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Child Abuse and Neglect and the Brain—A Review

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Developmental psychology and the study of behaviour and emotion have tended to be considered in parallel to the study of neurobiological processes. This review explores the effects of child abuse and neglect on the brain, excluding nonaccidental injury that causes gross physical trauma to the brain. It commences with a background summary of the nature, context, and some deleterious effects of omission and commission within child maltreatment. There is no post-maltreatment syndrome, outcomes varying with many factors including nature, duration, and interpersonal context of the maltreatment as well as the nature of later intervention. There then follows a section on environmental influences on brain development, demonstrating the dependence of the orderly process of neurodevelopment on the child's environment. Ontogenesis, or the development of the self through self-determination, proceeds in the context of the nature–nurture interaction. As a prelude to reviewing the neurobiology of child abuse and neglect, the next section is concerned with bridging the mind and the brain. Here, neurobiological processes, including cellular, biochemical, and neurophysiological processes, are examined alongside their behavioural, cognitive, and emotional equivalents and vice versa. Child maltreatment is a potent source of stress and the stress response is therefore discussed in some detail. Evidence is outlined for the buffering effects of a secure attachment on the stress response. The section dealing with actual effects on the brain of child abuse and neglect discusses manifestations of the stress response including dysregulation of the hypothalamic-pituitary-adrenal axis, and parasympathetic and catecholamine responses. Recent evidence about reduction in brain volume following child abuse and neglect is also outlined. Some biochemical, functional, and structural changes in the brain that are not reflections of the stress response are observed following child maltreatment. The mechanisms bringing about these changes are less clearly understood and may well be related to early and more chronic abuse and neglect affecting the process of brain development. The behavioural and emotional concomitants of their neurobiological manifestations are discussed. The importance of early intervention and attention to the chronicity of environmental adversity may indicate the need for permanent alternative caregivers, in order to preserve the development of the most vulnerable children.

Keywords: Attachment, brain development, child abuse, neglect, neurobiology, stress.

Abbreviations: ACTH: adrenocorticotropic hormone; ADHD: Attention Deficit Hyperactivity Disorder; CRH: corticotropin-releasing hormone; CSF: cerebrospinal fluid; DBH: dopamine beta hydroxylase; ERPs: event-related potentials; HPA: hypothalamic-pituitary-adrenal; PTSD: post-traumatic stress disorder.

Introduction

This review is concerned with examining impairments of the developing brain attributable to, or caused by, abuse and neglect, excluding nonaccidental injury that causes gross physical injury to the brain. An attempt has been made to review interesting and salient work published in the past decade, selectively citing studies of particular relevance to clinical work. As is clear, most of the source material for this review emanates from literature not specifically, or indeed in any way, concerned with child maltreatment. Child abuse and neglect are sometimes alluded to in passing, when mentioned at all. This is not intended as a criticism of the extensive and excellent work being carried out in the fields of neurobiology and developmental psychology. Rather, the challenge is for those of us working in the field of child abuse and neglect to seek out and make connections with these important and clearly relevant sources of knowledge. It is hoped that this review will go some little way towards this endeavour.

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Nature and Context of Child Abuse and Neglect

Child abuse and neglect are (wo)man-made phenomena which adversely affect a child's development and sometimes survival, and which should, at least in theory, be preventable. The definition of child abuse and neglect is not predicated on the intention to harm the child. In order for an experience to qualify as child abuse or neglect, it will be considered to be outside the norm of the usual interaction with a child and sufficient to be actually

or potentially harmful to the child. In the U.K., Significant Harm (Adcock & White, 1998) as defined in the Children Act (Department of Health, 1989) has been accepted as the threshold for recognition of child abuse and neglect. Significant Harm relies on evidence of *either* ill-treatment of the child that has caused or is likely to cause significant harm to the child, *and/or* impairment of the child's health and development which is attributable to ill-treatment or to the care that the child has or has not received.

The definition of child abuse and neglect includes both qualitative and quantitative aspects. It includes single events, repeated events, or a pattern of interaction that is characteristic of the relationship between the abuser, in this case often a parent or primary carer(s), and the child. Whereas physical and sexual abuse are in the nature of *events*, neglect and emotional abuse characterise the *relationship* between the carers and the child (Glaser & Prior, 1997). It is possible that event-type abuse, which is more likely to be traumatic in nature, leads to different effects on the brain than do chronic emotional neglect and abuse. Different forms of child abuse and neglect often coexist (e.g. Claussen & Crittenden, 1991; Ney, Fung, & Wickett, 1994). As Manly, Cicchetti, and Barnett (1994) point out, there are many different aspects of abuse and neglect including subtype, severity, frequency, and chronicity. The child's particular characteristics, be they age, gender, temperament, or disability, may make her more vulnerable to particular forms of abuse or neglect. An abuser or a neglectful parent are likely to have been affected adversely by their own past experiences (e.g. Harmer, Sanderson, & Mertin, 1999). Moreover, the abusing or neglecting person and the child(ren) are often living in a suboptimal social and, indeed, physical context (T. Boyce et al., 1998). There are factors working in parallel at different levels or systems (e.g. Bronfenbrenner, 1979) that contribute to the ultimate particular form of child abuse or neglect. The child's own attributes, the child's family context, and aspects of the maltreatment will all contribute to the later outcome for the child.

Effects of Child Abuse and Neglect

Over the last decade, evidence has continued to accumulate about the strong association between childhood maltreatment and social, emotional, behavioural, and cognitive adaptational failure as well as frank psychopathology, both in later childhood and adulthood (e.g. Cicchetti & Toth, 1995; Post, Weiss, & Leverich, 1994). Many of the papers published in prominent child maltreatment journals such as *Child Abuse and Neglect* have been concerned with various manifestations, associations, and outcomes of mostly—but not exclusively—sexual abuse. The concepts of multifinality and equifinality (de Haan, Luciana, Malone, Matheny, & Richards, 1994) are important. Multifinality recognises that similar, or even seemingly identical, experiences that different individuals undergo can and may well lead to different outcomes. Relatedly, equifinality describes the observed phenomenon that different developmental trajectories undergone by different individuals may, nevertheless, arrive at a common outcome. For these reasons, it is not possible to predict accurately the outcome of certain experiences. Moreover, some studies reporting associations of abuse with poor later functioning assume causality that may be misplaced (Rind, Tromovitch, & Bauserman, 1998).

Studies of children who have been abused. Examples of outcomes in childhood are included in seminal volumes such as Cicchetti and Carlson (1989) on the (causes and) consequences of child maltreatment, and include specific considerations such as the relationship between maltreatment and later peer relationship problems (Mueller & Silverman, 1989; Rogosch, Cicchetti, & Aber, 1995). The review by Kendell-Tackett, Williams, and Finkelhor (1993) of outcomes following sexual abuse has been helpful in pointing out, first and fortunately, that not all children who have been sexually abused are left with problems, and second that there is no "post child sexual abuse syndrome", the harmful sequelae showing considerable interpersonal differences.

Since, in humans, neglect often coexists with physical or sexual abuse, there have been few studies that have examined specifically the effects of emotional neglect on development. The longitudinal study by Egeland and Erickson (1987) included a proportion of children whose mothers were neglectful and/or emotionally unavailable, although there was also overlap with physical abuse. Follow-up findings show the emotionally neglected children to be socially withdrawn, inattentive, and cognitively underachieving in their elementary-school years (Erickson & Egeland, 1996).

A study of 25 children aged between 23 and 50 months (mean = 35 months) who were being raised in a Romanian orphanage were found to be seriously delayed in their cognitive and social functioning. This study used recognised and nontraditional tests and, interestingly, showed that the findings were not related to the Apgar scores at birth, age of entry into the orphanage, or length of time of residence in the orphanage, the mean here being 26 months (Kaler & Freeman, 1994). The cognitive developmental progress at the age of 4 years of Romanian children raised in orphanages and later adopted into families in the U.K. has been shown to be predicted by the age of entry into the U.K. Being adopted before the age of 6 months was protective of later development (Rutter et al., 1998).

There must be some debate about the extent to which maternal depression can be appropriately linked with child abuse and neglect. The later inclusion of some findings about the neurobiological consequences for the development of infants and children who have been cared for by mothers suffering from depression, is justified by the fact that these studies shed light on the effects of emotional deprivation and insensitive-intrusive care on the children's development. In a recent review, Weinberg and Tronick (1998) summarise findings about the effects of maternal depression on infant cognitive, behavioural, and emotional functioning, showing compromise of development in all three domains, effects that last beyond the mother's resumption of normal interaction with the infant.

Studies of adults abused in childhood. Notable among the evidence about adult sequelae of childhood maltreatment is the study by Mullen, Martin, Anderson, Romans, and Herbison (1996) of a community sample of women from New Zealand. The authors found that a history of any form of serious childhood abuse was associated with prior risk factors in the family, which were, in themselves, associated with negative outcomes in adult life. However, sexual, physical, or emotional abuse showed an independent association with adult mental

health problems, found on the PSE (Present State Examination) (Wing, Nixon, Mann, & Leff, 1977) to be in the depressive and anxiety areas. To a limited extent, different forms of childhood abuse were found to be associated with different adult psychopathology as well as personal and social problems. Thus, adult eating disorders were more commonly found following reported childhood emotional and sexual abuse. A history of sexual and emotional abuse by a male caregiver was associated with sexual difficulties in adulthood. Emotional abuse by the mother was associated with worse self-esteem and physical abuse with marital breakdown. The authors caution against an exclusive emphasis on sexual abuse.

In psychiatric patients, associations have been shown between a history of childhood physical and sexual abuse and adult psychopathology (e.g. Swett, Surrey, & Cohen, 1990). A higher incidence of post-traumatic stress disorder (PTSD) in Vietnam veterans has been shown to be associated with a history of childhood physical abuse (Bremner, Southwick, Johnson, Yehuda, & Charney, 1993). Similarly, Yehuda, Kahana, Schmeidler, et al. (1995) have shown that early trauma predisposes adults to suffer PTSD following traumatic event experiences in adulthood.

Childhood abuse as a risk factor for parenting. A history of childhood maltreatment in a parent's own past is now recognised as one important risk factor in the abuse of children (e.g. Widom, 1989). This is, however, not an inevitable outcome (Langeland & Dijkstra, 1995). Egeland and Susman-Stillman (1996) have found some significant differences between mothers who had been abused and went on to abuse their own children, and those who did not. High scores on the Dissociative Experience Scale (Bernstein & Putnam, 1986), idealised and inconsistent accounts of their childhoods, as well as attempts at psychological "escape" including early abuse of drugs and alcohol and attempts at self-harm, distinguished the 14 mothers who went on to abuse their own children from the 10 mothers who had been able to break the cycle of abuse. These latter mothers were able to talk about their past abuse in a coherent and integrated fashion, which enabled then to reflect on their style of parenting their own children. There are clear similarities here with findings from adults' attachment status on the Adult Attachment Interview (George, Kaplan, & Main, 1985), in which security of attachment is positively related to the *coherence* of the adult's account of their own childhood, rather than to the absence of maltreatment during childhood (Main, 1990). Further work on the relationship between childhood abuse and later sensitivity to a child's emotions shows that, in contrast to mothers who had an uneventful childhood, mothers with a self-reported history of physical abuse responded to a video of a smiling, but not a crying, infant with physiological arousal, as measured by increased skin conductance (Casanova, Domanic, McCanne, & Milner, 1994). This is a paradoxical finding that requires further exploration but which indicates an insensitivity and lack of attunement to infants' emotional cues in mothers who had a history of childhood physical abuse.

Despite the methodological weaknesses in some of the research on the effects of child abuse and neglect, there can be little doubt of its potential for adverse effects on the developing child. Questions remain, however, about neurobiological mechanisms by which abuse and neglect become linked with behavioural and emotional impairment. The remainder of this review will explore ways in which the developing brain responds to the external stimuli of the child's environment, in particular child abuse and neglect.

Environmental Influences on Brain Development

The process of early brain development is constantly modified by environmental influences. Child abuse and neglect constitute one aspect of these environmental influences, which present the maturing child's brain with experiences that will crucially—and potentially adversely—affect the child's future development and functioning. The younger the infant, the more these environmental factors are mediated by the primary caregiver(s). In order to consider these effects, it is necessary to summarise current knowledge about the processes of neurodevelopment in infancy and early childhood.

Brain Growth and Maturation

For obvious reasons, much of the work on the development of the brain has been carried out in animals, although increasing knowledge is being gained about human development.

The volume of the human brain increases more during the first year of life than at any other time in life (Gilles, 1993). The human brain grows from an average weight of 400 gm at birth to 1000 gm at 12 months, the growth spurt continuing to 24 months (Schore, 1994). From birth to 4 years of age, the cerebral cortex's use of glucose rises, reaching more than twice the glucose usage of adults' brain and continuing thus until the age of 10 years (Chugani, 1998). The stepwise *sequence* of neurodevelopment is genetically predetermined and not alterable by environmental forces. It proceeds from lower to higher brain centres, from the brain stem to the cerebral cortex, in a caudal to rostral direction (Nelson & Bloom, 1997). Most of the brain's neurons are formed and migrate to their assigned position during embryonic and early postnatal life. However, exceptions include the olfactory region (Huttenlocher, 1994) and hippocampal neurons in animals, including primates, which continue to be formed in adult life (Gould, McEwen, Tanapat, Galea, & Fuchs, 1997).

Neurotrophins are chemicals of central importance to the regulation of the survival, differentiation, and maintenance of function of neurons in the brain. The synthesis and secretion of neurotrophins is dependent on, and regulated by, neuronal activity, which is itself related directly to environmental input (Thoenen, 1995).

During the first 2 years of life, there is sequential growth, prodigious proliferation, and *overproduction* of axons, dendrites, and synapses in different regions of the brain[1]. This process is *genetically* determined. However, not all the synaptic connections survive, many being subsequently "pruned" due to lack of use (Singer, 1995). During this period of *plasticity*, or potential for change, the determination of which synaptic connections will

[1]*Neurons* are nerve cells, which communicate with each other by sending out "messages" from extensions of the cell body called *axons* and receiving "messages" into extensions called *dendrites*. The axon-dendrite point of communication is termed a *synapse*. *Synaptogenesis* is the creation of synapses.

persist is *environmentally* regulated, being dependent on information received by the brain. A competitive process operates, determining which neurons and neural connections will survive. The competition is, for instance, for potential binding sites on the receiving neuron. To quote Courchesne, Chisum, and Townsend (1994) "neurons that fire together, wire together". Synaptic connections that are not utilised gradually disappear. The progressive neuronal maturation and the establishment of synaptic connections are reflected in changes in the infant's increasing functional maturity.

Sensitive Periods

During early brain development there are sensitive periods during which particular experiences affect brain maturation. Although certain experiences are essential for orderly brain development to proceed, the occurrences of some noxious experiences will cause harm to the developing organism. Descriptively, sensitive periods could be conceived of as a brief opening of a window (Bateson, 1979) of vulnerability, of need, and also of opportunity. Sensitive periods have been observed to exist in the development of many different animals as well as in humans. Although generally applied to stages of early development, they can also occur later in life, for instance in animals (but not humans) at the point when maternal responsiveness needs to develop towards her young.

Bornstein (1989) points out that the study of sensitive periods has in the past often focused on associating an experience with an observed change, which is postulated to be a consequence of that experience. Bornstein suggests that an understanding of sensitive periods needs also to include (1) definition of the pathway by which the experience brings about change during the sensitive period; (2) details of the particular body system whose structure and functioning are affected during the sensitive period; and (3) description of the nature of the actual change. Applying Bornstein's terms to child development, the respective issues of interest here are (1) both positive and undesirable/noxious social and interpersonal interactions provided by the primary caregiving environment; (2) the particular body system under consideration here is the brain; (3) the actual changes considered include synaptic connections, and neurohormonal secretions and their receptors. The complex interconnections between different areas of the brain, each with their own timetable for critical periods of maturation, contribute to the varied outcomes and developmental complications of early detrimental experiences (Kandel & Jessel, 1991).

Greenough and Black (1992) distinguish between two aspects of this environmentally dependent maturational process of the brain. They describe one aspect as *experience-expectant*, that is, development that will not happen unless a particular experience occurs during its critical period. In this early phase, development is actually reliant on environmental influences. The predetermined sequences of expected experiences allow for an orderly process of synaptic connections, each stage building and depending on the establishment of the previous one. Greenough and Black further suggest that these early experiences have been selected through the process of evolution and are expected to occur reliably in the particular species and at a particular time in development. This species-typical development is genetically determined and its organisation is designed to buffer the developing brain in a regulatory and orderly development in the face of a variety of environmental influences (Bjorklund, 1997). In turn, typical and expectable environmental factors and circumstances are themselves species-specific, presumably evolved to ensure the stability of development. As far as the human infant is concerned, new stimuli are expected to be presented in a way which is "safe, nurturing, predictable, repetitive, gradual and attuned to the infant's or child's developmental stage" (Perry & Pollard, 1998).

The overproduction of synapses tends to be found in situations in which a source of information can be relied upon to guide the elimination of unused synapses. They include the handling of young infants, responsive gaze, and talking to the infant. The absence of these interactions with the infant would be unusual and contributes to the elimination of synaptic connections. Neglect and failure of environmental stimulation during critical periods of brain development may lead to permanent deficits in cognitive abilities. Experience-expectant development has been especially well studied in animals' visual cortex (e.g. Wiesel, 1982). In experiments now regarded as classical, Hubel and Wiesel (1979) showed that by temporarily blocking the visual input to one eye of a cat during a critical period of development, irreversible structural and functional changes are produced in the brain's visual cortex, leading to permanent impairment of vision in that eye. In humans, profoundly deaf children do not continue to vocalise in later infancy (Scarr, 1993) presumably because species-typical auditory experiences, which are required for the development of language, fail to reach the appropriate brain area. Irreversible reduction in visual acuity (amblyopia) occurs if an eye is deprived of visual input due to, for instance, a cataract or a squint beyond the age of 8–10 years (Taylor & Taylor, 1979).

The other aspect of brain maturation has been termed *experience-dependent* by Greenough and Black. Here too, environmental inputs actively contribute to brain structure, but unlike the experience-expectant process, here the experiences are not predetermined, nor are synapses anticipating the experiences at any particular stage. Experience-dependent processes generate new synapses in response to the environmentally determined experiences, which vary between individuals. For instance, rats reared for 30 days after weaning, in group complex environments were found to have 20–25 % more synapses per neuron in the upper visual cortex than rats reared socially or individually in standard cages (Turner & Greenough, 1985). More recent work has shown that in rodents, neurogenesis continues throughout adult life in the dentate gyrus of the hippocampus. Mice exposed to an enriched environment were found to have more new neurones in the dentate gyrus of the hippocampus than control mice (Kempermann, Kuhn, & Gage, 1997). Similar findings have been reported in adult rats trained in hippocampus-dependent tasks (Gould, Beylin, Tanapat, Reeves, & Shors, 1999). Both groups of authors found that these experience-dependent responses in the hippocampus enhance the survival of new neurons that had already been generated, rather than stimulating their production. In humans, Davidson (1994) raises the possibility that during an experience-dependent period of plasticity, exposure of the young child to particular affective interactions could lead to pre-frontal asymmetric structural and enduring changes in the brain that

would carry significant consequences for later behaviour and affect.

These individual experiences that contribute to brain development are an example of the nonshared environment about which Plomin, Owen, and McGuffin (1994) have written. They point out that the genetic studies of human behavioural dimensions and disorders provide the best available evidence for the importance of nonheritable, environmental factors to human development.

Neural Plasticity

The process of neural plasticity in response to learning and the acquisition of new memories continues throughout childhood and into adulthood. Although the processes of plasticity enable the brain's structure and function to continue to be modulated in response to environmental input and the organism's needs, there is evidence that plasticity in the adult brain is limited, no longer leading to structural changes and operating mainly by regulating the efficacy of certain connections between neurons (Singer, 1987). With increasing age, the balance between plasticity and stability is progressively weighted towards the latter. Maturation is associated with decreased structural responsivity in the brain to new information (Tucker, 1992) or to injury.

Synaptogenesis can be visualised by its active utilisation of glucose on PET (positron emission tomography) scanning (Chugani, 1998). Using this means, it has been possible to demonstrate that in humans, critical periods are proportionally longer. In contrast to animals, the course of human development is far more protracted and includes neotony, or the retention of embryonic or juvenile characteristics by retardation of development (Bjorklund, 1997). While this allows for a longer period of plasticity and maximal learning capacity, it equally prolongs the vulnerability for the developing child's brain. Synaptogenesis and pruning occur in functionally differentiated neural systems at their respective periods of maturation, at different ages early in the child's life (Thatcher, 1994). In some areas of the brain, maturation occurs more slowly and later than in other areas, extending into the second year of life in the frontal lobes. These areas are concerned with reasoning and abstract thought, and more global aspects of behaviour such as the regulation of goal-directed behaviour in time, as well as with affect inhibition (de Haan et al., 1994). In this area of development, object (and person) constancy are an example of what Greenough and Black (1992) term an *expected* experience. This is related to the secure base that Bowlby, in his conceptualisation of attachment, described as a biologically determined "environment of evolutionary adaptedness" (Bowlby, 1969).

Regulation of Infants' Affect and Arousal

An important aspect of the primary caregivers' interaction with the developing infant is to respond sensitively to the infant by gauging their emotion accurately. This is necessary in order for the caregiver to regulate the affect, arousal, and behaviour of the young infant, to help the infant deal with frustration, and to direct and focus the infant's attention. Young infants have not developed the capacity to regulate their own level of arousal and impulses, are unable to obtain their own gratification, and require help in learning to plan their actions. The development of these executive functions requires the maturation of the frontal lobes, from the end of the first year. The frontal lobes are involved with the expression and self-regulation of emotion including the inhibition of automatic or habitual emotional responses, and with regulating responses to emotionally arousing situations. This orderly development is dependent on appropriate input and sensitive interaction with the primary caregivers at the sensitive period. Using rat pups in the first days of life, Hofer has detailed the interactions between the pups and their mothers, showing that the maternal regulation includes both physiological and behavioural modulation of the pups (Hofer, 1994).

The early mother–infant interaction is thus a biobehavioural system. In the brain of the infant who sees the responsive mother's face, brain stem dopaminergic fibres are activated, which trigger high levels of endogenous opiates. These endorphins are biochemically responsible for the pleasurable aspects of social interaction and social affect and are related to attachment (Schore, 1996). The pleasurable arousal also activates the sympathetic nervous system. The sensitive caregiver's role is to modulate the infant's arousal, which could also follow intense displeasure, fear, or frustration, by calming the infant and restoring her or him to a tolerable emotional state (van der Kolk & Fisler, 1994), free of anxiety. One aspect of early child abuse and neglect is the absence of these sensitive interactions between the parent(s) and the young child. Some depressed mothers are withdrawn and disengaged in their interactions with their infants, whereas others are insensitive, intrusive, and sometimes angry (Cohn & Tronick, 1989). In the absence of experiences of external modulation of affect, the infant brain is unable to learn self-regulation of affect, part of the process of ontogenesis. Such deficits may only become apparent later, when the child is expected to have matured for that particular task and these deficits may then become manifest by aggression or hypervigilance.

Ontogenesis

Ontogenesis, which is defined as the development of the self through *self*-regulation, is an active process in development. Ontogenesis is conceptually located between two other interacting influences that determine the direction of development, namely the child's genetic endowment and the environment. Development therefore constitutes more than the resultant of the interaction between nature and nurture, with the notion of ontogenesis allowing for the modification of the process by the contribution and adjustment of the individual child (Cicchetti & Tucker, 1994). They point to the importance of an historical analysis in understanding the complex process of the brain's self-organising system. The nature of the resolution of developmental tasks and challenges, a process that may be more or less adequately accomplished, will determine what is integrated into the brain's structure and contributes, in a probabilistic way, to later adaptation.

Whatever the contribution of ontogenesis, it is far more effective to address adverse risk factors or actual illtreatment before, or at an early stage of the critical period of neural development than to attempt to alleviate the later effects. Animal studies clearly indicate that recovery may be limited if treatment for the precipitating causes of the abnormal or unanticipated neural activity is

offered after the closure of the critical period when neuronal "misconstruction" is completed (Courchesne et al., 1994).

Bridging the Mind and the Brain

Until recently, developmental psychology and neurobiology have been studied in parallel. Whereas the former is concerned with the observation and measurement of behaviour, cognition, and emotion, the latter is concerned with the study of cellular, neurophysiological, and biochemical processes in the brain and the autonomic nervous system. It is now increasingly possible to study simultaneously the neurobiological processes accompanying or underlying observed behaviour, by the use of a variety of neurophysiological measures and brain-imaging techniques[2] (for the latter, see review by Nelson & Bloom, 1997). These methods are enabling the apparent mind–brain dichotomy to be bridged. However, it is evident that the relationship between observed behaviour and measured physiological function is complex. Before considering the neurobiological correlates of child abuse and neglect in the following section, in this section a variety of neurobiological equivalents of observed behaviours, emotions, and psychological processes will be discussed, which are of relevance to the field of child abuse and neglect. While some begin from a neurobiological point of view, others commence from a psychological perspective.

Biogenic Amines

There are more than 30 neurotransmitters[3] in the central nervous system. Of these, the biogenic amines noradrenaline (norepinephrine) and dopamine (known collectively as the catecholamines) and serotonin (or 5-HT) have been studied in greater detail, since they are particularly involved in the regulation of several human behavioural systems which, in turn, help to regulate the interaction between the organism and its environment. The biogenic amines are synthesised in discrete nuclei in the brain stem and midbrain. Dopamine cell bodies are present in the substantia nigra and ventral tegmental areas of the midbrain; noradrenergic cell bodies occur in the locus coeruleus and the lateral tegmental areas of the brain stem; serotogenic cell bodies are located in the midline raphe regions of the pons and upper brain stem. Projecting axons from these nuclei extend to all higher brain centres, and it is likely that the biogenic amines are involved in regulating the function of higher brain centres. There are different ways by which neurotransmitter secretions become activated. It is, for example, postulated that peripheral adrenaline, produced as part of the stress response, stimulates receptors in the vagus nerve (part of the autonomic nervous system), which ends in the nucleus of the solitary tract in the brain stem. From there, messages are sent to the noradrenaline-producing locus coeruleus (LeDoux, 1996). The locus coeruleus is primarily activated from within the brain, from nuclei in the medulla (Aston-Jones et al., 1991).

The biogenic amine systems are hypothesised to operate in balance with each other in their regulatory functions (Rogeness, Javors, & Pliszka, 1992). There has been further amplification of Gray's work on behavioural facilitatory and behavioural inhibitory systems, which suggested that these behavioural systems are mediated by neurotransmitters (Gray, 1982, 1987). Rogeness and McClure (1996) have reviewed their own and others' empirical findings about the functions of these neurotransmitters in regulating behaviour and emotions and about possible early environmental influences on permanent changes in neurotransmitter levels. Dopamine is postulated to mediate the behavioural facilitatory system, activated by rewarding stimuli, or by aversive stimuli when escape or avoidance are possible. Dopamine is thus involved in approach, escape, and active avoidance as well as in predatory aggression (Quay, 1993). It is suggested (Rogeness et al., 1992) that noradrenaline and serotonin are involved in the mediation of behavioural inhibition in the face of lack of reward, punishment, or uncertainty. These two neurotransmitters are therefore involved in regulating dopamine dependent behaviour.

Attachment

Attachment is considered here since it is a fundamental aspect of child development and is affected by child abuse and neglect. There are some neurobiological correlates of attachment security, and it has also been shown to influence the infant's response to stress.

Attachment behaviour is defined as proximity-seeking behaviour by a dependent organism (infant or child), when he or she senses discomfort of any sort, including pain, fear, cold, or hunger. The child seeks to get closer to the attachment figure (parent or primary carer) on the assumption that the parent will be able to reduce the discomfort and restore the child's equanimity. It is a biological instinct (Bowlby, 1969). On the basis of the nature of the mother's or the primary caregiver(s)' responses to the infant's inevitable, normal, and repeated bids for a response to their attachment needs, the child constructs internal working models of self and parent (Bowlby, 1988). These models are beliefs by the child about herself or himself and predictions about how he or she will be treated by others.

There are well-validated measures of the nature of infants' and young children's attachment status, which begins to be formed in the middle of the first year of life. The child's attachment status is assumed to be based on the child's previous attachment experiences and thus reflects the child's internal working models. Attachment security is measured in infancy and early childhood by the Strange Situation Test (Ainsworth, Blehar, Waters, & Wall, 1978), which yields a secure category (B),

[2] *Electroencephalogram* (EEG) measures electrical brain activity generated by neuronal communication; *event-related potentials* (ERPS) are recordings of brain electrical activity over very short, discreet periods of time; *positron emission tomography* (PET) uses small amounts of injected radioactive-labelled glucose or oxygen to measure the degree of glucose or oxygen metabolism at specific sites in the brain, indicating activity at those specific areas; *functional magnetic resonance imaging* (fMRI) identifies active areas of the brain by their use of oxygen, which leads to the conversion of oxygenated to deoxygenated haemoglobin; *orthostatic challenge* means standing up suddenly after lying down.

[3] *Neurotransmitters* are chemicals in the brain which cross synaptic gaps from the axon of the transmitting neuron to the dendrite of the receiving neuron, activating the latter. For details about the activity of neurotransmitters at a synapse see Rogeness, Javors, and Pliszka (1992).

two insecure categories—anxious/avoidant (A) and anxious/insecure (C)—and a disorganised/disoriented category (D) (Main & Solomon, 1990). Following the addition of the D category, V. Carlson, Cicchetti, Barnett, and Braunwald (1989b) reanalysed the attachment relationships of a sample of maltreated and nonmaltreated 12-month-old infants and found a large over-representation of this disorganised category (82%) among the maltreated group, in comparison with 19% in the nonmaltreated group. More boys than girls were classified as (D).

Main and Hesse (1990) postulated that introjection of fear into the caregiving relationship leads to the (D) category. The frightened or discomforted infant seeks his attachment figure, who is at the same time the source of his discomfort. Alongside the (D) classification, Crittenden (1988) has added the (A/C) classification, also found more commonly among maltreated children. Most studies of attachment status in maltreated children have included physically abused and/or neglected children, and none have examined the attachment classification of sexually abused infants (Morton & Browne, 1998). This may be explained by the fact that in neglect, emotional abuse, and repeated physical abuse, especially of young children, the abuser and caregiver will, most likely, be the same person, whereas it is far more likely that the sexual abuser will not be the primary or sole caregiver of the child.

The measurement of attachment status in older children using the Strange Situation Test is not applicable. Alternative means, relying on the assessment of internal working models, have been developed using story-stems (McCrone, Egeland, Kalkoske, & Carlson, 1994), a projective task in which children are requested to complete beginnings of a number of stories.

Neurobiological correlates of attachment. Gunnar, Brodersen, Nachmias, Buss, and Rigatuso (1996) postulate that one function of a secure attachment relationship is to buffer or protect the developing brain from the potential deleterious effects of elevated glucocorticoids on the brain during the protracted postnatal brain development. This is the more so for infants rendered vulnerable due to a fearful or inhibited temperament. An interesting psychobiological attachment theory has been expounded by Kraemer (1992), suggesting a central role for biogenic amines as the mediators of secure or insecure attachment. There is also evidence of a complex relationship between attachment status and infant cardiac reactivity (Izard et al., 1991). Heart-rate variability (a measure of heart-rate pattern) was found to be higher in insecure infants.

Stress

Stress is defined as a stimulus or experience that produces a negative emotional reaction or affect, including fear and a sense of loss of control. Potent sources of stress in childhood have now been shown to include severe deprivation and neglect in early life and exposure to violence between parents, as well as the more obvious recognised forms of abuse. Much of the data on the effects of early deprivation on brain development comes from animal experiments. For example, extensive animal studies have shown that brief and repeated periods of separating a mother from her newly born offspring leads to a stress reaction expressed by increased glucocorticoid secretion with resultant death of hippocampal cells (e.g. Plotsky & Meaney, 1993). Conversely, increased licking behaviour of their pups by mother rats leads to decreased hippocampal cell loss in old age. Interestingly, this finding was initially attributed to brief periods of handling of neonatal rats by humans (Meaney, Aitken, Bhatnagar, Van Berkel, & Sapolsky, 1988); it was subsequently found that the mother rat responded to the human smell on her pups by licking them (Liu et al., 1997)! Further work with rats has shown that one day of maternal deprivation was sufficient to decrease brain-derived neurotrophic factor in the hippocampus and bring forward preprogrammed cell death (apoptosis) (Zhang, Xing, Levine, Post, & Smith, 1997). It is important to note that 1 day in the life of a new-born rat is equivalent approximately to 6 months of maternal deprivation in human infants.

The Stress Response

The stress response is a physiological coping response. It involves the hypothalamic-pituitary-adrenal axis, the sympathetic nervous system, the neurotransmitter system, and the immune system. There are individual variations, likely to be enduring, in the response to stress, which are based on differences in temperament (W. Boyce, Barr, & Zeltzer, 1992) as well as on prior experience. Prior experience can affect responses to stress by sensitisation, by determining the child's attachment security (Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996), and by shaping the child's perception of an experience and its meaning as stressful or not. Lewis (1992) describes three dimensions along which responsiveness to stress can be measured, namely threshold, dampening, and reactivation. Threshold represents the amount of stressful stimulation needed to produce a response. Dampening refers to the child's ability to stop responding to a particular stimulus once the threshold has been reached or passed. Reactivation refers to the child's ability to become aroused again after arousal and dampening have occurred. In support of temperamental influences, Lewis showed that in babies there was stability over the first 2 months of life for threshold and dampening levels, particularly in highly reactive babies whose response threshold to stress was low and whose dampening response was low. Although in Lewis' work, measures of stress responses were behavioural rather than neurobiological, it is likely that there are neurobiological correlates to these observed behaviours, which would suggest that some children will be more vulnerable to the effects of stress. These children would also be described and perceived by their carers as temperamentally difficult. They are therefore doubly vulnerable, first to their own inherent responses to stress, and second, when they are met with insensitive and punitive caregiving responses, which will be perceived by the infant or child as stressful.

Hypothalamic-pituitary-adrenal (*HPA*) *axis*. The HPA axis is a physiological pathway connecting the brain to the adrenal cortex, which secretes cortisol[4]. The hypothalamus secretes corticotropin-releasing hormone (CRH) that in turn stimulates the anterior pituitary gland

[4]*Adrenal cortex* is the outer shell of the adrenal gland, which is situated adjacent to the kidney; *cortisol* is a steroid; the *hippocampus* is a part of the temporal lobe of the brain.

to secrete adrenocorticotropic hormone (ACTH). This is released into the blood and, when reaching the adrenal gland, stimulates the cortex to produce and release cortisol into the circulation (Chrousos & Gold, 1992). The rate of secretion of cortisol is regulated by a negative feedback loop to maintain an optimal level. This means that as specific brain centres receive cortisol, they send messages via the HPA axis to reduce the level of cortisol secretion. Conversely, there are situations that require an elevation of cortisol in the body, and when certain signals are perceived by the brain, cortisol secretion increases via messages down the HPA axis. In the normal state, there is a diurnal variation in cortisol levels, with higher levels found in the morning, falling to lower levels in the afternoon. Cortisol levels can be measured noninvasively by assays of saliva and in the urine.

One aspect of the body's coping response to acute stress is an elevation of serum cortisol, a stress response that commences in early infancy. It has, for instance, been found that a more reactive HPA axis is associated with greater professional competence in air traffic controllers (Rose, Jenkins, Hurst, Livingston, & Hall, 1982) and with greater emotional and social competence in boys with haemophilia (Mattson, Gross, & Hall, 1971). Serum cortisol acts in a number of different ways and on most tissues and organs. Its actions include suppressing the immune response, increasing the level of circulating glucose, and dampening of fear responses to the stressor, as well as adverse effects on the hippocampus (see later). However, what is particularly interesting and important is the notion, proposed by Munck, Guyre, and Holbrook (1984), that the stress-induced increase in glucocorticoid (cortisol) levels protects not against the original stressor but, instead, against the body's normal and immediate responses to stress, with the aim of avoiding the over-reaction of these responses, to the detriment of the body's homeostasis.

Behavioural responses to stress. Cortisol level is only one measure of a stress response, behaviour being a further one. Interestingly, there is a differential response to the same stressor from the two measures. Gunnar, Brodersen, and Krueger (1996) showed a diverging stress response in infancy. Whereas there was a parallel decrease of both cortisol and behavioural responses to stress between 2 and 6 months, crying increased again by 15 months, while the cortisol response to stress had fallen to a lower level than in early infancy. Another example of this differential response is the finding that pacifying a young infant by, for instance, use of a dummy, which reduces crying, belies the fact that elevation of cortisol continues (Gunnar, 1992). Coping may take the form of a reduction in felt anxiety or distress, alongside (and possibly facilitated by, or at the expense of) elevated cortisol.

The sympathetic nervous system and catecholamines. Both the sympathetic nervous system and the catecholamines are activated by stress. Fear messages from the amygdala and hippocampus arriving in the medulla of the brain stem (LeDoux, 1996), and CRH from the hypothalamus, released by stress, stimulate the locus coeruleus and thus noradrenaline secretion in the brain, demonstrating the direct links between the adrenergic and the cortisol responses to stress (Southwick et al., 1993). Messages are also relayed by sympathetic nerves from the brain stem to the medulla of the adrenal gland, which secretes adrenaline and noradrenaline. The effects of these hormones include raising heart rate and blood pressure, sweating, and activation of the fight or flight response. As mentioned earlier, adrenaline probably also activates noradrenaline secretion in the brain via the vagus nerve. There are thus several connections between the peripheral sympathetic adrenaline and central (brain) noradrenaline actions in response to stress (Krystal, Southwick, & Charney, 1995), which explain the emotional as well as the physical experiences associated with stress. Whereas the catechol amines epinephrine (adrenaline) and norepinephrine (noradrenaline), whose production marks the sympathetic nervous system's response to stress, are secreted within seconds of the body sensing a stressor, glucocorticoids are secreted during the following minutes and take several hours to exert their effect (M. Howe, 1998). In preclinical studies, stress has been shown to enhance the release and metabolism of dopamine in the prefrontal cortex (Charney, Deutch, Krystal, Southwick, & Davis, 1993), one of whose functions is to produce coping responses to stress. Raised levels of noradrenaline and dopamine are positively associated with dysfunction of the prefrontal cortex (Arnsten, 1999), whose functions also include the planning and organising of actions using "working memory" and the inhibiting of inappropriate responses and attention to distractions ("executive functions"). This dysfunction leads to symptoms clinically recognised as Attention Deficit Hyperactivity Disorder (ADHD).

Long-term effects of the stress response. Very young animals and human infants show reactions to stress that, in some circumstances, may become enduring and, in others, can be modulated by maternal behaviour. In monkeys, infant–mother separation activates the HPA axis, leading to elevation of ACTH and plasma cortisol as well as to increased activity of the noradrenergic sympathetic nervous system, which includes elevation of heart rate. In some monkeys, this reaction may become sustained and this physiological arousal is accompanied by passive and withdrawn behaviour (Suomi, 1991). McEwen (1999) describes several more and less adaptive responses of the stress hormone axis to chronic stress. When faced with repeated or chronic stress, suppression of the stress response leads to a restoration of cortisol levels to within normal limits (Yehuda, Giller, Southwick, Lowy, & Mason, 1991) by down-regulating the HPA axis response. However, since cortisol also exerts an effect on the amygdala, which is concerned with actively responding to fear-inducing stimuli in times of acute threat, there may be a cost to the reduced cortisol levels, namely a dysfunctional, or less than optimal, response to frightening experiences, and feelings of passive fear (Hart, Gunnar, & Cicchetti, 1995). These are not uncommonly met with in children who have suffered long-term abuse (Shields, Cicchetti, & Ryan, 1994) and may be reflected in the (D) category of infant attachment.

Stress, Elevated Cortisol, the Hippocampus, and Memory

While being a necessary physiological response to acute stress, elevated cortisol may also be harmful. Direct evidence for the harmful effects on brain development of a reactive HPA axis, and consequent elevated cortisol levels, particularly in early life, first came from animal experiments. An indication of a similar mechanism in humans comes from Gunnar and Nelson (1994) who showed that in 12-month-old infants, there was a negative correlation between EEG event-related potentials

(ERPs), which reflect hippocampal activity in "laying down a memory", and salivary cortisol levels. In other words, it appeared that higher cortisol levels interfered with activity of the hippocampus.

In his paper entitled *Why stress is bad for your brain*, Sapolsky (1996) has succinctly summarised recent evidence indicating a significant correlation between sustained stress, excess cortisol, and damage to the hippocampus in humans. The hippocampus, part of the temporal lobe of the brain, is integrally concerned with memory (Squire, 1992). At the time of recollection, the hippocampus is believed to integrate the different aspects of a memory, as well as to locate the memory in time, place, and context (Bremner & Narayan, 1998). Whereas the left hippocampus is believed to play a more important role in verbal memory, the right side is more involved with visual memory (Bremner et al., 1995). The hippocampus has a high concentration of receptors for glucocorticoids. Primate hippocampal neurons are adversely affected by sustained high levels of cortisol, which promotes early degeneration of these neurons (Sapolsky, Uno, Rebert, & Finch, 1990). Exposure to high levels of cortisol causes atrophy of hippocampal dendrites, which is reversible when exposure is brief. Prolonged high levels of cortisol lead to hippocampal cell death, probably due to increased neuronal vulnerability to glutamate toxicity. Long-term elevated, but not toxic, cortisol levels render hippocampal neurons susceptible to the effects of commonly encountered threats to the brain, namely hypoxia, epileptic seizures, hypoglycaemia, physical trauma, and toxic chemicals.

High-dose cortisol medication has been shown to affect memory adversely, both in adults and in children. Bender, Lerner, and Poland (1991) showed that the verbal memory of asthmatic children on high doses of prednisolone was poorer than on low doses. Healthy adults have shown a decline in explicit memory with sustained increases in dexamethasone (a glucocorticoid) (Newcomer, Craft, Hershey, Askins, & Bardgett, 1994).

There are other brain regions with glucocorticoid receptors, including the cingulate gyrus, amygdala, and frontal brain regions. It is possible that some of these regions (although not the amygdala) may be adversely affected by excess cortisol levels early in life (Gunnar, 1998).

Buffers to the Stress Response and the Influence of Attachment Status

Gunnar (1998) suggests that in view of the potentially damaging effects of elevated cortisol levels on the brain early in development, mechanisms have evolved to lower reactivity of the HPA axis to stress. From animal (rodent) work, we learn that hypo-responsiveness to stress in the very early days of postnatal life is achieved by maintaining close contact between mother and pup (Suchecki, Rosenfeld, & Levine, 1993). Gunnar, Brodersen, and Krueger (1996) have shown that in 72 infants, the cortisol response to the same procedure (well-baby examination with inoculation) decreased from a high to a lower response between the age of 2 and 4 months, and further between 6 and 15 months. This change possibly reflected the child's capacity to recall the previous experience, a repetition of which may therefore not be as aversive. The salivary cortisol levels in 9-month-old infants, left with an unfamiliar babysitter for 30 minutes, did not rise if the caregiver was friendly, playful, and sensitive, in contrast to a cold and distant babysitter (Gunnar, Larson, Hertsgaard, & Brodersen, 1992).

It is postulated (Gunnar, 1998) that the equivalent protector, or buffer, of the HPA axis in human infants is the security of attachment with the primary caregiver. Thus, for example, Nachmias et al. (1996) have shown that 18-month-old children who had a secure attachment to their mother, who was present, showed no elevation of cortisol when responding fearfully to the approach of a stranger (a clown). This finding held whether the children were rated as constitutionally inhibited in new social situations, or not. By contrast, constitutionally inhibited *and* insecurely attached children showed a significant elevation in salivary cortisol when approached by the clown. It was also shown that for these latter infants, maternal intrusiveness and insensitive encouragement of the infant towards the clown contributed to the elevated cortisol response. Infants who showed a disorganised/disoriented attachment response were found to have higher cortisol levels *during* the Strange Situation Test (Hertsgaard, Gunnar, Erickson, & Nachmias, 1995). This test is a mild stressor compared to most experiences of child abuse and neglect and these results reflect the extent of these children's vulnerability to stress. The disorganised attachment pattern is associated with abuse and neglect (V. Carlson, Cicchetti, Barnett, & Braunwald, 1989a).

EEG Changes

Fox, Calkins, and Bell (1994) have shown particular EEG asymmetries between the electrical activity of the right and left frontal lobes in 4-month-old infants who had shown early difficulties in coping with the arousal induced by new stimuli. In some of these children, by 24 months, there had been a behavioural adaptation but the original EEG asymmetry endured. Whether these enduring physiological changes are indicators of continuing vulnerability in these children, despite the behavioural adaptation which they showed, is not known. Davidson (1994) has suggested that a particular form of positive emotion, associated with the motivation towards attaining a goal (e.g. enthusiasm), is manifested in the brain as activity in the left prefrontal cortex. In adults, enduring changes have been found in the pattern of EEG asymmetry between the left and right prefrontal lobes in patients who had suffered from depression but had made a symptomatic recovery (Henriques & Davidson, 1990). Similar patterns of asymmetries have been found in 3-year-old children who were temperamentally extremely inhibited and shy (Davidson, 1994).

Psychological Therapies and Neurobiological Changes

Alongside evidence of specific brain functioning and structure, which are the physiological concomitants of observed behaviour, there is evidence that behavioural therapies, as well as drug therapy (e.g. for obsessive compulsive disorder) bring about change on PET scanning (Baxter et al., 1992). This has important implications for intervention, underscoring the contribution of non-physical, psychological treatments to neurobiological change.

Effects of Child Abuse and Neglect on the Brain

Broadly and theoretically, during early brain development, neglect leads to deprivation of input needed by the infant brain at times of experience-expectant maturation, while abusive experiences affect brain development at experience-dependent stages. Both early neglect and abuse therefore have the potential to affect subsequent brain functioning. In practice, the distinction between omission and commission within child maltreatment is not as clear cut. Post and Weiss (1997) describe the "worst case scenario", not infrequently encountered, in which young children experience both abuse and neglect. Child abuse is a potent source of stress, and much of the literature on the relationship between child abuse and neglect and neurobiology has examined the effects of stress on the brain (e.g. De Bellis & Putnam, 1994). Deprivation has been found to result in a stress response as well as in deficits in development.

Trauma and abuse are not synonymous. There continues to be a considerable lack of clarity and tight operational definition about what distinguishes traumatic from stressful events (Shalev, 1996). Most would agree that trauma includes the following ingredients: (1) it seriously threatens the health or survival of the individual; (2) it renders the individual powerless in the face of overwhelming fear or arousal; (3) it overwhelms the individual's coping capacity; and (4) it violates basic assumptions about the environment's (human or physical) benevolence and safety (adapted from Eisen & Goodman, 1998). Interesting work has shown, using PET scanning, that when patients suffering from PTSD were presented with vivid accounts of their own traumatic experiences and showed autonomic arousal, there was concomitant heightened activity in their right amygdala and associated areas of the temporal and frontal cortex, as well as in the right visual cortex. At the same time, Broca's area in the left hemisphere, the area concerned with language, was "turned off" (Rauch et al., 1996). The authors suggest that this provides a neurobiological illustration of the clinically encountered tendency in PTSD to re-experience emotions as physical states rather than as declarative verbal memories.

Much abuse and neglect, whilst stressful, is not perceived by the child as trauma, if only because of the very predictable and chronic nature of some forms of maltreatment. While PTSD is not infrequently found in children who have been maltreated (De Bellis, Keshavan, et al., 1999), it is by no means an invariable consequence. van der Kolk and colleagues consider that the diagnosis of PTSD is most appropriate for traumatised adults, and that children develop much more complex reactions, which are not easily subsumed under that diagnosis (van der Kolk, Weisaeth & van der Hart, 1996). Chronic abuse and neglect are likely to have a pervasive effect on a child's psychological and biological regulatory processes rather than to lead to discrete conditioned behavioural and emotional responses such as are found in PTSD (van der Kolk, 1994). However, a set of criteria for diagnosing PTSD in young children under the age of 4 years has been developed and shown to have good inter-rater reliability (Scheeringa, Zeanah, Drell, & Larrieu, 1995). The set of criteria relies on observed behaviours and has been tested prospectively on 12 young children known to have undergone significant trauma, some of which would be clearly regarded as child abuse.

The ensuing section will commence with a discussion of aspects of the stress response to various forms of child maltreatment. Next, other aspects of neurobiological dysfunction in relation to child abuse and neglect, but not reflecting a stress response, will be considered.

Neurobiological Stress Responses to Child Abuse and Neglect

HPA axis responses. Golier and Yehuda (1998) summarise a number of studies mostly suggesting that some years after experiencing trauma, including sexual abuse, lower cortisol levels are found in conjunction with a possibly enhanced negative feedback in the HPA axis. In childhood studies, findings have been found to be discrepant about the response of the HPA axis to maltreatment. Measures include ACTH response to injected CRH, total level of cortisol being secreted, and diurnal variation of cortisol level.

1. Hart et al. (1995) found that, in comparison to nonmaltreated children, a group of 33 maltreated children aged 4 to 6 years, who were also less socially competent, were shown *not* to have elevated salivary cortisol levels in situations of stress brought on by conflictual social interactions, which suggests a blunting of the HPA axis. This lack of HPA responsiveness may have evolved as a protective factor for the brains of these very vulnerable children. Alternatively, it may reflect lack of novelty of, or familiarity with, stressful situations to which these maltreated children have therefore become habituated and do not respond physiologically.

2. As part of a longitudinal study of sexually abused girls using a self-selected sample of girls of mean age 11, an average of 5 years after sexual abuse, De Bellis, Chrousos, et al. (1994) found dysregulation of the HPA axis with a blunted ACTH response to ovine corticotropin-releasing hormone (oCRH), but without increased cortisol secretion. The 13 girls were no more depressed than a comparison group at the time of the study, although 54% had a history of severely depressed mood and self-harming behaviour. A hypothesised explanation for this finding is that the previous stress of the abuse had caused CRH hypersecretion with consequent adaptive down-regulation of the HPA axis.

3. Hart, Gunnar, and Cicchetti (1996) have found that 131 9-year-old children who had been, and possibly were still being, maltreated showed slightly elevated afternoon salivary cortisol levels, which may have been related to the anticipatory stress of returning to an abusive home. Those maltreated children who were classified as depressed using the Child Depression Inventory (Kovacs, 1992) showed attenuated morning cortisol levels. The authors point out that maltreatment is not a unitary concept, and that their results replicate those found by Kaufman (1991) for depressed maltreated children. This is in contrast to depressed children who have not been abused, in whom an alteration in HPA axis functioning has not been found.

4. Further findings have been reported from a more recent study by Kaufman et al. (1997), in which they compared ACTH response to CRH stimulus in three groups of children, mean age 9.5 years. Thirteen were depressed with additional histories of physical and/or sexual and/or emotional abuse; 13 were depressed without a history of abuse; and 13 were normal matched controls. The depressed children were recruited from inpatient and outpatient psychiatric clinics. Results showed no differences in the cortisol response to the CRH

stimulus between any of the groups. However, while there was no difference between the ACTH responses of the control, depressed nonabused, and depressed abused children who were now living in a stable environment, seven depressed abused children who were continuing to experience active emotional abuse showed a significantly elevated ACTH response. The authors suggest the possibility, supported by animal experiments, that stress in early life, in combination with acute or ongoing adversity, leads to a raised ACTH response to CRH. In the absence of a comparison group of nondepressed, abused children who continued to experience abuse, the contribution of depression to these findings is not clear. In the De Bellis, Chrousos, et al. (1994) study described above, there was no indication of ongoing adversity and this supports the explanation postulated here.

5. The picture is further complicated by findings recently reported by De Bellis, Baum, et al. (1999). They found that 18 prepubertal children (mean age 10.4 years) who were suffering from PTSD following previous significant abuse, and who were now living in stable situations, showed increased levels of 24 hour urinary cortisol in comparison to healthy controls (but not in comparison to nonabused anxious controls). The difference in this sample of maltreated children is that they suffered from PTSD, although adults who suffer from PTSD show lower urinary cortisol levels (Yehuda, Kahana, Binder-Brynes, et al., 1995). The authors suggest that their findings may be explained by a lack or immaturity of adaptation of the HPA axis.

6. The study of the effects on human infants of extreme deprivation, in particular the emotional and tactile caregiving aspects, has been carried out on infants reared in Romanian orphanages. Postulating a stress response, M. Carlson and Earls (1997) report that at the age of 2 years, these children did not show the usual diurnal variation of cortisol levels that was found in home-reared Romanian comparison children. The children in the orphanages had significantly lower morning cortisol levels, which remained elevated relative to the lower afternoon levels, of the comparison children. The deprived, orphanage-reared children also showed significantly poorer performance on the Bayley Scales of Infant Development and the Denver Development Screening Test.

In summary, there is evidence of impairment in the HPA axis following, and during continuing experiences of, various forms of abuse and neglect, some showing raised levels of cortisol with others showing protective adaptation expressed by the presence of normal levels of cortisol. What is not clear is the implication for later functioning of continued dysregulation of the HPA axis.

Hippocampal volume. Bremner et al. (1997) have reported 12% *left* hippocampal volume reduction in 17 adult male and female survivors of severe childhood physical and sexual abuse who now suffered PTSD, in comparison with a nonabused group. There was, however, no associated memory impairment. Stein, Koverola, Hanna, Torchia, and Mclarty (1997) similarly found statistically significant *left* hippocampal volume reduction (5%) in 21 women who reported experiences of severe childhood sexual abuse, in comparison to 21 subjects who had experienced no childhood abuse. Seventy-one per cent of the subjects suffered from PTSD and 71% from a dissociative disorder. Severity of the latter correlated positively with degree of hippocampal volume reduction. Interestingly, there was no associated impairment of memory functioning. The respective researchers, as well as Sapolsky (1996), point out that, for understandable reasons, there is currently no conclusive evidence for a causal explanation in the direction of abuse leading to hippocampal damage, presumably from excess cortisol secretion brought on by the stress of the abuse, although results from many animal experiments, including primates as well as rodents, would support this possibility.

The relationship between hippocampal atrophy and adult short-term memory recall remains unclear. As Stein et al. (1997) suggest, it is possible that the relatively small magnitude of the hippocampal damage found in adult survivors of childhood abuse does not impair explicit memory, or may be compensated for during childhood development by the process of neural plasticity. This would explain why trauma (e.g. military combat) first encountered in adult life, when neural plasticity is no longer functioning sufficiently, will affect short-term memory (Bremner et al., 1997). Differential hippocampal response to stress at different stages of development might also explain why the left and right hippocampi, respectively, were found to be affected by early and late trauma. What this does not explain is why in one of the studies (Bremner et al., 1995) there was short-term memory recall deficit in adulthood following childhood abuse. The association between hippocampal atrophy and adult PTSD following either childhood or adult trauma may be explained by the suggestion that metamemory, the integrative function of the hippocampus, particularly for emotionally charged memories of trauma, may be affected as reflected by the partial hippocampal atrophy, leading to the phenomena associated with PTSD. Although there is evidence of damage or shrinking of the hippocampus following traumatic events, amnesia associated with hippocampal damage is usually confined to subsequent events, while retrograde memory, that is, memory for events preceding the hippocampal damage, is spared (Squire, 1992). Also, interestingly, Schacter, Koustaal, and Norman (1996) report a series of 22 women who experienced prolonged and severe child sexual abuse and who showed reduction of volume of the left hippocampus on MRI (magnetic resonance imaging). Yet, both their memories for the abuse and their current memory functioning were intact.

Catecholamine response.

1. Urinary catecholamine excretion was measured by De Bellis, Lefter, Trickett, and Putnam (1994) in the longitudinal study of sexually abused girls mentioned above (De Bellis, Chrousos, et al., 1994). Twelve sexually abused girls were found to secrete significantly greater amounts of homovanillic acid, a metabolite of dopamine, than a comparison group, indicating higher catecholamine activity. Interestingly, only one girl met DSM-III-R criteria for PTSD. In their further study reported above, De Bellis, Baum, et al. (1999) also showed that abused children suffering from PTSD excreted significantly greater concentrations of baseline noradrenaline and dopamine in comparison to nonabused anxious and healthy controls, measures correlating significantly with duration of abuse. These findings are presumed to indicate an enduring stress response. Increased levels of urinary catecholamine excretion have been found in adult PTSD (Southwick et al., 1993).

2. Perry (1994) has reported decreased platelet adrenergic receptors in a small group of children with PTSD following serious abuse, a finding suggesting down-regulation of the peripheral adrenergic receptors in response to higher levels of circulating catecholamines. Perry also found increased resting heart rate, and abnormal return of heart rate to baseline levels after an orthostatic challenge, suggesting an overactive sympathetic nervous system in these children. These findings of a continuing effect on catecholamine functioning following abuse primarily apply to children with PTSD. Whether these effects would be found without the PTSD and whether they abate following treatment is less certain. In his uncontrolled trial of medication using clonidine, Perry found an improvement in arousal symptomatology as well as in basal heart rate in the children suffering from PTSD. However, recent guidelines for treatment of children and adolescents with PTSD state that "there is no empirical support for the use of any particular medication to specifically treat PTSD in children" (Cohen, 1998).

3. In psychiatrically hospitalised boys who had experienced significant neglect with or without abuse in the first 3 years of life, an association has been found with reduced levels of plasma dopamine beta hydroxylase (DβH) (Galvin et al., 1991). This enzyme is involved in the conversion of dopamine to noradrenaline. The reduced blood level of the enzyme, which is correlated with DβH level in the cerebrospinal fluid (CSF), is believed to be long-lasting. Galvin et al. postulate that the early neglect and abuse which these boys suffered led to an overstimulation of the noradrenergic system due to the stress response with enzyme induction. Subsequent reactive repression of enzyme activity leads to the findings of lowered DβH level. Rogeness and McClure (1996) report similar findings in a group of children (mean age 10.5 years) hospitalised for psychiatric treatment. They found reduced plasma DβH levels as well as lowered blood pressure in association with a history of early neglect, with or without abuse. These findings bear similarities to those found in rhesus monkeys. Infant monkeys deprived of their mother's care were found to have lower levels of cerebrospinal fluid (CSF) noradrenaline and its metabolites than control monkeys (Higley, Suomi & Linnoila, 1992; Kraemer, Ebert, Schmidt, & McKinney, 1989).

4. Galvin, Stilwell, Shekhar, Kopta, and McKasson Goldfarb (1997) have gone on to show that among psychiatrically hospitalised boys, those maltreated before the age of 3 years, and those who had lower serum DβH, showed more interference with an aspect of conscience development, namely the valuation of authority- and peer-derived rules of conscience. These difficulties correspond closely with essential features of conduct disorder. In fact, the same group of researchers had previously reported an association between low serum DβH and undersocialised conduct disorder, as well as with a history of early maltreatment, in a group of boys hospitalised in a psychiatric hospital (Galvin et al., 1995). The authors postulate that the findings regarding processing of values of conscience requires an intact behavioural inhibition system that is, in part, mediated by noradrenaline.

5. Some traumatic forms of child abuse and neglect are repeated experiences. This includes the witnessing of domestic violence, being the recipient of direct physical threat or abuse, and being the victim of some forms of sexual abuse. Following maltreatment, some aspects or reminders of the experience become cues capable of evoking apprehension and fear, even when not accompanied by or following the trauma. Fear is perceived in the amygdala (LeDoux, 1994). The recognition of these cues as danger signals is conveyed to the amygdala, which sets off a fear response (Gallagher & Chiba, 1996). Children might thus become hyper-aroused, experiencing raised heart rate and feelings of anxiety when faced with an apparently neutral occurrence or stimulus, which might include a particular smell or a sound associated with the abuse. The children are often not actually aware of the source of the arousing cue. Moreover, their threshold to reacting to stress is lowered, and their reaction shows sensitisation to early indicators of potentially frightening or threatening cues (Perry, Pollard, Blakley, Baker, & Vigilante, 1995). Some of these children show behaviour that symptomatically resembles ADHD and which is a manifestation of post-traumatic arousal. This hypervigilance and hyperactivity is seen equally commonly in girls and boys who have been abused, unlike ADHD without trauma, which is far more common in boys. The extent to which this behaviour is the same entity as the commonly encountered disorder is not clear.

6. When interacting with their depressed mothers, infants have been observed to be less active, vocalize less, and show more gaze aversion than a comparable group of infants of nondepressed mothers. Dawson, Hessl, and Frey (1994) also found increased heart rate, a physiological measure of being stressed, in infants of depressed mothers when the infants were engaged in social interaction, either with their mother or with another adult. This physiological stress response could be the result of both increased sympathetic adrenergic activity or lowered vagal (parasympathetic) tone, which was also noted by Field, Pickens and Fox (1995). In the infants of depressed mothers, the physiological stress response was not, however, associated with behaviourally observable distress, in contrast to infants of nondepressed mothers who do show a rise in heart rate when displaying negative affect. Stress hormones, both cortisol and noradrenaline, have been found to be elevated in depressed mothers and infants (Field, 1998). Infants of depressed mothers also show less distress when separated from them.

Parasympathetic nervous system response. A very different reaction to trauma, which is found particularly in very young children and in girls, is described by Perry et al. (1995). Here, the child faced with a frightening experience, and unable to escape, "resorts" to dissociation, disengaging attention from the present reality. In this process the vagus nerve, the parasympathetic part of the autonomic nervous system, becomes activated, leading to a slowing of the heart rate and a fall in blood pressure. It is postulated that as part of the dissociation process, endogenous opiates, associated with dopamine systems that arise in the brain stem and are activated by stress, alter the perception of painful stimuli (Abercrombie & Jacobs, 1988). As with the arousal response, children will later react to cues or apparently minor reminders of the past traumatic experiences by dissociating. Clinically they are described as having brief, blank, and inattentive spells, which interfere with their functioning.

Serotogenic response. Kaufman et al. (1998) also measured serotogenic functioning in their study reported above (Kaufman et al., 1997), and found a raised level of

plasma prolactin secretion in 10 depressed-abused children, compared to depressed-nonabused and normal controls. The findings held both for children who were no longer being abused and for those still being emotionally abused. It is therefore difficult to determine whether this finding is considered to be part of a stress response to previous abuse or whether it is associated with familial and experiential factors as well as with current psychopathology.

Other Neurobiological Responses to Child Abuse and Neglect

Cerebral volume. Using MRI scans, De Bellis, Keshavan, et al. (1999) have also recently measured the size of brain lateral ventricles and various brain structures in 44 maltreated children suffering from PTSD and 61 healthy, nonabused controls, individually matched for age, size, Tanner stage, gender, and handedness. Their mean ages were 12 years. Some of the children had also participated in the study reported by De Bellis, Chrousos, et al. (1994). Compared to the controls, the children with PTSD were found to have 7% smaller cerebral volumes; the total midsagittal area of the corpus callosum, particularly the middle and posterior regions, were smaller; and total lateral ventricles and cortical and prefrontal cortical CSF volumes were larger. The brain volume was correlated positively with age of onset of PTSD and negatively with duration of the abuse. The volumes of the left and total lateral ventricles correlated positively; and the area of the total corpus callosum correlated negatively with duration of abuse. PTSD symptomatology correlated positively with ventricular volume, and negatively with intracranial volume and total corpus callosum midsagittal area. The authors discuss possible explanations for their findings, suggesting that these brain size changes could be due to the traumatic early childhood experiences, and therefore possibly related to increased catecholamine concentrations (Simantov et al., 1996; Todd, 1992) and possibly raised cortisol levels. Impoverished environments and lack of mental stimulation in the early lives of these children could also be contributing factors. As the authors show and discuss, there is a positive correlation between IQ measures and brain size. An important implication for these abused children with PTSD is, therefore, an impairment in their cognitive functioning.

It is important to note that this childhood study did not find a predicted decrease in hippocampal volume, in contrast to adult survivors of childhood abuse. De Bellis, Lefter, et al. (1999) discuss explanations for the differences in hippocampal volumes between children and adults, both of whom had suffered childhood abuse and PTSD. Differences may be due to differences in methods of measurement. In preclinical rat studies, age-dependent changes in sensitivity to the neurotoxicity of glutamate receptor blockers have been found such that cell death in corticolimbic regions did not occur in immature animals, but increased towards adulthood (Farber et al., 1995). Moreover, in human adults the extent of hippocampal atrophy following major depression correlated positively with the total life-time duration of depression (Sheline, Wang, Gado, Csernansky, & Vannnier, 1996). These findings indicate that brain changes depend both on maturational factors and course of illness.

Functional, structural, and chemical changes in the brain. There have been diverse examples of an association between functional, structural, and chemical changes in the brain, and a history of child abuse and neglect, several of which are summarised here.

1. Particular relationships have been found between the ERP responses of maltreated and non-maltreated children to affect-containing stimuli. Specifically, pictures of happy and angry faces interspersed between neutral pictures were shown under 2 conditions to 23 maltreated and 21 non-maltreated children aged 9 years. The children were instructed to press a button when seeing either angry or happy faces. While being as accurate in their responses, the maltreated children were slower. Unlike the non-maltreated children, they were also found to have higher amplitude of ERPs when instructed to respond to the angry, rather than the happy, faces (Pollak, Cicchetti, Klorman, & Brumaghim, 1997). The implication is that being presented with negative affect carries a different meaning to maltreated children and elicits a physiologically measurable different response. This may be adaptive in abusive situations but may become maladaptive when used indiscriminantly in different settings.

2. In a group of 115 psychiatric inpatient children, a significant association has been shown between a history of child physical, sexual, or psychological abuse, and EEG abnormalities in the left side of the frontal and temporal region of the brain (Ito, Teicher, Glod, & Ackerman, 1998; Ito et al., 1993). This follows an earlier study by the same group which showed that, using a questionnaire designed to test limbic system dysfunction in adults, adult psychiatric outpatients with a history of childhood physical or sexual abuse had a significantly higher score, indicating limbic system dysfunction (Teicher, Glod, Surrey, & Swett, 1993). The limbic system includes the amygdala, hypothalamus, hippocampus, and prefrontal cerebral cortex.

3. There are early and continuing EEG changes in both infants and their depressed mothers. The pattern is one of relatively increased right frontal lobe activity, which has been recorded from 1 week of age, through to 3 years of age (Jones, Field, & Fox, 1997). Similar EEG changes have also been shown by Dawson, Frey, Panagiotides, Osterling, and Hessl (1997). They describe the EEG changes in 13–15-month-old infants of depressed mothers as relatively decreased left frontal lobe EEG activity. The authors point out that the left frontal lobe is specialised for the expression of positive emotions such as joy, whereas the right frontal lobe is concerned with sadness and other negative emotions. The right frontal region is specifically activated during withdrawal-related negative affective states (Davidson, Ekman, Saron, Senulis, & Friesen, 1990).

4. A preliminary study with 10 non-patient adult subjects who had experienced early trauma and 10 comparison subjects found that the traumatised subjects showed greater right-sided brain activity when recalling a traumatic memory than did the comparison group (Schiffer, Teicher, & Papanicolaou, 1995). Although the numbers were small, the authors speculate that their findings indicate that traumatic memories may be preferentially stored in the right cerebral hemisphere.

5. In comparison to depressed and normal children, sleep disturbances have been found in prepubertal children who had been physically and sexually abused and who had been referred for inpatient or outpatient psychiatric treatment. The disturbances included difficulty in falling asleep and increased activity during sleep.

The disturbance was worse in the physically abused children and was found to be related to the abuse rather than to PTSD (Glod, Teicher, Hartman, & Harakal, 1997).

Much of what has been discussed above about the deleterious effects of trauma, abuse, and neglect on the developing brain and subsequent child development has been amplified descriptively in intelligible lay language in a new book by Karr-Morse and Wiley (1997). The book is replete with reputable references as well as quotes from extensive conversations with researchers in the related fields.

Implications for Future Practice

Early recognition of infants and young children whose development is rendered vulnerable by neglect, exposure to trauma, or direct abuse is an important step. Living in the presence of parental violence is one particularly common situation, in which young infants may not be considered as victims. Emotional neglect (Erickson & Egeland, 1996) has only latterly acquired the recognition it deserves, as has the fact that maternal depression is one common context in which this occurs. Zeanah, Boris, and Larrieu (1997) rightly point out the complex interactions between risk and protective factors that must be encompassed in the understanding of the development of psychopathology. They also point to the caregiving relationship as the mediator of both extrinsic and intrinsic risk factors. When, in child maltreatment, the caregiver also abuses or neglects the child, the mediating relationship itself is the source of risk.

As has been illustrated, the process of early brain development is constantly modified by external events which impact on that process. These environmental factors commence their influence *in utero*. In this review, only the contribution of the environment postnatally was considered. There are pragmatic reasons for this choice, since one purpose of this review is to point to areas of possible intervention to minimise harm to the child's development. As is evident, in the field of child abuse and neglect there is not infrequently a conflict between the interests of the parent or abuser and the child, which at times requires the legal mandating of intervention in favour of the child. At least in the U.K., there are situations in which we currently have no means other than education to intervene effectively in such undesirable practices as drug and alcohol abuse in pregnancy, despite evidence of the harmful consequences to the development of the future child (Jacobson & Jacobson, 1994; Mayes, Bornstein, Chawarska, Haynes, & Granger, 1996). Thus, in a recent case in the U.K., the Court of Appeal adjudicated that the rights and wishes of the mother prevail over those of her unborn child, even if the expression of these wishes will be to the detriment of the future child (St George's Healthcare NHS Trust v. S., 1998).

Nevertheless, it is possible to recognise active foetal abuse. Condon (1987) found that 8% of 112 pregnant women and 4% of their male partners acknowledged the urge to hurt or punish their unborn child. Kent, Laidlaw, and Brockington (1997) describe five depressed, pregnant women who repeatedly actively punched their own pregnant abdomen, as well as acknowledging negative feelings towards their unborn child. All the mothers had contemplated or actively sought termination of the pregnancy. Three of these mother–child relationships remained very troubled after birth. As the authors point out, active enquiry about possible foetal abuse, even in the absence of clear maternal depression, is indicated. This would allow for the possibility of actual prevention of very early child neglect or abuse. In rats, at least, adoption has been shown to reverse the effects of prenatal stress (Maccari et al., 1995).

It is important to continue to study factors leading to positive outcomes for these children. For instance, using the concepts developed by Block and Block (1980), Cicchetti, Rogosch, Lynch, and Holt (1993) found that ego-resiliency, ego-overcontrol, and self-esteem each contributed to better overall adjustment in a group of 129 disadvantaged, maltreated children aged 8–13 years. However, only ego-overcontrol differentiated between the maltreated and a disadvantaged, non-maltreated comparison group. This is encouraging, since it is probably more feasible to encourage children to develop strategies of gaining control over their actions and responses than to become more flexible. However, as Block and Block point out, both ego-control and ego-resilience are likely to be temperamentally determined. Moreover, self-esteem is a resultant of both good nurturance (Harter, 1983) and personal efficacy and achievement and, while predictive of good adjustment, self-esteem is therefore both dependent on some contributors to good outcome and an independent contributor to outcome. In the light of the stability of resilient and nonresilient functioning (Cicchetti & Rogosch, 1997), which may be partially explained by the poor quality of attachment relationships found in maltreated children (Cicchetti & Barnett, 1991), self-organization by the child needs to be encouraged and fostered by those intervening in abuse and neglect. This needs to include the construction of a coherent account by the child of her or his own experiences. Future prospective research will need to continue to test the hypothesis that a greater and earlier direct investment in children who are maltreated leads to enduring improvement in their functioning.

Conclusions

There is considerable evidence for changes in brain function in association with child abuse and neglect. The fact that many of these changes are related to aspects of the stress response is not surprising. The neurobiological findings shed some light on the many emotional and behavioural difficulties which children who have been abused and neglected show. Hyperarousal, aggressive responses, dissociative reactions, difficulties with aspects of executive functions, and educational underachievement thus begin to be better understood.

The findings from neurobiological studies of brain development dealing with experience-expectant periods lead to an assumption of a deficit model, in which the lack of input to the developing child at certain critical stages of development will result in delay or absence of development of certain skills. It is therefore interesting to note that empirical findings about the effects of deprivation point to stress responses as much as to deficits.

The neurobiological findings go some considerable way towards explaining the emotional, psychological, and behavioural difficulties which are observed in abused and neglected children. The stress response offers one explanatory model for the neurobiological findings. This is particularly so for abuse that is traumatic. However, in

other instances it is not yet clear how, or to what extent, child abuse and neglect bring about the neurobiological changes. Some of the explanations may lie with experience-dependent brain development, in which the nature of early experiences shape neural connections in the maturing brain. The chronic nature of much emotional abuse and neglect negates the potential for development and change afforded by neural plasticity.

Changes in the family's social context and in the child's immediate caregiving relationships, as well the child's own adjustment, all influence the later outcome for the child's development. Findings from the Rochester Longitudinal Study, summarised by Sameroff (1998), paint a picture of the outcome for children growing up in families of low socioeconomic status. The study identified 10 risk factors that were believed to impinge adversely on the children's development. Four of these risk factors could be regarded as aspects of emotional abuse and neglect. No single risk factor, but increasingly in combination of 2 or more, the 10 risk factors were found to correlate with poor outcome for the children at ages 4, 13, and 18 years, on measures of cognitive, social, and emotional competence. There was very strong continuity in the existence of the risk factors over the period of the study. Composite measures of the children's mental health and competence respectively at 1, 4, and 13 years of age did not protect or predict the child's ultimate competence and mental health independently of the risk factors identified. The disadvantaged and disadvantaging environment therefore proved more powerful than the emotional health and personality of the child at every age.

Since brain development is integrally related to environmental factors, active early intervention (e.g. Zeanah & Larrieu, 1998) offers the greatest hope for children's future. The evidence on the protective effects of secure attachment in the face of stress clearly indicates a target for concern and treatment. In support of family preservation, there is a tendency to continue to attempt to bring about changes in parent–child interaction. When these are ultimately declared ineffective, adoption is contemplated. Although for the most vulnerable children, adoption offers an alternative avenue, the good prognosis for successful outcome is inversely related to the age of the child at adoption (D. Howe, 1998). Preclinical studies with rats support this finding (Barbazanges et al., 1996).

However, the most exciting challenge for the future is to find new ways of utilising the rich evidence about the relationships between child abuse and the brain in ways that will benefit children.

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