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Annual Research Review: Parenting and children's brain development: the end of the beginning

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After questioning the practical significance of evidence that parenting influences brain development – while highlighting the scientific importance of such work for understanding *how* family experience shapes human development – this paper reviews evidence suggesting that brain structure and function are 'chiselled' by parenting. Although the generalisability of most findings is limited due to a disproportionate, but understandable focus on clinical samples (e.g., maltreated children with post-traumatic stress disorder (PTSD)) and causal inferences are difficult to draw because of the observational nature of most of the evidence, it is noteworthy that some work with community samples and very new experimental work (e.g., parent training) suggests that tentative conclusions regarding effects of parenting on the developing brain may well be substantiated in future research. Such efforts should focus on parenting in the normal range, experimental manipulations of parenting, differential susceptibility to parenting effects and pathway models linking parenting to brain development and, thereby, to behavioural development. Research on parenting and children's brain development may be regarded as at 'the end of the beginning'. **Keywords:** Brain, parenting, EEG, fMRI, MRI, amygdala, hippocampus, experience, emotion.

The effect of parenting on children's development has been the subject of empirical study for more than half a century. Over this period investigations have become ever more sophisticated. As appreciation developed for the importance of the temporal ordering of putative cause and effects in research designs, prospective longitudinal studies in which parenting measures preceded the assessments of child 'outcomes' came to take precedence over cross-sectional studies in which parenting 'predictors' and child outcome were measured at the same point in time, including such studies in which parenting was assessed retrospectively. Owing to evidence amassed principally by behaviour geneticists, students of parenting have also come to appreciate that even well-designed longitudinal studies do not afford strong – or at least indisputable – causal inferences due to the possibility that effects of parenting may be the result of shared genes that influence both parenting and child functioning (Plomin, DeFries, McClearn, & McGuffin, 2008). The fact, however, that genetically informed studies chronicle parenting effects, typically of the non-shared-environment variety, clearly indicates that well-documented links between parenting and child development are not all a function of genetic effects 'masquerading' as environmental ones ((Plomin et al., 2008). Even more compelling in this regard is experimental research that systematically manipulates parenting and documents its indisputably causal influence on child behaviour and development (e.g., van den Boom, 1994).

Unless one believes in magic, it is difficult to conclude on the basis of the evidence available that parenting does not affect the developing brain, in terms of either structure or function – or both. After all, how else would parenting or any experience for that matter influence a developing organism's behaviour, cognitions, emotions and even, in some instances, physiology and health? From this perspective, many behavioural scientists, including developmentalists, who are not brain scientists often wonder what all the fuss is about with regard to brain development. Although as scientists they very much appreciate the reason to investigate exactly *how* experiences, including parenting, affect brain development and, thereby, behaviour and well-being, it seems somewhat strange that the documentation of effects on the brain can pack more of a punch, especially of the journalistic or policy-making variety, than documenting effects on behavioural, cognitive, social and/or emotional functioning and physical health and well-being. After all, if parenting and other developmental experiences influenced the developing brain but such effects did not extend to functioning in the real world, would there be any reason for policymakers and practitioners to regard evidence of such as important or especially meaningful?

Two critical points follow from this rhetorical question. First, understanding of influences on the developing brain and brain development, including parenting, carries important implications for multiple aspects of human development and functioning. But, second, the chronicling of links between parenting and brain structure and function, including of

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course causal not just statistical-associational ones, is no more important, from the perspective of either basic or applied science, than documenting such links between parenting and children's development more generally. As it turns out, the study of parenting and brain development is not even yet in its infancy; it would be more appropriate to conclude that it is still in the embryonic stage, if not that which precedes conception.

Nevertheless, as we plan to show, there is ever-emerging evidence that experience shapes the developing brain in humans. In this review, we focus virtually exclusively on research that has endeavoured to measure parenting in some manner – but not characteristics of parents known to influence parenting, like maternal depression – and structural and/or functional aspects of the brain. As almost no work actually involves repeated brain measurements, little of the work truly qualifies as research on brain *development*; we nevertheless use such terminology interchangeably with that of 'the developing brain'. Of note, too, is that we do not consider hormones or genetics and their role in shaping parenting and/or brain development to any substantial degree.

As will become apparent, most of the research linking individual differences in parenting with individual differences in brain structure and function that is considered herein involves truly adverse experiences of the kind that no one would ever purposefully impose on fellow humans in order to evaluate causal influence. Some of this work actually involves parenting – in the form of maltreatment. And an even smaller portion involves parenting in the so-called 'normal range', measured as part of community studies rather than clinical ones in which children are selected for study because of their exposure to especially problematic environmental conditions. What should become clear is just how limited our knowledge remains today. Before proceeding to consider effects of experience – and particularly effects of parenting – on brain structure and function, a brief overview of brain development is provided to set the stage for what is to come thereafter.

Brain development overview

Here we offer an overview of mechanisms and milestones in brain development. We focus on aspects of the brain and brain functioning that figure importantly in the available research to be reviewed on parenting effects on the brain, including the cerebral cortex, the amygdala and hippocampus. For each we describe prenatal development of structures to provide a background as to the level of brain development at point of birth and how this is achieved. We then discuss what is known about postnatal brain development and the aspects which are influenced by experience. In most instances we focus on studies of humans; we do, however, include reference to work with other species, including non-human primates and rats, to illustrate points when data on humans are not readily available. For interested readers, a very comprehensive overview of brain development can be found in Stiles (2008).

Development of the cerebral cortex

The cerebral cortex is a flat sheet of cells about 2.5 cm thick covering the outer surface of the brain (Pakkenberg & Gundersen, 1997). It consists of six layers, each made up of particular types of cells and connections to and from other cells. It is estimated that the human adult neocortex contains approximately 20 billion neurons, each connected to about 1,000 other neurons, thereby creating a network with trillions of connections! It is generally believed that different regions of the cortex develop and differentiate at different rates, with respect to both anatomical and functional characteristics.

The key events in human cortical development include the production of brain cells, their migration from their birth place to their appropriate position in the cortex, and their differentiation. In humans cortical neurons are produced before birth during the sixth to 18th week after conception. At the peak of proliferation, it is estimated that 200,000 neurons are generated every minute! Once formed, neurons typically migrate to the correct position in the cortex by moving along the long fibres of cells called radial glia, which act like ropes extending from the inner to the outer surface of the brain (Rakic, 1988).

Once neurons find their way to their final position, they begin to differentiate and take on their mature characteristics. One aspect of differentiation is the growth and branching of dendrites, which increase in size and complexity with development. The dendrites of a neuron are like the antennae that pick up signals from many other neurons and, if the circumstances are right, pass the signal down their axon and on to other neurons. The pattern of branching of dendrites is important because it affects the amount and type of signals the neuron receives. Neurons also form axons, their primary outgoing pathways that must often extend long distances to reach their targets. Growth cones on the tip of axons help to direct axon movement by sensing guidance molecules, while cell adhesion molecules help to anchor the axons to the tissue substrate.

Many cortical neurons also become myelinated. Myelin, a fatty sheath that surrounds neurons and helps them transmit signals more quickly, begins to form around neurons in the third trimester. Although much of this process is complete by the end of the second postnatal year, it continues even into adulthood in some areas of cortex. Myelinated axons send signals at velocities that are about ~50–100 times faster than unmyelinated axons (Brinley, 1980, cited in Markham & Greenough, 2004).

The points of communication between neurons are called synapses, and these begin to form in the cor-

tex in the early weeks of gestation (Zecevic, 1998). The generation of synapses occurs at different times in different cortical areas. For example, the maximum density of synapses is reached at about four months in the visual cortex but not until about 24 months after birth in the prefrontal cortex (Huttenlocher, 1979, 1990; Huttenlocher & Dabholkar, 1997). Neurons use neurotransmitters to communicate across synapses. The acquisition of specific neurotransmitters and receptors by a neuron involves both processes that are determined intrinsically by the cell and those that are the result of the extracellular environment in which the neuron finds itself. The most common neurotransmitters in the cerebral cortex are the excitatory neurotransmitter glutamate, which is expressed in about half of cortical neurons, and the inhibitory neurotransmitter gamma-aminobutyric acid (GABBA) which is expressed in 25–40% of cortical neurons.

At the same time that the brain is growing and increasing in size and complexity, seemingly 'regressive' events are also occurring. One example is the elimination of synapses. During the process of synapse formation, the number of synapses increases above the level observed in adults and remains at this level for some time. Then, synapses are eliminated until the adult number is reached. For example, in certain parts of the visual cortex the density of synapses per neuron peaks at about 150% of the adult level at about age four months and then starts to decrease at the end of the first year of postnatal life to reach the adult level by about age 4 (Huttenlocher, 1990). The timing of this process is different for different areas of cortex. This loss of synapses, referred to as 'pruning', does not reduce the range of behaviours but may be related to stabilisation of important networks of neurons in the brain and the differential strengthening of circuits based on both experience and genetics. This process may provide a neural basis for 'experience-expectant learning', a type of environmental influence on brain development discussed in more detail below.

To summarise, the production of cortical cells and their migration to their appropriate position occur mainly prenatally (for discussion of neurogenesis in the adult mammalian brain see Song et al., 2005). Differentiation of brain cells, involving synpatogenesis and synapse elimination, dendritic branching, acquisition of neurotransmitters and myelination, begins prenatally but continues postnatally.

These early developmental changes associated with neuronal migration, synapse formation, pruning and myelination may contribute to the general changes in grey and white matter volumes that have been used as markers of brain development during childhood and adolescence. Generally, white matter volume increases over childhood into adulthood (Giedd et al., 1999; Hua et al., 2009; Wilke, Krägeloh-Mann, & Holland, 2007). There is limited evidence for regional differences in this process, though with advances in magnetic resonance imaging (MRI) measures of white matter integrity this picture may change. With respect to grey matter, most studies indicate that volumes initially increase in the first years of life. For example, grey matter increases by 149% over the first postnatal year (Knickmeyer et al., 2008), though after about eight years grey matter begins to decrease (Giedd et al., 1999; Giedd, 2004; Hua et al., 2009; Wilke et al., 2007). Measures of cortical thickness also show thinning with development (Sowell, Thompson, & Toga, 2004). Measures of cortical grey matter development do tend to vary by cortical region, generally displaying a pattern whereby primary sensory and motor areas develop earlier than frontal or superior temporal regions (Sowell et al., 2004; Gogtay et al., 2004).

Aspects of neuronal differentiation that occur postnatally may be influenced by postnatal experience, and be one of the mechanisms by which children's experience in the environment, including the parenting to which they are exposed, shapes brain development. This has been well documented in rats, with experiments showing that animals raised in enriched conditions have greater dendritic arborisation, increased dendritic spine density and more synapses per neuron in a number of brain areas than animals raised in impoverished environments (summarised in Markham & Greenough, 2004). The increase in dendrite length contributes to the increase in cortical thickness also observed in rats raised in enriched environments (Wallace, Kilman, Withers, & Greenough, 1992). These changes persist well beyond exposure to the enriched environment and do not reflect general changes in somatic development. Similar changes can also be observed in adult or older animals (Markham & Greenough, 2004).

There is also evidence that experience can influence white matter (Ullen, 2009). Studies in rats show that environmental experience has an influence on myelination in the corpus callosum, discussed more fully in the next subsection: post-weanling rats raised in more complex environments have greater myelination in the splenium (the part of the corpus callosum that contains visual cortical neurons; Juraska & Kopcik, 1988). Rhesus monkeys raised in complex environments also have larger corpus callosa (Sanchez et al., 1998) and in humans extensive piano practice beginning in childhood increases fractional anisotropy (a measure believed to correlate with degree of myelination) in cerebral white matter (Bengtsson et al., 2005). Rat studies suggest that these effects of experience on myelination may be limited to development, as they are not found in mature rats exposed to complex environments (Markham, Herting, Luszpak, Juraska, & Greenough, 2009). This is an important point because, if the same applies to humans, it could indicate that there is a critical period during which alterations in parenting are particularly effective in influencing this aspect of brain development.

Corpus callosum

The corpus callosum deserves special attention as it has been the focus of several studies comparing the brains of maltreated and non-maltreated children considered later. The corpus callosum is the most prominent white matter structure in the brain and contains about 200 million myelinated fibres, most of which connect corresponding areas of the left and right hemispheres. It is generally thought to function to integrate the activities of the two hemispheres. In line with the general trend for cortical white matter to increase over childhood, research indicates that all subregions of the corpus callosum increase in volume over childhood into young adulthood, though there may be some regional variation in the rate of growth (Hasan et al., 2009).

Subcortical development

Generally speaking, subcortical structures develop earlier than cortical structures. This section focuses on the subcortical structures relevant to the studies described in this paper, the amygdala and hippocampus.

Amygdala. The amygdala is a subcortical group of 13 interconnected nuclei located in the anterior portion of the medial temporal lobe. (For a more detailed review of amygdala development, see Payne & Bachevalier, 2009.) The lateral nucleus is believed to be particularly relevant to social processing, because anatomical studies of monkeys show that it receives input from the pulvinar, a subcortical pathway that is thought to mediate rapid orienting to socially relevant stimuli, and also because it receives, from the cortex, inputs of highly processed visual information regarding faces, facial expression, gaze direction and body movements. The lateral nucleus projects back to cortical areas via the basal nucleus, both to higher-order cortical areas as well as primary sensory ones. It is thus able to modulate various parts of the cortical network for social processing, including early sensory regions such as the fusiform gyrus.

The human amygdala is first observed by five weeks' gestation, with its nuclei becoming discernible by the early stages of the second trimester. Data regarding the development of the connections of the amygdala come primarily from studies of monkeys. This research suggests that most of amygdale–cortical connections are already established by the time of birth or soon afterwards (Amaral & Bennett, 2000), including reciprocal connections with the inferior temporal cortex (Webster, Ungerleider, & Bachevalier, 1991). However, these connections do undergo some change over the first postnatal year. In infant monkeys the inferior temporal inputs to the lateral nucleus of the amygdala are more widespread than in adults, and become more refined from one week to three months (Rodman, 1994; Webster et al., 1991). For example, at a time when temporal cortex anterior to area TE remains immature, the infant amygdala receives additional inputs from areas posterior to TE. A functional interpretation of this anatomical refinement is that the amygdala receives increasingly refined and detailed visual information over this period (Payne & Bachevalier, 2009).

Myelination in the human amygdala begins in the first months of life, with some aspects appearing mature by 10 months of age (Brody, Kinney, Kloman, & Gilles, 1987; Kinney, Brody, Kloman, & Gilles, 1988). Studies of monkeys indicate, however, that mature levels of myelination of amygdala output fibres are not reached until at least three years after birth (Machado & Bachevalier, 2003). Together, these findings suggest that the amygdala's influence over other brain areas influence increases during the first postnatal years. Neuroimaging studies also indicate a protracted period of grey matter development from 4 to 18 years. The volume of grey matter increases over this time, though some studies find such changes are restricted to the right amygdala and are observed only in girls (reviewed in Payne & Bachevalier, 2009; Ostby et al., 2009; Wilke et al., 2007). The amygdala is also connected to the orbitofrontal cortex, which plays an important role in social and emotional behaviour, though little is known about the development of this connection.

Hippocampus. The hippocampus is a layered structure located on the floor of the lateral ventricles that is believed to be important for spatial navigation, learning and memory. It consists of the CA1–4 regions of Ammons' horn which contain mainly pyramidal cells and the dentate gyrus. The perforant pathway from the entorhinal cortex provides the main input to the hippocampus. Formation of hippocampal neurons and their migration to their positions occurs earlier for the CA fields than the dentate gyrus (Seress, 2001). In the CA fields, cells are mainly formed by 15 weeks and completed by 20–24 weeks, with cell migration finishing prenatally. By contrast, in the granule cell layer of the dentate gyrus neuron formation continues as late as 34–36 weeks' gestation and cell migration continues until one year postnatally. Overall about 30% of granule layer neurons begin to proliferate and establish their connections only postnatally. The elements of the basic hippocampal circuit which connects dentate gyrus to CA3 fields, CA3 to CA1, and then CA1 providing an output route, are in place at birth but continue to show significant developments until at least 5 years of age (Seress, 2001).

MRI studies indicate that the hippocampus increases in size over the first years of life, showing, for example, a 13% increase from age 1 to 2 years (Knickmeyer et al., 2008). Research examining the development of the hippocampus from the preschool period into early adulthood reveals regional varia-

tions, with the posterior hippocampus subregions increasing in volume and the anterior subregions showing loss (Gogtay et al., 2006).

Animal research demonstrates that stress and the glucocorticoids secreted during stress can be neurotoxic to the hippocampus. However, this has not been empirically documented in human samples. One small study of 14 children showed that posttraumatic stress disorder symptoms and cortisol levels at baseline subsequently predicted hippocampal volume reduction over a 12–18-month period (Carrion, Weems, & Reiss, 2007). Other work also indicates that parenting can influence children's neuroendocrine response to stress (e.g., Kertes et al., 2009), providing a potential mechanism by which variations in parenting could impact the developing brain via influences on hormonal responses which in turn influence the brain.

Experience and the developing brain

Even though the brain is substantially shaped by genetic processes (Rakic, 1988), it remains the case that brain development occurs in interaction with the environment (Greenough, Black & Wallace, 1987; O'Leary, 1989). 'To understand neuropsychological development is to confront the fact that the brain is mutable, such that its structural organisation reflects the history of the organism' (Luu & Tucker, 1996, p. 297). The balance between genetic and environmental influences on brain cortical development changes over development and also differs across cortical regions (Lenroot et al., 2009). To be appreciated as well is that cortical development and organisation are no longer regarded as passive processes solely dependent on genetics and environmental input, but rather are self-organising, guided by self-regulatory mechanisms (Cicchetti, 2002).

Brain development has been described as a complex scaffolding of three types of neural processes (Black, Jones, Nelson, & Greenough, 1998). First are gene-driven processes, ones considered more or less impervious or insensitive to experience. Such processes protect the developing brain, guide neuron migration, and target many of their synaptic connections, while also determining differentiated functions (Rakic, 1988).

Second are experience-expectant processes, taking place when the brain is primed to receive particular classes of information from the environment – and thus 'expectant'. These correspond to critical or sensitive periods during which an overabundance of synapses characterises the brain (or brain structure), ones which are eventually reduced. The period of synapse overproduction is a genetically programmed occurrence that allows for the emergence of basic skills which are then used in interaction with the environment to guide the subsequent elimination of excess synapses (Huttenlocher, 1994). This process of pruning is itself regulated by competitive interactions between neuronal connections (Courchesne, Chisum, & Townsend, 1994), such that those neurons that remain inactive or are rarely activated are eliminated, whereas those that are actively stimulated by experience are strengthened and maintained (Edelman, 1987; Greenough et al., 1987). This brain malleability or plasticity is a function, then, of both timing and thus the basic developmental programme guiding the brain and the individual's encounters with the environment (i.e., experience). As a result, severe deprivation or other experiences that are in some sense abnormal and not species typical may adversely and enduringly affect brain structure, function and development (Black et al., 1998).

Experience-dependent synapse formation, the third process under consideration, is a function of the individually unique experience of the individual, typically taking place later in time than experience-expectant processes (Cicchetti, 2002). In consequence, each person's brain comes to reflect, at least in part, his or her unique experiential history. Moreover, 'experience-dependent synaptogenesis is localised to the brain regions involved in processing information arising from the event experienced by the individual' (Cicchetti, 2002, p. 1413). These processes are less subject to the stringent temporal constraints – and opportunities – than experience-expectant ones. Rather than involving, then, the overproduction and subsequent pruning of synapses, a process restricted to early development, this third brain development mechanism involves formation of new synapses and/or the modification of existing ones and can take place, to greater or lesser degree, across the life course. As a result, many sources of influence can be envisioned, ranging from everyday social experience, especially if repeatedly encountered, to planned interventions, such as psychotherapy or occupational training.

To be appreciated, of course, is that such influences can maintain, even enhance normal functioning but, at the same time, adversely affect it. 'Early stresses, either physiological or emotional, may condition young neural networks to produce cascading effects through later development, possibly constraining the child's flexibility to adapt to new challenging situations with new strategies rather than with old conceptual and behavioural prototypes … Accordingly, abnormal perturbations at one stage of brain development hinder the creation of some new structures and functions, distort the form of later-emerging ones, make possible the construction of ones that normally never become manifest, and/or limit the elaboration and usage of structures and functions that had appeared earlier' (Cicchetti, 2002, p. 1428). Clearly, then, there are many ways in which brain development can go awry. Not to be forgotten is that children vary in the extent to which they prove resilient to adversity, whether it takes the

form of poverty, community violence, parental abuse and neglect, or harsh discipline.

Indeed, recent theory and evidence suggests that individuals differ in their susceptibility to environmental influences (Belsky & Pluess, 2009a, 2009b), with some being more and some being less affected by conditions that both undermine well-being, broadly conceived, or enhance it (Belsky, 1997, 2000, 2005; Boyce & Ellis, 2005). In other words, whereas some individuals are substantially affected, 'for better *and* for worse', by, respectively, positive and negative experiences (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007), others are far less affected and may even be immune to the effects of the very same experiences. An ever-growing body of research indicates that phenotypic factors (e.g., temperament), endophenotypic factors (e.g., physiological reactivity) and genetic factors function as 'plasticity markers' and distinguish those who are more and less prone to environmental influence of perhaps many kinds (Belsky, Jonassaint et al., 2009; Belsky & Pluess, 2009b; Obradović & Boyce, 2009).

This new and emerging perspective on why and whether, not just how, early experiences, including parenting, may affect life-course development carries implications for the study of the effects of parenting on brain development. Most importantly, it implies that failure to distinguish those likely to be more and less influenced by parenting could result in researchers both over- and under-estimating effects on brain development, with effects on those most susceptible being under-estimated and effects on those least susceptible being over-estimated. As we will see, only a single study cited in the conclusion of this report has considered this possibility. Thus, as will be noted when this work is discussed, one important direction for future work will be to consider interactions between parenting and phenotypic, endophenotypic and/or genetic plasticity markers when it comes to evaluating effects of parenting on brain development.

Effects of parenting on the brain

The possibility that maltreatment (in its myriad varieties: emotional, physical, sexual, neglect) could affect brain development is suggested by research showing that maltreated children and adolescents with mood and anxiety symptoms (i.e., PTSD symptoms) show evidence of altered catecholomines and hypothalamic–pituitary–adrenal (HPA) axis activity (Carrion et al., 2007; De Bellis et al., 1999a, 1999b). And this is because elevated levels of catecholamines and cortisol may lead to adverse brain development through the mechanisms of accelerated loss (or metabolism) of neurons, delays in myelination, abnormalities in developmentally appropriate pruning, and/or the inhibition of neurogenesis (De Bellis et al., 2002). Certainly consistent with this argument is behavioural evidence that maltreated children show a variety of intellectual and academic impairments (e.g., Perez & Widom, 1994; Pianta & Egeland, 1994), as well as neuropsychological deficits, including impairments in executive functioning and attention (Beers & De Bellis, 2002) and everyday memory (Moradi, Doost, Taghavi, Yule, & Dalgleish, 1999). In what follows, we first consider research on maltreatment and how it may affect brain structure, before turning to evidence pertaining to brain processes. As all the research to be reviewed is non-experimental, causal inferences can be made only with extreme caution**.** In some cases the work to be reported is based on studies of children growing up in extremely deprived Romanian orphanages; in some respects such experience can be likened to extremely severe (parental) neglect. But because such deprivation involves much more than just limitations in caregiving, it is no doubt mistaken to equate it completely with – and thus expect exactly the same effects of – the kind of parental neglect typically encountered by child protection workers dealing with troubled families.

Brain structure

Evidence that maltreatment, sometimes when coupled with PTSD, appears to influence brain structure comes from a series of studies carried out in the laboratories of De Bellis and Teicher (see below). Some of this work focuses on corpus collosum, some on the hippocampus, some on the amygdala and the most recent on cortical grey matter regions, adopting a whole brain approach. Before saying more about this groundbreaking work, it must be appreciated that owing to the clinical settings in which most of this research has been conducted, much of the evidence to be presented is limited by reliance on clinical samples consisting of abused individuals with a specific form of psychopathology, often PTSD, as already noted. In consequence, much of the work considered in this section may overestimate effects of abuse by selecting the most adversely affected individuals, confounding abuse-related differences with disorder-related differences or mis-identifying brain abnormalities that were risk factors for developing a specific disorder when exposed to trauma rather than regions altered by exposure (Tomoda, Navalta, Polcari, Sadato, & Teicher, 2009a). The work can be regarded as important nevertheless, owing to the fact that it is based on prior early-experience research with animals. Indeed, the research considered first pertaining to the corpus collosum is informed by such work showing that stressors and experimenter handling affect this brain structure in rats, especially in males (Berrebi et al., 1988), as well as experiments with rhesus monkeys showing that males isolated from the typical social group show substantial reduction in the midsaggital area of the corpus collosum (Sanchez et al., 1998).

Cortical grey and white matter: regional analyses

As just mentioned, the corpus callosum is one region of white matter that has received particular attention in studies of the neural correlates of child maltreatment. Although the clinical consequences of reduced corpus callosum area are not fully understood, reduced size is associated with diminished communication between brain hemispheres, perhaps reflecting, if not causing, reduced integration (Teicher, Tomoda, & Andersen, 2006). Certainly consistent with this possibility is Schiffer, Teicher, and Papanicolaou's (1995) early work using auditory evoked potentials to study laterality and hemispheric integration of memory in adults with and without a history of childhood maltreatment, all of whom were well functioning at the time of assessment. When asked to actively recall, first, a neutral or work-related memory and then, with associated affect, a disturbing memory from childhood, both hemispheres appeared to be equally involved in normal individuals. In adults with childhood trauma, results were entirely different. A marked suppression of the evoked potential response over the left hemisphere (indicative of increased left hemisphere processing) occurred during recall of the neutral memory but, during recall of the disturbing childhood memory, there was a substantial shift in laterality. Evoked potential response was suppressed over the right hemisphere, indicating enhanced right hemisphere activation, thereby suggesting that early maltreatment is associated with increased hemispheric laterality and decreased hemispheric integration. Teicher et al. (2006) suggest that this may contribute to psychiatric illness – or reflect it.

In one of the first studies to examine potential effects of maltreatment on the corpus callosum, Teicher and associates (1997) examined the MRI records of 51 of 115 consecutive paediatric patients who had such records and who had normal intelligence; the mean age of the children was almost 13 years and maltreatment status was based on medical records. All anatomical measurements of the corpus callosum were obtained from the midsaggital image; regional volume of the corpus callosum was corrected for brain volume (to take into account age and gender). Physically abused males and neglected males each showed a roughly 25% reduction in the relative volume in region 4 of the corpus callosum which largely interconnects right and left motor cortex, with neglect also being associated with a similar reduction in region 3 which interconnects pre-motor regions. In view of the fact that abnormally large regions of the corpus callosum can also reflect pathology, it seems noteworthy that physically abused females had a nonsignficant 17% increase in region 4 volume and significant increases in regions 1 (89%) and 6 (51%); the latter connects superior temporal/posterior parietal regions. Neither psychological nor sexual abuse proved related to corpus collosum measurements and total brain size was also unrelated to any abuse condition.

Subsequent work by De Bellis and associates (1999b) comparing 44 maltreated children and adolescents suffering from PTSD with 61 matched controls on measurements obtained from an anatomical MRI brain scan, as well as assessments of psychiatric and neuropsychological functioning, reveals other apparent effects on brain structure and function. Matching was done on age, gender, handedness, height, weight, pubertal status and race; controls had no history of disorder or of trauma or maltreatment. The participants in this research were judged to be similar to most studies of maltreated children that find significantly increased rates of internalising and externalising disorders in abused children. Maltreated/PTSD children had significantly smaller intracranial and cerebral volumes and, after adjusting for socioeconomic status (SES), proportionately smaller intracranial and cerebral volumes, than comparison children. Moreover, total midsagittal area of the corpus callosum, particularly its middle and posterior regions (4, 5, 6 and 7), proved smaller than controls. Of note, too, is that the longer the duration of maltreatment, the smaller the intracranial volume and total corpus callosum, as well as its middle and posterior regions, clearly suggesting a dose–response relation. Important from a psychological perspective is that the smaller these structures, the greater PTSD cluster symptoms of intrusive thoughts, avoidance, hyperarousal and dissociation proved to be.

Effects of maltreatment/PTSD have also been reported for the lateral ventricles. Consistent with evidence that lateral ventricular enlargement is related to many psychiatric disorders (i.e., childhood- and adult-onset schizophrenia, Alzheimer's disease, alcoholism, bipolar disorder, major depression with psychosis), longer durations of abuse proved related to *increased* lateral ventricular enlargement (De Bellis et al., 1999a, 1999b). There was also evidence, consistent with animal studies cited earlier, that many of the chronicled adverse effects of maltreatment/PTSD were more pronounced in, or even restricted to, males. Such results accord with the view that males are more vulnerable to adversity.

In a second study of an independent sample of 28 maltreated children and adolescents with PTSD and 66 healthy, non-maltreated controls, De Bellis and associates (2002) replicated – and extended – many of the findings just highlighted. The maltreated/PTSD subsample had smaller intracranial, cerebral and prefrontal cortex, prefrontal white matter, and right temporal lobe volumes and areas of the corpus callosum and some of its subregions (2, 4, 5, 6 and 7) than controls. The total midsagittal area of the corpus callosum and middle and posterior regions remained smaller in the index group. As in the prior study, brain volumes correlated negatively with duration of abuse and males seemed more vulnera-

ble to adversity with regard to some brain measurements (e.g., lateral ventricular volume). Some of the findings emanating from the investigators' previous inquiry could not be replicated, however, particularly ones linking brain structure measurements with PTSD symptoms (e.g., negative associations between PTSD cluster symptoms with intracranial or cerebral volumes and positive associations with ventricular volumes).

In a third study linking maltreatment-related paediatric PTSD with brain structure, this one of 61 medically healthy children with chronic PTSD secondary to abuse and 122 healthy controls, all 4–17 years of age who had participated in the prior De Bellis et al. (1999b, 2002) investigations, De Bellis and Keshavan (2003) detected smaller midsagittal area of the corpus callosum subregion 7 (splenium) in the index group. Moreover, these same maltreated PTSD children did not manifest the normal age-related increases in the area of the total corpus callosum and its region 7 which was evident in the comparison sample. Most notably, males in particular seemed adversely affected, showing smaller cerebral volumes and corpus callosum regions 1 (rostrum) and 6 (isthmus) and greater lateral ventricular volume increases when compared to their healthy counterparts. These latter findings led the investigators to conclude that 'maltreated males with PTSD show more evidence of adverse brain development' than their female counterparts (De Bellis & Keshavan, 2003, p. 114).

Further evidence that maltreatment is associated with reduced corpus callosum area comes from Teicher and associates (2006). In preliminary work, Teicher et al. (1997) reported a substantial reduction in the midsaggital area of the corpus callosum in psychiatrically ill children with a history of abuse or neglect, with males again being more adversely affected than females. In later research on 51 children admitted for psychiatric evaluation (28 with abuse or neglect) and 115 healthy controls, Teicher and his collaborators (2004) found, after controlling for age and midsaggital area, that the corpus collosum area of the abused/neglected children was 17% smaller than controls and 11% smaller than fellow psychiatric patients who had not been mistreated; the two comparison samples did not differ from each other. Additional analyses revealed neglect to be the strongest experiential factor associated with (15–18%) reductions in corpus callosum regions 3, 4 5 and 7; sexual abuse was the strongest factor associated with reduced corpus collosum region in girls.

In light of the apparent effects of maltreatment, including both abuse and neglect (and sometimes PTSD, too), on diverse measurements of the corpus callosum, it would seem somewhat surprising that no such effects emerged when the focus of inquiry was on the kind of extreme neglect and deprivation experienced in the first years of life in Romanian orphanages. In this work by Mehta and associates (2009) on 14 adolescents adopted into English homes before age 3.5 years, magnetic resonance imaging revealed no overall or subregional differences on the midsagittal slice when comparisons were made to 11 agemates without such adverse early experience. Perhaps the failure to 'replicate' the abuse/neglect findings under consideration should have been expected given the earlier comment that there is risk associated with equating the kind of neglect which child protection workers typically encounter with what children experience in some orphanages.

Regional analyses do indicate that formerly institutionalised children show reduced volumes in specific regions of the cerebellum. In research by Bauer and associates (Bauer, Hanson, Pierson, Davidson, & Pollak, 2009), 31 9–11-year-olds raised in orphanages for 4–77 months after birth and adopted when they were between 10 and 92 months old were compared to similar-aged, never-institutionalised controls. Post-institutionalised children showed reductions in the left and right superior-lateral lobe of the cerebellum but not in six other cerebellar regions analysed. Of developmental significance is that these smaller volumes predicted poorer performance on tests of visual memory and planning.

Cortical grey volume: whole brain approach

As previous work indicates that children suffering extreme neglect and deprivation in their first years of life – by being raised in Romanian orphanages – have smaller head circumferences than controls, it seems unsurprising that such children, as adolescents, also show reduced grey and white matter volumes in a recent MRI study (Mehta et al., 2009; see also Eluvathingal et al., 2006). Of note, too, is that, in the most recently reported work being carried out in Teicher's lab, attention has shifted from investigating the size of particular brain regions to a whole brain approach to identify, using voxel-based morphometry, alterations in regional grey matter volume (GMV). Moreover, in order to overcome some of the inferential problems posed by studying clinical populations, the most recent investigations recruit individuals from the community regardless of their psychiatric status (or lack thereof). In one such study, Tomoda and associates (2009a) compared 23 unmedicated females with histories of sexual abuse and 14 healthy controls of equivalent age (range: 18–22 years) and socioeconomic status with no history of trauma. GMV was reduced by 12.6% and 18.1% in, respectively, right and left primary visual (V-1) and visual association cortices of abused individuals, results which also emerged when nine abused females who met criteria for an Axis 1 psychiatric disorder were excluded from analysis. Moreover, not only did longer exposure to sexual abuse before age 12 – a cut-off based on prior human and animal work on the development of the visual system – predict

greater reductions in grey matter, but GVM of left and right V-1 correlated positively and significantly with an overall index of visual memory. A marginal relation also emerged linking GMV in left V-1 with the capacity to distinguish targets from non-targets on the Go/No-Go-Stop Continuous Performance Task. These findings suggest that sexual abuse, by reducing grey matter in select areas of the brain, adversely affects select aspects of psychological functioning. To be appreciated, however, is that the investigators did not predict exactly which grey matter areas might be affected by sexual abuse and were thus left to speculate as to the basis of their findings. Perhaps, they concluded, the child's brain may seek to reduce abuse-induced stress by attenuating the development of sensory systems and pathways relaying recurrent aversive or traumatic experience.

In a second study using voxel-based morphometry to measure regional GVM, Tomoda and associates (2009b) turned their attention away from sexual abuse, indeed away from abuse per se, to harsh (but apparently not abusive) corporal punishment as reported by a community sample of 18–25-year-olds. When 23 individuals with exposure to a minimum of three years of such experience, involving at a minimum 12 episodes per year, 10 of which involved objects, were compared to 22 healthy controls with at most minimal such experience using high-resolution T1-weighted MRI, apparent effects of rearing history also emerged. Relative to the latter group, children with extensive histories of harsh corporal punishment manifest GMV reductions of almost 20% in the right medial frontal gyrus, almost 15% in the left medial frontal gyrus and a little more than 15% in the right anterior cingulated gyrus. These regions are part of the medial rostral prefrontal cortex. Work cited by the investigators indicates that this general area of the human brain plays a crucial role in social cognition, such as person perception, self-knowledge and mentalising, as well as functional organisation, including internal monitoring of one's actions. Moreover, the specific regions related to rearing experience in this study have been linked in other imaging research to addiction, suicidal behaviour, depression and dissociative disorders. GMV in these identified regions did not correlate with psychiatric symptoms, however, though they did relate positively and significantly with performance IQ. It remains possible, of course, that the null findings pertaining to psychiatric symptoms reflected limited statistical power more than anything else. Not to be forgotten in drawing conclusions from this small-sample work is the general scientific principle that absence of evidence (of the link to psychiatric symptoms) should not be regarded as evidence of absence (of such links).

White matter: whole brain approach

All the maltreatment work considered through this point chronicles putative effects of physical and sexual maltreatment, as well as neglect, on brain structure. Recent research by Choi and associates (Choi, Bumseok, Rohan, Polcari, & Teicher, 2009) extends the study of maltreatment effects to a central feature of emotional maltreatment, namely, verbal abuse. Diffusion tensor imaging was used to determine whether such rearing experience was associated with abnormalities in white matter tract integrity by comparing 16 healthy young adults reporting high levels of verbal abuse while growing (but not to other forms of maltreatment) and 16 healthy controls, after screening 1,271 healthy young adults for exposure to childhood adversity. The specific focus of this inquiry was based on research summarised above pertaining to the corpus callosum, the brain's most extensive white matter tract. Diffusion tensor imaging, which analyses the restricted diffusion of water molecules, affords a more detailed assessment of fibre tracts than conventional MRI, providing a powerful technique for investigating the role of neural connectivity in health and disease (Catani, 2006).

After controlling for parent education and income, group differences in fractional anisotropy for three white matter tract regions emerged favouring the comparison cases (i.e., greater fractional anisotropy in each area). Indeed, analysis indicated that a history of verbal abuse was strongly associated with reduced fractional anisotropy in the left superior temporal gyrus (which was itself positively related to verbal IQ and verbal comprehension), the cingulum bundle by the posterior tail of the left hippocampus (which was itself negatively correlated with ratings of depression, dissociation and limbic irritability), and the left body of the fornix (which was itself negatively correlated with ratings of somatisation and anxiety). Of note is that levels of verbal abuse reported in this particular study were not especially high, leading the authors to surmise that the high-verbal-abuse group would qualify as controls in other studies.

What remains unclear, according to Choi and associates (2009), is why parental verbal abuse was associated with fractional anisotropy, as it is unlikely that such treatment directly affects the number of axons because this is generally established early in childhood. One hypothesis advanced was that verbal abuse affects axon diameter, microtubular structure, and the proportion of myelinated and unmyelinated fibres that constitute a component of the pathway and that these pathways are established later in development (Keshavan et al., 2002) and appear susceptible to effects of experience during preadolescence and peripubertal periods (Juraska & Kopcik, 1988). In any event, as the authors conclude, results proved consistent with the hypothesis that 'the brain is chiseled in precise ways by exposure to adverse early experiences. Diminished fibre integrity, aberrant crossing patterns, alterations in axonal diameter, or extent of myelination along portions of these pathways' may

underlie some of the psychiatric and neurocognitive sequelae of child abuse (Choi et al., 2009, p. 233).

Work by Eluvathingal and associates (2006) examined connectivity of white matter pathways in the limbic systems at age 7–11 years in a group of Romanian children with normal intelligence who had been institutionalised and then adopted between the ages of 17 and 60 months, and in control children matched in age who were never institutionalised. Overall, previously institutionalised children showed lower connectivity than control children, with the difference reaching statistical significance for the uncinate fasciuculus which connects the limbic system with the frontal lobes. The authors suggest that the lowered connectivity could be caused by lower levels of myelination, fewer fibres, or disorganisation of the pathway.

In view of the correlational nature of virtually all of the human evidence reviewed through this point, a recent randomised controlled trial to evaluate the effects of training parents of preterm infants in reducing stressful experiences on brain development must be considered important (Milgrom et al., 2009). Evidence indicated that such training was associated with enhancement in DTI measures of maturation and connectivity of white matter at term equivalent age, but with no effects on grey or white matter volumes or short-term medical outcomes. Clearly, more work of this kind is what is required before strong causal inferences can be drawn regarding ways in which parenting shapes brain development.

Subcortical structures

Attention is now turned to two subcortical structures, the hippocampus and the amygdala, to further consider possible effects of parenting on brain structure.

Hippocampus. Work not focused on humans and/or parenting per se provides grounds for anticipating adverse effects of maltreatment on the hippocampus. Classical studies by Sapolsky and McEwen demonstrate that this brain structure is vulnerable to prolonged exposure to stress hormones (Sapolsky, Krey, & McEwen, 1985). In particular, stress and corticosteroids can alter pyramidal cell morphology markedly (Sapolsky et al., 1990), producing pyramidal cell death, while suppressing the production of new granule cells (Gould & Tanapat, 1999). Just as importantly, stressful variations in maternal care by rat dams affect neuroendocrine control mechanisms, including adrenocortical response (Levine, 1967; Sapolsky & Meaney, 1986), with similar findings reported in primates (Maestripieri, Lindell, Ayala, Gold, & Higley, 2005). Of note as well is that effects on hippocampal development have also been chronicled in rats (Andersen & Teicher, 2004).

As it turns out, early clinical studies document links between maltreatment and hippocampal volume. In a preliminary report of magnetic resonance imaging-based measurements of hippocampal volume in PSTD cases related to childhood physical and sexual abuse, a reduction in left hippocampal volume was documented (Bremner et al., 1997), a finding replicated by Stein and associates (1997) in a study of women victimised by childhood sexual abuse. Of note also is more recent work chronicling a 15–18% reduction in left hippocampal volume in women with a history of pre-pubertal physical and/or sexual abuse and depression relative to healthy control or depressed women lacking histories of maltreatment (Vythilingam et al., 2002). Rao and associates (2010b) recently reported somewhat related findings, examining the effect of early adversity, defined in part by (child and/or parent report of) degree of physical neglect, emotional abuse/assault, physical abuse/assault and sexual abuse/assault to which adolescents had been exposed before age 11. After controlling for chronic stress during adolescence, greater early adversity predicted smaller left hippocampal volumes in teenagers with no personal history of depression.

The aforementioned work by De Bellis and associates (1999a, 1999b, 2002), however, failed to replicate these hippocampal results, with the same being true of Carrion et al. (2001). Teicher et al. (2006) observe that numerous hypotheses could be advanced to account for why exposure to childhood abuse seems to be linked to reduced hippocampal volume *in adulthood*, but normal hippocampal volume in childhood. One possibility that received support in research on rats suggested that the normal pruning of synapses may lead to effects not proving detectable until later in life (Andersen & Teicher, 2004, 2009). Timing of maltreatment may be another factor that helps to explain the (seemingly inconsistent) findings at hand.

Indeed, when Andersen and associates (2008) examined volumetric MRI scans from 26 women with repeated episodes of childhood sexual abuse and 17 healthy female comparisons, all of whom were 18–22 years of age, age of victimisation proved central to illuminating which region of the brain was affected in this preliminary study. Hippocampal volume was most reduced when childhood sexual abuse occurred at 3–5 years of age, but also at 11–13, periods of time associated with the overproduction phases of human hippocampal grey matter (Gogtay et al., 2006). Conceivably, then, at least if studies of the rat are to serve as a guide, early stress prevents the normal peripubertal overproduction of synapses in select regions of the hippocampus (CA1, CA3), but does not prevent pruning; and this leads to an enduring deficit in synaptic density by late adolescence/early adulthood (Andersen & Teicher, 2004).

The ages associated with hippocampal reductions certainly suggests that brain regions have unique windows of vulnerability to the effects of traumatic stress. Indeed, the notion of early vulnerability of the

hippocampus, even if delayed in manifestation, is consistent with morphometric measures that show that the hippocampus has obtained 85% adult volume by 4 years of age (Giedd et al., 1996). The idea that the period of 3–5 years represents a time when the hippocampus is especially influenced by experience is echoed in a recent study examining the influence of variation of early parental care and environmental stimulation on hippocampal volume in adolescence in families with no evidence of abuse or neglect (Rao et al., 2010a). This work examined a group of 49 children participating in a longitudinal study in which the Home Observation for Measurement of the Environment (HOME) scale was administered at 4 and 8 years of age and hippocampal volumes assessed at 14 years of age. Parental nurturance, but not environmental stimulation, at 4 years of age were related to later hippocampal size. By contrast, neither HOME measurement at 8 years related to later hippocampal measures. Somewhat counterintuitive was the finding that *more* parental nurturance at age 4 was related to *smaller* hippocampal volumes in adolescence. As noted by the authors, this negative association between parenting and hippocampal size during childhood could be regarded as consistent with results from studies of paediatric PTSD, as these tend to show no difference in, or sometimes larger, hippocampi in children with PTSD compared to controls.

Further evidence of the influence of early rearing on hippocampal volume comes from the work of Buss and associates (2007). Low birth weight significantly predicted smaller hippocampal volume in adulthood, but only in females retrospectively reporting poor maternal care. These findings were seen to suggest that good maternal care buffers the adverse neurodevelopmental consequences of prenatal risk, thereby providing evidence of a positive effect of maternal care on brain development, at least in the case of children otherwise at risk (of smaller hippocampal volume).

Amygdala. Perhaps surprising and of interest is that many studies have failed to document relations between maltreatment and amygdala volume (Andersen et al., 2008; Bremner et al., 1997; De Bellis et al., 1999b, 2002; Stein et al., 1997). Research with children from Romanian orphanages adopted early in life into English homes, however, did reveal enlarged amygdala volumes at adolescence, particularly in the right hemisphere, relative to continuously family-reared controls, potentially underpinning disrupted affective processing (Mehta et al., 2009). Especially interesting was that left amygdala volume proved to be strongly associated with time spent in institutions, such that the longer the stay – and thus older age at time of adoption – the smaller the volume. These findings, relative to the null ones emanating from studies cited above, once again caution against equating the kind of neglect and deprivation experienced in institutions with that which social workers encounter in troubled families.

Another recent study, this one of mothering behaviour in the normal range, also discerned an apparent effect of parenting on amygdala volumes (Whittle et al., 2009). Adolescent boys whose mothers reacted with punishing responses to their offspring's positive affect during pleasant event-planning interactions, but not during conflictual problem-solving interactions, showed larger right amygdala volumes. Just as importantly, larger amygdala volumes predicted, in turn, adolescents' aggressive behaviour when interacting with their mothers in a problem-solving task (Whittle et al., 2008). Evidence like this clearly suggests how parenting comes to predict – and apparently influence – behavioural development (i.e., parental punishment → larger amygdale volumes → child aggression). Moreover, it underscores the need extend studies of parenting and brain development by including measurements of real-world performance.

Interim conclusion

Clearly there is repeated indication that, as expected, exposure to maltreatment, whether it takes the form of physical, sexual or emotional abuse, or the kind of extreme neglect and deprivation demarcated by experience in Romanian orphanages, is related to brain structure. Not always clear from this work, however, is whether causal inferences can be drawn. This would seem to be especially the case where PTSD is associated with abuse, as it is difficult to determine whether PTSD is the cause or consequence of the brain measurements obtained, though it is not difficult to imagine multiple and reciprocal pathways of influence. Given how little work to date focuses upon non-extreme or pathological parenting, that is, parenting in the 'normal range', it seems noteworthy that some of the findings reviewed dealing with such experience are not inconsistent with those emerging from studies of more extreme rearing conditions. This raises the possibility, though cannot yet confirm it, that effects and perhaps even processes of influence detected in studies of extreme environments may prove to be more or less generalised to less extreme conditions. Obviously, much more work is called for before such a conclusion could be embraced with any confidence.

Brain function/process

Relatively little research has directly examined how variations in parenting, including extreme circumstances such as maltreatment, affect brain function. Existing studies have mainly utilised electroencephalographic (EEG) and event-related potential (ERP) approaches, though a few exceptions have used other brain imaging modalities.

EEG studies

Early work documented increased levels of EEG abnormalities, especially in fronto-temporal regions and on the left side of the brain, in children with histories of maltreatment (Davies, 1979; Ito et al., 1993). Subsequent studies used quantitative methods such as EEG coherence to investigate such abnormalities in more detail. EEG coherence evaluates the degree of synchrony between brain activity recorded at two electrodes across a selected portion of the EEG frequency. One useful measure that can be computed from such analysis is called short-distance coherence. Decreases in this index are believed to reflect increased cortical differentiation and thus increased brain complexity. Decreases in short-distance coherence have been related to enhanced language functioning in normal children (Mundy et al., 2003). A second useful measure is long-distance coherence, which is believed to increase with myelination and development of connections between distant cortical regions (Thatcher, 1992; Thatcher, North, & Biver, 2005). MRI studies support the idea that normal development is characterised by a weakening of short-range functional connectivity and strengthening of long-range functional connectivity (Supekar, Musen, & Menon, 2009).

In one early investigation, 15 hospitalised, 6–15-year-old victims of severe physical or sexual abuse were compared to 15 non-abused agemates on measures of EEG coherence (Ito, Teicher, Gold, & Ackerman, 1998). Abused children had higher left hemisphere coherence in the alpha (high-frequency) range compared to non-abused controls, but there was no difference between the groups in right hemisphere coherence. This result, together with further analyses examining the rate of decay of coherence over electrode distance, suggested that the cortex in the left hemisphere was less differentiated in the abused children than in controls. The fact that findings were similar for physical and sexual abuse subgroups was regarded as evidence that the detected EEG abnormalities were not a consequence of direct physical injury.

Another way to quantify the EEG is to compute the power in defined frequency bandwidths. In one investigation of alpha-band activity in 44 maltreated children and 43 non-maltreated children aged 6–12 years, the former showed greater right relative to left activity in parietal regions whereas the latter did not show this asymmetry (Curtis & Cicchetti, 2007). Although these results were considered consistent with other work documenting increased right hemisphere activity in individuals with PTSD, no assessment of PTSD was made in this inquiry. In addition, maltreated females showed greater right than left hemisphere activity over frontal regions. This result was interpreted in line with prior work associating this EEG pattern with withdrawal and negative affective style, and thus linked to the internalising symptomatology often associated with maltreatment.

Quantitative EEG has also been studied in children experiencing extreme neglect and deprivation in Romanian orphanages. Marshall, Reeb, Fox, Nelson, and Zeanah (2008) examined a group of children aged 42 months who had, at a mean age of 2 years, been randomly assigned to placement in foster care or remaining in institutions. Measures of EEG coherence were assessed in the theta, alpha and beta frequency ranges for fronto-temporal, fronto-occipital, fronto-central and fronto-parietal combinations. Coherence was lower in the right hemisphere for the group in foster care compared with the group who remained institutionalised, a result similar to that reported above for maltreated children, in that more nurturing environments were associated with lower coherence. To be noted, however, is that the findings which provide much stronger grounds for drawing causal inferences than do those from observational studies diverge from such prior work in that the differences in coherence were observed over the left hemisphere in the maltreatment study, but over the right in the institutionalisation study. A further important finding of Marshall et al. (2008) was that, within the foster care group, lower short-distance coherence in the alpha and beta ranges was related to earlier placement into foster care.

In studies of EEG power, institutionalised Romanian children aged 5–31 months showed increased low frequency band (theta) power, particularly over posterior brain regions, and decreased high frequency band (alpha and beta) power, particularly over fronto-temporal regions, compared to age-matched never-institutionalised Romanian children (Marshall et al., 2004). Similar patterns of EEG power have been reported in a group of internationally adopted, post-institutionalised children compared to age-matched never-institutionalised agemates (Tarullo, Chatham, & Gunnar, 2007). This result might reflect a delay in development, as alpha power normally increases with age, or it may reflect a general hypo-activation of the brain, possibly due to lack of appropriate stimulation (Marshall et al., 2004). Marshall and colleagues also found hemispheric asymmetries, with greater absolute theta and beta power over the right temporal and occipital regions compared to the left in the non-institutionalised group, but a lack of asymmetry in the institutionalised group.

In a subsequent investigation, Marshall and associates (2008) again examined EEG in the same children after they had been randomly assigned at a mean age of 2 years to foster care or remaining in institutions. There were no overall differences in power for either low or high frequency bands between the groups. This apparently negative finding might have occurred because of a policy of non-intervention, whereby after the initial random assignment to foster care or institution, some infants

in the institution group were subsequently returned to their families or placed in foster care, with data analysed in accord with initial group assignment.

Despite the absence of *between*-group differences, analysis *within* the foster care group revealed earlier foster-care placement to be related to increased alpha power. Given that Marshall and colleagues (2004) had previously found reduced alpha power in younger children while they were living in institutions (see above), this increased alpha power in the foster care group was regarded as evidence that foster care had a positive influence on brain development. Cognitive functioning was also superior for children placed in foster care at an earlier rather than later age, though no evidence emerged consistent with the hypothesis that EEG variables mediated this rearing effect on cognitive performance (i.e., foster-care placement → EEG → cognitive functioning). What this should make clear is that it cannot be presumed that just because a rearing experience proves related to a brain process and to a phenotypic outcome, the former effects mediate the latter.

ERP studies

Event-related potentials (ERPs) are a subset of the EEG that reflect the brain's processing of a discrete event, such as the brief presentation of a visual image or sound. Several ERP studies have examined how maltreatment or institutionalisation affects children's processing of emotions in faces. In one of the first such inquiries, ERPs were recorded while 23 maltreated and 21 non-maltreated 9-year-olds viewed pictures of happy, angry and neutral faces after being directed to press a button in response to the happy face in one test session and to the angry face in another (Pollak, Cicchetti, Klorman, & Brumaghim, 1997). As expected from prior work, the P300 component was larger for target than non-target faces. However, for non-maltreated children the size of the P300 was the same whether happy or angry was the target; by contrast, for maltreated children the P300 was larger when angry was the target than when happy was the target. A direct comparison between the groups showed that the P300 did not so much differ for angry targets but proved smaller in the maltreated group than the non-maltreated group for happy targets.

A subsequent study used a similar task and age group but with happy, fearful and angry faces where each emotion served as target and non-target equally often across a set of three test sessions (Pollak, Klorman, Thatcher, & Cicchetti, 2001). In this work, the P300 was larger for the angry target face in maltreated compared to non-maltreated children but there were no differences between the groups for the happy or fearful targets. A third ERP inquiry generated evidence that physically abused children pay more attention than normal to task-relevant visual or auditory anger cues and task-irrelevant auditory cues (Shackman, Shackman, & Pollak, 2007). Furthermore, the degree of attention allocated to the angry faces statistically mediated the relationship between physical abuse and child-reported anxiety (Shackman et al., 2007).

Considered together, this body of work suggests that maltreated children process facial emotion differently when they are required to attend to anger, and that they process auditory information about anger differently whether or not they are required to attend to it. Behavioural research supports the interpretation that these maltreated children show increased levels of attention and enhanced perception of anger. For example, in an attentional cuing task, physically abused children demonstrated delayed disengagement when angry faces served as invalid cues and increased attentional benefits on valid angry trials (Pollak & Tolley-Scholl, 2003). In a different task in which children had to identify facial emotion from perceptually impoverished stimuli, abused children accurately recognised anger early in the formation of the facial expression, when few physiological cues were available. The speed of children's recognition was associated with the degree of anger/hostility reported by the child's parent (Pollak, Messner, Kistler, & Cohn, 2009). Clearly, then, at the level of both brain and behaviour, maltreated children appear hyper-vigilant to cues to anger.

Behavioural studies suggest that this altered processing of anger is particularly related to experience of physical abuse rather than other forms of abuse. For example, one investigation of emotion recognition found that physically abused children performed well, especially with angry expressions, suggesting a particular sensitivity to this expression. By contrast, the neglected children had generally difficulty in differentiating facial expressions of emotion (Pollak, Cicchetti, Hornung, & Reed, 2000). These data suggest that specific kinds of experiences, rather than simply the general presence of stress or maltreatment, have differential effects. Recall, however, that the ERP studies considered earlier did not find such a differentiation between neglected and physically abused children in terms of response to anger, possibly because of a lack of statistical power to do so (Pollak et al., 2001).

ERPs in response to facial expressions of emotion have also been assessed in institutionalised children who have experienced extreme neglect and deprivation. In one such study, ERPs to happy, sad, angry and fearful faces were recorded in 5- to 31-month-old institutionalised Romanian children and a similarly aged group of Romanian children who had never been institutionalised (Parker et al., 2005a, 2005b). Institutionalised children showed overall decreased amplitudes of the N170 Nc and PSW responses and, unlike controls, did not show a decrease in Nc amplitude with age. These results appear consistent with the notion that institutiona-

lised children show brain hypoactivation, as well as a distinctive trajectory of brain development. Institutionalised children also showed an absence of hemispheric lateralisation for the positive slow wave, whereas controls showed a larger response over the right hemisphere. Emotion did not influence the Nc or PSW components but did influence two early components believed to reflect perceptual processing, a frontal 'N170' component (believed not to be the face-sensitive N170 component because of its anterior topography) and a posterior 'P250' component. The control group showed the largest N170 response to sad and smallest to fear, and the largest P250 response to fear and smallest to happy. The institutionalised group manifest a roughly opposite pattern, with the largest N170 response to fear and smallest to happy and sad, and largest N250 response to happy and sad and smallest to angry. The authors speculated that these results might reflect an overactivity of the response of the amygdala to fearful expressions.

Subsequent work, however, failed to replicate these findings, clearly casting doubt on this interpretation, as no differences were detected in the ERP correlates of emotion processing in institutionalised compared to never-institutionalised children (Moulson, Fox, Zeanah, & Nelson, 2009b). Nevertheless, Moulson et al. (2009b) did present evidence of hypoarousal in institutionalised children who displayed smaller amplitudes for the P1 bilaterally and the N170 and P400 components over the right hemisphere compared to the never-institutionalised group. Latencies for the P1 and P400 components were also longer among the institutionalised children relative to the never-institutionalised children, thus chronicling slower information processing in children with a history of institutionalisation (Moulson et al. 2009b).

After these initial baseline measures were collected, the institutionalised children, as previously noted, were randomly assigned to be placed into foster care or to remain in the institution. At 30 and 42 months of age, ERPs were once again collected during presentation of emotion face stimuli. Results revealed that P1 and P400 amplitudes of children in the foster care group were midway between the institutionalised and never-institutionalised children, suggesting that foster care may be normalising these components. Interestingly, neither age at placement in foster care nor duration of time there contributed to this outcome.

ERPs in institutionalised children also have been recorded during face identity recognition tasks. In one such study, ERPs were measured while institutionalised Romanian children (ranging from 5 to 31 months in age) or never-institutionalised Romanian children viewed pictures of either their caregiver's face (mother or preferred institutional caregiver) or a stranger's face (Parker et al., 2005a). The institutionalised children displayed attenuation in their N170, Nc and PSW components and increases in their P250 component compared to never-institutionalised group. Both groups of children had a normative increase in the Nc amplitude to the face of a stranger compared to the caregiver's face. In contrast, the institutionalised children displayed an abnormal pattern for the PSW component, in which they showed a tendency towards a decrease in amplitude to the stranger's face compared to the familiar caregiver's face while the never-institutionalised children showed an opposite pattern.

A subsequent study comparing institutionalised and never-institutionalised children aged 5–31 months found only a reduction in amplitude of the P1 component, but not other components, in the institutionalised group (Moulson, Westerlund, Fox, Zeanah, & Nelson, 2009a), and the only evidence of recognition of the familiar face was a faster latency of the P400 to the caregiver's face in the younger (<21 months) but not the older (>21 months) never-institutionalised children. Children were reassessed at 30 and 42 months, by which time some of the institutionalised children had been randomly assigned to foster care. Results showed that by 42 months the P1 amplitude was still larger in the never-institutionalised compared to institutionalised children, with the foster care group in between. All groups showed evidence of face recognition at 30 and 42 months, with larger and faster Nc's to the strangers' faces compared to caregivers' faces.

Overall, the EEG and ERP research reviewed suggest that early adverse experience can affect brain function. Studies of maltreated children provide evidence of altered EEG coherence and cerebral asymmetry; studies of institutionalised children also provide evidence of altered EEG coherence and cerebral asymmetry as well as reduced-amplitude components, slower information processing and altered cerebral asymmetry. Reductions in component amplitude and alterations in EEG power observed in institutionalised children may reflect delayed development or general brain hypo-activation. Findings of atypical cerebral asymmetry and altered EEG coherence in both groups may reflect influences of adverse experience on brain differentiation, though this interpretation remains to be fully investigated. With respect to emotion processing, studies of abused children provide consistent evidence of atypical processing of anger, but studies of institutionalised infants and toddlers do not provide consistent evidence that brain processing of facial emotion or facial identity per se is atypical. A recent neuropsychological study of 8–9-year-old children adopted from institutions when they were 12 months or older did find evidence of a mild (less than one standard deviation from the mean) but statistically significant impairment in face learning/recognition in this group (Pollak et al., 2010), perhaps suggesting that such deficits become more marked with age.

MRI studies

MRI is a noninvasive method that can provide high-spatial-resolution structural ($\sim 1mm^3$) images of the brain (or other body parts). Analysis of such images allows segregation of grey and white matter structures and measurement of their characteristics such as volume or thickness, with recent variants of conventional MRI such as diffusion tensor imaging (DTI) allowing even more detailed visualisation of white matter. Functional magnetic resonance imaging allows indirect measurement of brain activation by measuring changes in brain activation. Compared to ERP measures described above, it provides more detailed spatial information about the regions activated, but more limited temporal resolution.

One fMRI study has examined longer-term relations between early parenting experience and later emotion processing, at least as revealed by research in which childhood experience is reported retrospectively in adulthood (i.e., non-longitudinal study). Thus, this work examined how the quality of family life in childhood seemed to affect adults' brain responses to facial emotions by comparing adults who grew up in risky families characterised by harsh parenting to those who grew up in more loving, 'non-risky' environments (Taylor, Eisenberger, Saxbe, Lehman, & Lieberman, 2006). Adults who grew up in non-risky families showed amygdala activation while observing fearful/angry faces and activation of right ventral-lateral prefrontal cortex that negatively correlated with amgydala activation during emotion labelling. By contrast, adults who grew up in risky families showed little amygdala activation during passive observation and a strong positive correlation between right ventral-lateral prefrontal and amygdala activation during labelling. The authors concluded that harsh parenting affects processing of threat stimuli, such that there is a tuning out or lack of response to such stimuli when viewed passively, and an atypical activation when forced to view them. Questions can be raised, however, about the source of the effect in question, as more than just harsh parenting was used to define the concept of a risky family environment.

Summary, conclusions and future directions

Parenting is determined by multiple forces emanating from the child, the parent, and the social context, forces that both combine and interact to amplify and buffer each other's effects (Belsky & Jaffee, 2006). Although there is a large and ever-growing literature examining how parenting influences children's behavioural development, relatively little is known about how parenting influences children's brain functioning and development. As a result, this review has, by necessity, drawn heavily, though not quite exclusively, on research focusing on child maltreatment and institutionalisation and how they relate to the developing brain. Overall, the findings of this work suggest that these parenting conditions of extreme adversity, including institutionalisation, are associated with reductions in cortical grey and white matter volumes and measures of white matter microstructure. Findings for subcortical structures are more complex and varied, with the hippocampus showing effects of early adversity only later in development, beginning from the transition into adulthood from adolescence, and the amygdala often (but not always) showing no effects. It is possible that subcortical structures such as the amygdala are less influenced by environmental variations than the cortex or the hippocampus, which is sometimes described as a 'primitive cortex'. This is certainly not a conclusion that could be confidently embraced at this point, however.

With respect to function, most studies to date have employed electrophysiological techniques which are thought to measure primarily cortical activity and which do not afford conclusive identification of the specific sources underlying recorded activity. This body of work suggests that early institutionalisation, regarded here as a marker of extreme parental neglect and deprivation, is related to general brain hypo-activation, but not necessarily specific difficulties with emotion perception as assessed by face processing. In contrast, child maltreatment, in particular physical abuse, is associated with enhanced neural processing of anger/threat-related stimuli. Future studies using fMRI or in which EEG measures are combined with MRI measures can provide more detailed information about how such functional abnormalities are related to structural abnormalities.

It is not surprising that the first research examining parenting effects on brain development has focused on extremely adverse experiences, namely, maltreatment and institutionalisation. After all, if evidence suggestive of parenting effects on brain structure and function did not emerge when exposure to such adversity was compared to parenting in the normal range, one would be hard pressed to expect variation within the latter to make much difference to children's brain development, as is often assumed to be the case. But now that so much progress has been made in the first stage of inquiry, it seems appropriate to conclude that research in this area of inquiry has reached 'the end of the beginning'.

Work is now needed to determine whether and how variation in parenting in the normal range affects the brain development of children not exposed to extreme adversity. Certainly Whittle et al.'s (2009) recent effort in this regard suggests that such enterprises should prove fruitful, thereby allowing greater generalisation of findings and conclusions. Until more work of this kind is carried out, it will be impossible to know whether evidence emerging from

studies of extreme adversity apply to most parents and children. The kind of work being called for would do well to move beyond just measuring constructs like 'harsh parenting' to ensure that a wide range of potential influential features of parenting are examined. It is certainly imaginable that effects on the brain of warmth, harshness, sensitivity, responsiveness, monitoring, to name just a few well-studied parameters of parenting, will not all be the same.

But as investigators turn, hopefully, to investigating parenting and child development in the normal range, it would be most useful to move beyond observational studies which yield correlational findings. In view of the fact that a great deal of intervention research demonstrates that parenting can be systematically manipulated, with discernible effects on child behaviour, the time would seem to have come to add brain measurements to such study designs. It seems critically important that Andersen and colleagues (2008) have moved in this direction. Not only does such work afford stronger causal inferences about effects of parenting on brain structure and function – that is, evidence that experience 'chisels' the brain (Choi et al., 2009, p. 233) – but it enables investigators to extend such links to behaviour.

As noted in the introduction, without (eventual) evidence that discerned effects of parenting on brain structure and function come to influence actual behavioural functioning, there would seem to be grounds for questioning the significance of this entire field of study. Until such evidence emerges, the fundamental proposition that effects of parenting – or other environmental factors for that matter – on the brain illuminate *how* development operates will remain just a hypothesis. In point of fact, even observational-correlational studies linking parenting with brain measurements would do well to include behavioural 'outcome' measurements, broadly conceived, as some of the reviewed studies have done, so that putative pathways of influence from parenting to brain development to behaviour could be examined, even if only correlationally (e.g., path analysis).

Future research should also consider the very real possibility that parenting – and other environmental factors – does not affect the brains of all children equally and thus that there is differential susceptibility to environmental influences (Belsky & Pluess, 2009a, 2009b; Boyce & Ellis, 2005; Obradović & Boyce, 2009). Intriguingly, Gatt and associates (2009), in studying the interaction of the brain-derived neurotrophic factor (BDNF) Val66Met polymorphism and early life stress (including 'abuse, neglect, family conflict') in predicting brain and arousal pathways to syndromal depression and anxiety, detected evidence of such. BDNF is a member of the nerve growth factor family and is involved in promoting neuronal differentiation, synaptic connectivity, and neuronal repair (Vinberg et al., 2009). Individuals carrying at least one Met allele had the lowest levels of hippocampal and amygdala grey matter volume if they had been exposed to high levels of stress, but the highest levels if they had not been exposed, whereas those carrying only Val alleles (Val/Val) evinced no effect of early life stress whatsoever.

Noteworthy is the fact that the investigators failed to call attention to the 'for better and for worse' patterning of their results, just like many others studying GXE interactions (Belsky & Pluess, 2009b), thus highlighting only genetic vulnerability – in the face of adversity – of those carrying Met alleles. Investigators in the future would do well to remain open to the possibility that it is not just the case that some children, for genetic or other organismic reasons (e.g., temperament), are more susceptible to the negative effects of adversity than others, but that those most vulnerable to adversity may also be those most likely to benefit from supportive and enriching environmental conditions. This proposition could certainly be tested vis-à-vis parenting effects on the developing brain by means of experimental intervention to enhance parenting.

The final point to be made concerns the perhaps restricted focus of this review on effects of parenting on *children's* brain development, without regard to reciprocal processes whereby the experience of parenting influences the brain functioning of adults. Work on the neural bases of maternal behaviour in humans, in which mothers, non-mothers, and sometimes fathers are presented with pictures of their own infants or same-aged unfamiliar infants (Bartels & Zeki, 2004; Leibenluft, Gobbini, Harrison, & Haxby, 2004; Nitschke et al., 2004), recorded infant cries (Lorberbaum et al., 2002; Seifritz et al., 2003), or videotapes of infants (Ranote et al., 2004), demonstrate that many of the same hypothalamic, limbic and coritical sites important for emotional or social (face) processing or for regulation of maternal behaviour in other mammals are implicated in response to infant stimuli. When cast in individual difference terms, such findings highlight the possibility that variation in the parenting experience, perhaps due to variation in child behaviour, could affect parents' brain functioning. Quite conceivably, then, when the next phase of parenting–brain-development research is reviewed, scholars will be in a position to delineate not only effects of parenting in the normal range on children's brain development, but how variation in the parenting experience influences the brains of adults doing the parenting.

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Key points

- Brain structures develop at different rates, so they are differentially sensitive to developmental experience, including parenting, at different points in time.
- Most studies illuminating putative parenting 'effects' on brain structure and function are of children exposed to child maltreatment and severe deprivation in institutions. Evidence clearly suggests that both brain structure and functioning can be adversely affected by such experience.
- Experimental interventions will afford stronger causal inference than observational studies. Research on parenting 'in the normal range' is needed.
- Work that incorporates phenotypic outcomes would afford evaluation of whether parenting effects on the developing brain mediate parenting effects on behaviour, cognition, emotion and health.
- Consideration should be given to the hypothesis that children vary in their susceptibility to parenting effects on the developing brain.

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