on some measures (e.g., amygdala volume, EEG power) there is evidence that placement in families before about two years of age is, over time, associated with outcomes comparable to (although still below that of) same-age family-reared children; while on other measures (e.g., executive functions), there is little evidence that given the first half year in institutional care, placement before age two is associated with functioning comparable to age-matched family-reared children, even after a number of years of non-institutional experience (see Chapter 6). Because such data have critical implications for policy, more research is clearly needed examining brain structure and functioning related to dosage, timing and duration of institutional care, quality of institutional care, and age at placement in more species typical rearing environments (e.g., a family).

¹It is very likely that the expectable environment consists of more specific experiences but such speculation is beyond the scope of this chapter.

Furthermore, because the long-term development of children with histories of early institutionalization will depend on a) the specific ages during which they were institutionalized, b) how long they were institutionalized, and c) the exact features of the environment (i.e., what children were deprived of), more attention needs to be paid to understanding how different types and timing of deprivation impact neurobehavioral development. Moreover, these three dimensions must be set against a backdrop of a child's genetic makeup and his or her prenatal experience (e.g., was the mother adequately nourished? Was the fetus exposed to alcohol or other teratogens?). Unfortunately, these last two dimensions are rarely known in most studies of post-institutionalized children because genetic information was not obtained and because no reports exist about prenatal development. However, the combination of these three factors—genetic makeup, prenatal experience, and postnatal experience—likely lead to developmental programming effects that may well set the stage for years to come (see Rutter et al., 2004, for elaboration).

Implications

There are many implications of this research. For example, many children living throughout the world (including Western Europe and North America) experience deprivation associated with neglectful parents. Although perhaps not quite as severe as the conditions in many institutions, a significant number of these children still experience profound neglect, and their developmental outcome may be quite similar to children raised in institutions. There is an urgent need for societies to respond to the needs of such children, and doing so may be informed by the results of this research.

A second implication of this work applies to the child protection systems in much of the world. We know the longer a child lives under adversity, the more that child is at risk and the more difficult it will be to redirect that child's development along a typical trajectory. Most child protection systems, however, pay little heed to this clear evidence, and fail to move children into permanent homes quickly or to remove them from abusive homes sooner (Chapters 7, 8).

Finally, the lessons learned from the BEIP, the ERAS, and work by Gunnar, Pollak, and colleagues should be noted by the many countries engaged in war or ravaged by disease. How the world will handle the thousands of children currently being orphaned in Africa, Afghanistan, and Iraq is unclear, although it is frequently the impulse of such countries (motivated by financial, cultural, or practical forces) to place such children in institutional settings rather than to develop high-quality foster care or adoption systems (Chapters 7, 8). Wasil Noor, deputy minister of social welfare in Afghanistan, estimates that of the 1.6 million orphaned Afghani children, more than 10,000 are living in institutional care. Approximately 85% of these children, he estimates, have surviving parents (often both). The government has recently launched a deinstitutionalization program, which reunites children with their families.²

²Personal communication with Aaron L. Greenberg, Coordinator, Better Care Network UNICEF/Child Protection Section, New York, May 15, 2007.

Overall, we have known for more than half a century that children reared in institutions are at great risk for atypical development. Most of this work has been descriptive in nature, with little study of the biological mechanisms responsible for deficiencies in development. Advances in neuroscience now make it possible to elucidate why, from a neurobiological perspective, children reared in institutions are at risk. Having laid the groundwork for a more mechanistic approach to understanding the effects of such early adversity on development, the next step will be to develop interventions targeted at the neural circuits that have been altered by institutional life, with the ultimate goal to use the science of early development to change the policies countries adopt to address their abandoned or neglected children. To do so, of course, will require that we improve our understanding of function-structure-circuit relations so that we know precisely *which* behaviors and circuits to target.

Future Directions

We offer a number of recommendations about future research.

First, on the basic science side, it is imperative that we continue to employ a variety of neuroimaging tools to examine brain structure and function among currently and previously institutionalized children. Second, whenever possible, information obtained on the brain should be complemented by genetic information, including both genetic variants (such as Single Nucleotide Polymorphisms [SNPS] and copy number variants [CNVs]) and epigenetics. Third, it is imperative that we dig deeper into the neuroendocrine and immune systems, if only to demonstrate the long-term health outcomes of early adverse experience. Fourth, we need to improve, as much as possible, our understanding of the timing and conditions experienced by the children in these neuroscience studies to better explicate issues of sensitive periods and protective/risk factors as they unfold over time. Finally, longitudinal studies employing state-of-the-art tools are needed to provide a developmental examination of the impact of early deprivation on neurobehavioral development.

In terms of translational science, although the number of children being adopted internationally has fallen off in recent years, institutionalized children continue to be adopted, increasingly within their native countries. It is critical that we make good use of our science to educate parents and the clinicians who ultimately see these children about the possible sequelae of early institutionalization. Second, we should use the latest knowledge of these sequelae to educate governments about what is in the best interest of children. Although efforts are being made to improve institutional life in some countries, we have known for over a half century that being raised in an institution carries risks and is no substitute for being raised in a family that is able to provide for the child's basic physical and social needs.. Governments need to be better informed about how to take care of their orphaned or abandoned children, and alternatives to institutional care must be put in place whenever possible.

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