Medical Hypotheses 136 (2020) 109502

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

An innate brainstem self-other system involving orienting, affective responding, and polyvalent relational seeking: Some clinical implications for a "Deep Brain Reorienting" trauma psychotherapy approach

F.M. Corrigan*, J. Christie-Sands

Trauma Psychotherapy Scotland, 15 Newton Terrace, Glasgow G3 7PJ, United Kingdom

ABSTRACT

Underlying any complex relational intersubjectivity there is an inherent urge to connect, to have proximity, to engage in an experience of interpersonal contact. The hypothesis set out here is that this most basic urge to connect is dependent on circuits based in three main components: the midbrain superior colliculi (SC), the midbrain periaqueductal gray (PAG), and the mesolimbic and mesocortical dopamine systems originating in the midbrain ventral tegmental area. Firstly, there is **orienting** towards or away from interpersonal contact, dependent on approach and/or defensive/withdrawal areas of the SC. Secondly, there is an **affective response** to the contact, mediated by the PAG. Thirdly, there is an associated, affectively-loaded, **seeking** drive based in the mesolimbic and mesocortical dopamine systems. The neurochemical milieu of these dopaminergic systems is responsive to environmental factors, creating the possibility of multiple states of functioning with different affective valences, a polyvalent range of subjectively positive and negative experiences.

The recognition of subtle tension changes in skeletal muscles when orienting to an affectively significant experience or event has clinical implications for processing of traumatic memories, including those of a relational/interpersonal nature. Sequences established at the brainstem level can underlie patterns of attachment responding that repeat over many years in different contexts. The interaction of the innate system for connection with that for alarm, through circuits based in the locus coeruleus, and that for defence, based in circuits through the PAG, can lay down deep patterns of emotional and energetic responses to relational stimuli. There may be simultaneous sequences for attachment approach and defensive aggression underlying relational styles that are so deep as to be seen as personality characteristics, for example, of borderline type. A clinical approach derived from these hypotheses, Deep Brain Reorienting, is briefly outlined as it provides a way to address the somatic residues of adverse interpersonal interactions underlying relational patterns and also the residual shock and horror of traumatic experiences. We suggest that the innate alarm system involving the SC and the locus coeruleus can generate a pre-affective shock while an affective shock can arise from excessive stimulation of the PAG. Clinically significant residues can be accessed through careful, mindful, attention to orienting-tension-affect-seeking sequences when the therapist and the client collaborate on eliciting and describing them.

Introduction

This paper will aim to review emerging unserstandings of the importance of brainstem systems in early, developmental, relational trauma and the potential for treatment of the clinical sequelae. These understandings, as discussed previously [1,2], represent potentially a major paradigm shift in psychiatric disorders more broadly given their ubiquity and commonness and their role in the development of a range of so-called syndromal diagnoses. For example, many psychiatric presentations occur after adverse separation experiences; syndromes such as depression, anxiety, panic disorders and substance abuse being precipitated by deaths and other losses. While these events may be intrinsically grief-inducing the consequences for health and well-being are often more severe when they evoke echoes of earlier-life distress. Adverse occurrences in the neonatal period, infancy, or later childhood create the templates for distress that is somatically recalled by later events such as relationship break-ups, deaths, and losses of function with illness and ageing. This idea has a long history within psychodynamic psychotherapy, so is not new, although recently restated in terms of affective neuroscience and memory reconsolidation [1–3]. Animal models of enhanced forgetting of infantile memories demonstrate that those early memories have not been permanently erased but can be recovered through hippocampal stimulation [4]. Although somatic memories of attachment experiences relevant to the establishment of relational templates are the subject here, such work does add translational research support to the idea that early adversity is not completely eradicated but leaves roots that may later require therapeutic attention.

Working with the adult sequelae of early adversity has led to a focus here on the brainstem responses to attachment disruptions and relational shocks, chronic neglect, and other traumas occurring during critical periods of the brain's maturation. The concept of attachment shock is introduced for those experiences which were suddenly and

* Corresponding author.
E-mail address: fmcorrigan@aol.com (F.M. Corrigan).

https://doi.org/10.1016/j.mehy.2019.109502
Received 31 August 2019; Received in revised form 11 November 2019; Accepted 16 November 2019

unpredictably unpleasant and which carried a high-energy impact. Developing brain circuits have their functional capacity altered, if not impaired, by adverse events, including those of an interpersonal nature. The molecular mechanisms involved in the brainstem, such as those which form topographic maps in the superior colliculi (SC) [5], or those which contribute to fear responses through parvalbumin-positive neurons in the SC [6,7], are beyond the scope of this paper so the focus is on hypothetical patterns of sensitisation in the most significant networks. As the capacity for affective responding develops far earlier than the ability to regulate emotional expression through top-down cortical control, so sensitised responses to particular cues can form predictable sequences that become more embedded with repeated evocation. Intense affective experience drives implicit learning which is expressed later in life through often unanticipated responses to events; these may even become part of the temperament or personality [8]. When the emotions in very early life are so intense as to be overwhelming then dissociative responses occur [9] and further modify the trajectory of an individual's social and interpersonal learning. The focus is not on the sensory affects, such as disgust, or on the distress created by hunger and thirst, though these may be pronounced and significant when there is neglect and inspire fear of not having the resources to survive, but on the basic affects [10] that the chronic neglect and abuse can instigate: fear, anger, grief [10] and shame [11,12]. The presence or absence of positive affects stemming from the joy of playfulness or the sense of being cared for and nurtured [10] also has a bearing on the later affective state of the adult. Clinical experience with adults who have relational conflicts and who are found to have somatic memory residues of adversity in early life is combined with a perspective informed by developmental neuroscience and parent-infant research. It is proposed that the themes are readily explicable in terms of what is known about the intrinsic capacity for orienting to others, for basic affective responding, and for the resulting modifications of drive and motivation.

There is a growing body of literature on human relationality arising from different but complementary fields of scholarship [13–27]. Much of this literature highlights contemporary transformations of classical attachment theory into a theory of mother-infant emotional regulation as a vital component of physiological state regulation and of relational well-being [21]. Prenatal adversity [28,29] and early disruptions in bonding and attachment are understood to sensitise evolving regulatory networks, with often profound lifetime implications. The capacity for emotional regulation, thought to be dependent on a relationally optimal context for secure attachment with the primary caregiver(s) during the first two years of life, is strengthened through development of the prefrontal cortex [25]. That is, the developing brain is experience-dependent and experience-expectant and evolves Neurosequentially from lower subcortical systems through to higher, more complex, cortical systems [26,27]. These different neural systems develop, organise, and become fully functional at different times during a child's early life with each brain area having its own unique timetable for optimal development. When the developing nervous system is impacted by intrauterine insult (e.g. early prenatal exposure to neurotoxic stress, drugs and alcohol) together with severe postnatal neglect (e.g. impaired bonding and multiple attachment disruptions and attachment shocks) its functional capacity will be compromised [26,27]. The mechanisms by which prenatal depression [29] and stress [28] translate into altered emotion regulation are still to be fully described but it seems clear that disruptions of neurochemical modulators of brain growth and development in utero and/or the absence of positive interpersonal cues (gaze, affect and vocal synchrony) during bonding may lead to significant relational disturbances throughout life. An example of the latter is that congenital blindness disposes to the development of autistic spectrum disorders [30] through an impairment of the developing brain systems which facilitate communication with others. Likewise, separation from the mother at birth may introduce unexpected and unfamiliar sensory experiences which activate alarm and defensive systems through the intermediary of the innate connection system based in the SC. The "natural preferences" [17,31] towards the sound, sight and scent of the mother are not satisfied.

While this body of research maps the general neurobiological architecture and provides compelling explanations for the implications of early neglect and trauma it is equally important for the purposes of this paper to consider how raw sensory and affective experiences within the primary attachment relationships are imprinted into patterns for orienting towards and seeking relational contact, connection and communication. The work of both Stern and Trevarthen focuses on articulating the emotional subtleties and musical qualities of relational communications in the richly intersubjective world of the infant. For Trevarthen, the new-born is not only making experience but is actively 'seeking' relational exploration [31]. Indeed, he argues that the quality of those early intersubjective signals demonstrates that the infant is primed to seek and discover as well as to make and use experience. In 'Diary of a Baby' Stern [18] offers an insight into the subjective world of the infant through a series of 'autobiographical' segments linked to developmental changes. In this, he captures the infant's fleeting attention as it moves from one raw sensory experience to another. The baby is uniquely equipped at birth with 'natural preferences' [16] which provide sensory templates priming the urge to orient towards or away from certain experiences as well as to seek and discover mutual relational experiences. Raw data are lived on a felt sensory level with orientation, however fleeting, to the stimuli occurring before there are any affective responses to them.

Thus, in fields of enquiry relating to mother-infant intersubjectivity, 'shared' and rich emotional experiences are believed to be active and emergent from the moment of birth and relevant for optimal brain development. We cannot do justice to the varied and continuing research in this area as our focus is on the impact of adversity on the relational nervous system as that is expressed through orienting patterns as well as through affective and seeking experiences. An adult may then find that moments of relational contact, connection and communication are highly evocative of early bonding experiences or attachment disruptions but that the links are so deep as to be hidden from conscious enquiry into them. While the foundational template for attachment is considered to be embedded in the SEEKING system [10], the valence of which confers an individually sensitive priming of the urge to attach, we consider here also that orienting, however unconscious or covert, to the significant sensory experiences has contributed to the drive and motivation to connect with another. Panksepp [10], ever wide-ranging in perspective while encyclopedic on neuroscience detail, wrote that it would be foolish to attribute the endless desires of the human heart to one brain system. Nevertheless, they all require the dopamine systems ascending from the midbrain to give them interest and excitement, enthusiasm and pleasure. These systems are immediately responsive to homeostatic imbalances, through information fed from the lateral hypothalamus, and responsive to environmental contingencies. The resulting drive and motivation, valenced as positive or negative, to search and investigate with energy and interest, led Panksepp [10] to name this the SEEKING system and to describe its main pathway as the mesolimbic dopamine system [32].

Early adversity imposes a trajectory upon which the basic urge to attach may become conflicted throughout life: opposing action tendencies occupying parallel circuits in a mammalian SEEKING system that has evolved to ensure survival through attachment. However, it is also argued here that opponent urges can be present in the immediate orienting response. As the body orients towards and seeks relational contact, connection and communication, the 'somatic signature' of conflicted urges can emerge: a simultaneous urge to reach out and to pull away, for example. Adverse experiences during infancy, perhaps those that are painful, distressing and strengthened by frequent repetition or emotional intensity, then lead to a conflicted orienting response in addition to conferring a valence on fundamental templates of the urge to attach. These may become part of the brain's organising templates for attachment capabilities and then be inappropriately construed as characterological, rather than experience-based. A simultaneous urge to connect and to withdraw mediated by different areas of the SC prepares the body in opposing ways which are incomprehensible to purely cognitive scrutiny. When basic affects originating in the PAG and hypothalamus are engaged by orienting to connection and by the urge to attach there is the potential for further distress in adult relationships: sadness, rage, fear or shame being elicited by close contact with another person. The brainstem-based, self-other connection model provides a way of viewing clinical presentations derived from adverse relational experiences in early life when these underlie the adult's attachment patterns. It also provides a concise way of identifying and understanding an individual's interpersonal conflicts.

Three main brainstem components of the intrinsic connection system

Orienting

A therapeutic focus on the pain of early relational disruptions and other adversity [33,34] identified two main brain systems – basic affective and mesolimbic SEEKING - as influential in the long-term distress. However, this misses out the key component of orienting to another at the initiation of contact and throughout the continuation or development of an interaction. Orienting patterns may have their origins in early sensory bonding experiences that emerge during the third trimester when foundational templates for attachment are forming. The newborn infant can turn his/her head in response to a communication [18] but perhaps this is not surprising when the foetus can apparently orient towards parts of its body and make associated, directed, movements as early as 10 weeks gestational age [35], long before full cortical development. Disruptions in sensory bonding during early post-natal life, for example through separation from the mother or neglect by her, can then lead to conflicted orienting impulses in the earliest experience of relational intimacy and attachment.

During the third trimester there is evidence of orientation to the sound of the maternal voice and evidence of a fetal motor response to the maternal voice through arm, mouth and head movements [36,37]. The olfactory system develops during the third trimester as fetal swallowing and thumb sucking bathe the olfactory mucosa in amniotic fluids and after birth the mother's odour may provide a source of soothing and a prompt for nursing; the amniotic fluid smell prompts suckling in the early days and this in turn contributes to bonding and attachment. Thus, early sensory communications which promote the development of the sensory systems in utero are also laying a foundational template for bonding. Multisensory integration through the SC [38] is a key component of the neural hub for prenatal and postnatal bonding.

The new-born baby's initial contacts with others are based in sensory processes. The infant has preferences for sensory stimuli, in different modalities, associated with the mother and seeks proximity selectively to her [39]. That is, the recognition of sensory stimuli specific to the mother is necessary for the orienting towards her *before* there can be the directed seeking of proximity to her. The sensory interactions permit activation of, and access to, the extensively-described capabilities for seeking, discovering and experiencing mutuality in relationships [16,21,40]. From the moment of birth babies have a proprioceptive capacity for awareness of the position of their body and a kinaesthetic awareness of their own body movements – and they have visual and auditory abilities for tracking their parent's movements. Very early micro-orienting behaviours are evident through changes of gaze direction and tiny head movements, and full motor control of both gaze direction and head movement develops around the end of the third month. Head and eyes tend to move together, although they often have different communicative impacts depending on head position. For example, the head almost imperceptibly moving forward with a slight upward tilt may positively signal 'approach' while small side movements of the head may communicate aversion or flight. Stern [16] suggests that the gaze and face aversions more typically involved in peripheral monitoring are not truly indicative of complete flight actions. (This would fit with our thesis that such movements are determined by circuits through the SC while flight responses are mainly driven by circuits through the PAG.) Head lowering signals submission, collapse or withdrawal while full head turning expresses a more typical avoidance response. Such expressive orienting actions are dependent on the flow of communication with the caregiver, the neurorelational dialogue between infant and parent that is promoting maturation of the relevant brain areas. The interconnection of the innate systems for connection and defence means that there can be sensitisation of both simultaneously when interactions are challenging.

As the visual-motor system matures the infant's communicative repertoire becomes more primed to relationally engage or disengage caregivers [16]. The infant's alert face often coincides with smooth movements, eyes and head orienting towards caregiver, fleeting smiles and vocalisations [41]. By constrast, during periods of withdrawal there are fewer vocalisations, smiles, and movements – and face and eyes are turned away. Also, as early as three or four months, the infant has the skills for head movements expressive of mixed or ambivalent communications. Where there are no evident disruptions in bonding and attachment the mother's repertoire of facial expressions is generally infant-appropriate, in order to modulate the rich multisensory and emotional flow of the interactions. In contrast, blank facial expressions coupled with gaze aversion are a clear and potent signal of lack of interest. The classic 'still face' experiments [42] demonstrate that the baby, when met with a blank/still face, continues briefly to reach out in an approach gesture but soon withdraws. Such confusing and contradictory experiences can lay the foundation for conflicted urges to attach as they may activate both approach and withdraw tendencies of the SC and the negative affects mediated by the PAG. Withdrawal and orienting away-from are different as a movement for turning away may retain a covert orienting towards the source of the attachment conflict. However, both are based in collicular responses. The SC, with its layered organisation, is the single structure at the deepest level of the brain in which this kind of sensorimotor transformation, from sensory input to movement response, occurs [43]. Before the affective response to an interpersonal stimulus there has to be an overt or covert orienting to it. Therefore, in addition to the affective response stimulated by the PAG/hypothalamus and the seeking response driven by ML-DA during attachment, there is an additional focus here on the orienting mechanism based in the SC. Specific patterns of orienting-affective-seeking responses are being learned very early in life.

Orienting for approach or defence – preparatory muscle tension, often transient

Dean et al. [43] reported that stimulation of the rodent SC could lead to approach, with tracking or pursuit movements, or defensive movements of avoidance or flight. The upper layers of the SC receive visual information from the retina and the visual cortex while auditory and somatosensory stimuli are mapped in deeper layers. Intermediate and deep layers also control the movement of the eyes towards the stimulus. However, in addition to eye movements the SC mediate a range of defensive responses to threatening stimuli, especially useful in situations in which a rapid movement may ensure survival. Ipsilateral projections from the SC direct sudden movements, ranging from cringing to running, away from a stimulus, while contralateral projections direct movements towards a stimulus. More recent work proposes that there is a threshold mechanism in the SC for initiating PAG defensive responses when the perception of threat reaches a certain intensity [44]. There may, however, be vestigial defensive responding, or tension changes preparatory to and facilitatory of defensive and approach movements, based in the human SC.

Another assumption here, partly based in clinical observation, is that approach behaviours are often affiliative rather than predatory. This is a crucial point because different areas of the SC, at least in rodents, are engaged for predatory approach and for defence [45]. As is the case for defensive action urges there appear, in the human, to be tension changes preparatory to attachment movements which we assume to have their origins in the downward projections from the SC to the ventromedial tegmentum, a brainstem area responsible for the setting of musculoskeletal tension levels [46]. There is likely to be some functional segregation for the separate functions of approach and defence, as is seen in rodents [45], but so far there is no work on approach-for-attachment movements in laboratory animals to demonstrate the separate areas for attachment and defence which we hypothesise to be present – and highly relevant clinically. The human SC have extensive connectivity with the cortex for responding to complex stimuli according to an internal map of the body, as has been shown in the rubber hand illusion [47], so have the capacity to initiate responses to a wide range of stimuli. The linkage of neuroanatomical and functional aspects of expressive attachment actions is not foregrounded in contemporary parent-infant research although such clarification will promote greater understanding of any relational difficulties subsequent to adversity.

Defensive responding following orientation to threat and approach behaviour for connection

Studies on the active and passive defensive responses observed through electrical or chemical stimulation of the PAG (e.g. [48]) miss out, by their nature, the definition of how these responses are generated naturally. However, the importance of the SC in combining sensory information in such a way that the PAG is activated to initiate flight in response to threat is described in a study of mice exposed to looming stimuli [44]. Activity of glutamatergic neurons in the deep layers of the SC reaches a level at which the dorsal PAG is activated and flight is stimulated. Nevertheless, Dean et al [43] reported a range of defensive responses to stimulation of the SC which was apparently independent of spread to the adjacent PAG. This is important clinically because our experience is that orientation to threat engages rudimentary muscle tension in ways which would facilitate movement for orienting (e.g. neck tension for movements of the head), defence (e.g. tightening of the muscles of the arms for the creation of a barrier through pushing), and attachment (e.g. tension preparatory to reaching movements of the arms). Disruption of the rhythm and synchrony of early gaze communications when there is impaired bonding or attachment shock will alter the muscular tension that prepares the infant for the movement of reaching out. Non-specific bracing and pre-movement impulses, whether for connection or withdrawal, arise just before the affective and fuller defensive responses of fight, flight or freeze mediated by circuits through the PAG. As tension level changes preparatory to orienting and defensive movements appear clinically to precede the affective response we have put the "T" for orienting, pre-defensive, or pre-connection tensions between the "O" of orienting and the "A" of affect in the OTAS sequence described further below.

The rapid sensorimotor orienting sequences direct gaze and approach movements and precede affect, vocalisations, and the initiation of more complex seeking behaviours which then unfold towards the attachment figure. The micro-gestural patterns of infants serve to actively direct the mother or caregiver [17] and the newborn's delicately organised sensorimotor movement patterns suggest that human infants are born to participate in a relationally intentional dialogue of movement [41]. These movements, it is suggested here, are based in orienting approach movements whose fundamental substrate lies in the SC and their motor or pre-motor outputs. The sensorimotor dialogue unfolds as the infant begins to orient towards or away from mother/caregiver and a pattern of expressive micro-movements is visible in the head, face and eyes during the first four weeks after birth [49]. These delicately coordinated movements may be seen as an early form of expressive orienting providing a relational platform for bonding and attachment.

Heightened affective moments, both positive and negative, promote learning through enhanced salience and serve to organise patterns of response. Early bonding and attachment experiences have lifelong consequences in shaping emotional strengths and vulnerabilities [25–27] and early neglect, notably during the first two years of life, has a profound impact on the organisation and function of developing brain systems [31]. The infant's social and emotional experiences in relationship help to support the complex regulatory nature of affective states [50] and provide a scaffold for the maturation of neural organisation.

Affective response

As we have seen, the infant's attachment to the mother is characterised by the seeking of proximity to her and by distress when there is separation from her [39]. Nursing by the mother is important in establishing the multisensory linking that guides the infant's subsequent seeking of her; olfactory cues are dominant in the rat while visual cues, the mother's face and facial expression, are more important to the human infant. Thus, the second component of the brainstem-based innate self-other connection system is the basic mammalian affect system of the midbrain and hypothalamus as described by Panksepp [10]. This can introduce positive affects such as PLAY/joy into contact but can also lead to FEAR, GRIEF and RAGE. Shame, as an advanced form of separation distress, is included here as a basic affect [12] with an action urge to hide and with visceral emotional distress engaging the nociceptive functions of the PAG and hypothalamus. Because these brain structures devcelop early the infant can experience fear, rage, grief, and shame within the primary caregiving relationship. Also the positive affective responses to sensory stimuli, such as mother's voice, are mediated by the PAG and its opiate receptors responsive to social engagement [22].

Both Stern [17] and Trevarthen [49] offered ways of exploring and understanding human relationships from birth which included the rhythm and synchrony of affective communications. A few moments following birth babies have been known to focus their gaze with intense interest at the mouth and eyes of the maternal caregiver while simultaneously making delicate hand gestures and sharing small affect-laden vocal sounds. By around two months they grow more intensely interested in and responsive to the quality and tone of affective interactions [50]. During simulation of the classic 'still-face' experiments [42] the baby shows a range of responses which include: actively turning away from contact, physical agitation, withdrawal as the body appears to lose vitality, and facial expressions of confusion and distress. Similar conflicted orienting patterns may be seen in adults with histories of early attachment disruptions. The importance of the SC acting in conjunction with the PAG for the affectively-loaded turning towards or away from another person is then clear.

Templates for disturbances within relationships can be established early as the internal working models (IWMs) described by Bowlby [51]. These orienting-tension-affect-seeking sequences can be triggered later in life by contacts that share some specific quality with the early experience. Although these IWMs are often viewed from the standpoint of their cortical/cognitive components the focus here is on the brainstem substrates that have been delineated in infancy. Considering the different basic affects generated in the PAG and hypothalamus allows us to consider some examples. When GRIEF has been dominant in early attachments subsequent relationships may be imbued with sadness, pessimism, disappointment or despair. When there is FEAR that any relationship will end in grief the preoccupation may be with the inevitable ending and there will be constant anxiety and insecurity about what will go wrong. When RAGE is dominant there can be dismissiveness, sarcasm, belittling, and a general refusal to acknowledge the importance of any attachment. Shame leads to an avoidance, a hiding away, even within a relationship, as the intrinsic sense of worthlessness reduces the capacity for recognition of needs to which there might otherwise be some sense of entitlement [12]. Compound affects lead to even more complicated interferences with the relational experience; for example, FEAR and RAGE together give rise to behaviours that are testing of the relationship, simultaneously pushing away while fearing the eventual GRIEF when those actions are successful in provoking the feared response. Such pain also occurs when there have been disorganised attachments in early life and different affects are readily triggered in complex compounds in response to complicated communications. Adult attachment patterns can be understood in terms of the habitual affective responses to the orientation within an interaction. For example, when there are simultaneous sequences for approach with CARE/Nurturing and withdrawal with FEAR there is a conflict at a midbrain level which is not easily discerned through a therapeutic approach based in top-down cognitive control concepts.

Neglect, the lack of sensitively-attuned, appropriately-timed, repetitive nurturing experiences, gives rise to a different pattern of stress/threat responding, when compared with abusive experiences, in developing brain systems [26]. Emotional neglect sufficiently severe that it promotes dissociative responses is perhaps less compounded by amnesia when there are no episodes of terror on top of the continual lack of affection and care. We consider below the possible additional role of the projections from the dorsal raphe nucleus in the severe isolation of emotional neglect in infancy. Overall our working hypothesis is that if the anatomical systems are in place and the neurochemicals are available then the impact of early adversity can be overcome by a counteractive environment that is safe and predictable and, if necessary, by developmentally-sensitive therapeutic interventions.

Happy or unhappy seeking of connection: the polyvalent mesolimbic system

The third main component of the brainstem-based innate self-other connection system is the SEEKING disposition and the different conditions within which it can function, depending on environmental factors leading to separation distress [52] or shame [12]. The mesolimbic dopamine system (ML-DA) drives exploratory and goal-directed behaviour through dopamine (DA)-promoted oscillations in basal-ganglia-thalamocortical circuits, activity which is reduced in depressive disorders. Addictions are largely dependent on appetitive memories and a compulsive determination to reinstate a non-dysphoric or even euphoric condition [32]. High extracellular dopamine concentrations induce euphoric states while low extracellular dopamine concentrations are associated with aversive states [53]. Normal seeking of attachment frequently requires something between these extremes and the urge to attach is considered here as the valenced state of drive and motivation towards relational connection which is based in the ML-DA and in the thalamo-cortical responses to its activations. Anaclitic depression resulting from early and traumatic attachment disruptions likely is a manifestation of altered SEEKING function in later life [52]. Feldman [54] has presented a comprehensive and detailed review of the neurobiology of human attachments which centres on the interaction of the ventral and dorsal striatal dopamine systems and the pivotal role of the neuropeptide oxytocin in the learning relevant to bonding. Oxytocin is co-active with dopamine in the nucleus accumbens not only for the internalisation of rewarding interactions with another person but also for the amygdala-mediated social actions appropriate to the relationship as it is remembered. In utero an “Intrinsic Motive Formation” [22] arising in the brainstem underlies organised, intentional movements of the fetus even before connection with the outside world. The infant is born ready to respond with movement to the social encounters of the outside world, including the ability to disengage from them through gaze aversion [55].

Although dopamine neurons of the medial amygdala are involved in approach for exploration or avoidance of a threat [56] it is the nigrostriatal dopamine system which mediates the organised approach behaviours required for connection/attachment and defensive responding. The basal ganglia reptilian complex described by MacLean [57] enacts movements through the release of action sequences [58]. Clinically, there may be a discrepancy between the activation of the motivational and the movement systems. In some post-traumatic states there is a highly threatened state desperately seeking safety or rescue combined with an inability to make effective movement that is different from a freeze. Also there are states of anger that lead to activation of thinking rather than motion; these may contribute to insomnia and ruminative states. The dorsal striatum is part of a cortico-striato-thalamo-cortical circuitry which can be dysfunctional in obsessive-compulsive disorder [59]. There appears in some patients to be a lack of functional integration of such cortex-based circuits [60] with functionally relevant subcortical circuits through the striatum involved in orienting and defensive behaviours [61]. Repetitive and aroused thinking becomes separated from the affectively-charged experiences at its origin as if the upper-level, cortical, loops have taken on an energetic life of their own.

Bivalence of the mesolimbic dopamine system (ML-DA) was demonstrated [62] in laboratory animals which had part of the system geared to fearful behaviour while another part was still in affiliative mode for relational activity. Watt and Panksepp [52] described different neurochemical states of the ML-DA in separation distress and this leads to our consideration of the ML-DA as polyvalent rather than bivalent, at least in humans. That is, there are gradations of ML-DA activity in response to whether the environment disposes more to affiliative or to defensive behaviours; these reflect the proportion of comfort or discomfort induced by external stimuli. The brain does not have an on/off binary position for peaceful co-existence or defensive responding. There is also a range of neurochemicals other than dopamine which influence the resulting mood: endogenous opioids, cannabinoids, oxytocin, for example. This complexity confers an adaptability for an environment in which there are many people with whom we have varying levels of felt safety or felt threat; in which the temperature and the noise vary quickly and intensely; and in which we may be simultaneously thinking of rewarding or painful relationships. Thus the SEEKING of attachment can take on many affective forms, even without PAG/hypothalamus inputs. It is likely that the ML-DA is also instrumental, in animals, for hunting so we are extending the proposed polyvalence of the system to not only cover the many forms of attachment SEEKING that are positive but also those that are harmful to others. For example, predatory rage may be affectively coloured with arrogance when the self is felt to be superior and deserving. Also, rage derived from the protest phase of separation distress is a switch from the perception of needs not being met to the focus on the needs being justified and the blaming of others. In this example, the pain of separation has triggered protest which is self-focused but the subsequent defensive rage is other-focused; “you are not doing enough to meet my justifiable needs”. If this perspective is combined with a grandiose valuation of the self, perhaps itself an adaptive or compensatory response to neglect, there emerges an increased rage which is other-focused. The attacking behaviours have moved beyond the purely defensive response to the immediate pain of abandonment into more complex behavioural, affective and cognitive interactional structures.

Compassion and other positive affects

The more complex states of mind with fine cognitive detail and emotional nuamce contributing to subtlety in communication are often rightly to the fore in psychotherapy. The higher order functions of the self are, nevertheless, often coloured by deeper level activations such as those which occur with triggered negative affects. Likewise, it is argued here, positive affects such as CARE/Nurturance can also engage the SEEKING system so that drive and motivation are energised in the service of personal goals other than freedom from fear or rage or grief or shame. Watt & Panksepp [52] describe hopefulness as a willingness to endure and struggle with adversity and to pursue rewarding activities in the face of adversity, a motivational state that likely has a substrate in a positively valenced ML-DA. Gilbert [63] defines compassion as an essential kindness which combines an awareness of the suffering of oneself and others with a an intention to relieve that suffering. The wish that all beings be freed from suffering therefore has an outward-loooking drive and a mixed-valence state of empathy for the distress of others recruits activation within the nucleus accumbens [64]. However, one brain imaging study of compassion which showed involvement of the midbrain and hypothalamus, in addition to areas of cortex, did not find involvement of the nucleus accumbens [65]. Positively-valenced states of the mesolimbic and mesocortical dopamine projections may confer a feeling of energy and drive onto the sense of self as they are key components of the cortical-subcortical midline systems of the self [66]. Positive self-energy may be a felt experience from the clearing of negative affects and the re-valencing of the ML-DA as attachment disruptions are resolved. Nevertheless, Gilbert[67] cautions against an over-stimulation of the drive system and encourages balance with the social safeness system. In the brainstem-based model, caring and safeness are considered to be dependent on circuitry through the dorsal and ventral PAG, respectively, with neurochemical influences favouring positive valence on ascending systems to thalamus, basal ganglia, and cortex.

Although we are conceptualising the SEEKING system as energising the fundamental urge to attach we propose that the brainstem's interface between the external world and the individual interacting with it represents the most fundamental capacity for self-other connection. The brainstem-based interface develops specific orienting patterns, sometimes conflicted and sometimes affectively-informed, for rapid reactions to particular relational stimuli. The midbrain information hub can process cortical efference [68] and turn it into motor and autonomic output through links with subcortical and spinal cord mechanisms.

Key implications of damage and disruption to the brainstem-based self-other connection system for treatment of developmental trauma

The SC form a powerful midbrain centre for processing multisensory integration as they contain topographical maps of the visual, auditory and somatosensory systems [38,69]. With their inputs from many cortical and subcortical areas they constitute a hub of widespread networks which are not fully formed and functioning in the newborn's brain but which develop and mature in response to rich sensory experiences [70]. As the development and maturation of collicular networks involved in multisensory integration are experience-dependent, and experience-sensitive, these networks likely contribute to the sensory processing difficulties in young children who have suffered ill-effects from prenatal exposure to alchohol and drugs. Deficits in sensory processing often leave children hypersensitive or hyposensitive to a range of sensory cues, giving rise to auditory, tactile and proprioceptive difficulties. For example, prenatal exposure to the anticonvulsant valproic acid induces deficits in colliculi-dependent behaviours [71]. In the absence of sensory-rich bonding and relational experiences the infant may fail to develop the full capacity for mature sensory integration and suffer the interactional consequences of this failure. Thus, abnormal functional development of the SC may contribute to relational and other difficulties in children whose sensory processing problems are a direct result of prenatal and postnatal adversity. The alignment of visual and tactile maps in the SC [72] creates a sensitivity to mother's face and allows for the early detection of micro head, eye and mouth movements. The baby is innately primed to recognise human faces at birth and to seek eye contact with others and has the capacity to turn towards or away from these depending on the collicular activations. During the third trimester the SC have the functional maturity that supports some control of eye movements and facial expressions [72] and they contribute to the motor responses to relational stimuli in neonates. The SC can therefore be seen as a brainstem structure involved in the development of early relational communications and social interactions, the basis of an innate connection system. Their role in the development of subcortical and cortical structures and functions essential for optimal social communication indicates a potential significance for the pathogenesis of autistic spectrum disorders as has been proposed in an extensive analysis by Jure [30].

Shock, horror, memory – and neurotransmitter systems ascending from the brainstem

Working clinically with hypothesised brainstem sequences and patterns stored as a result of prior experiences of attachment disruption or trauma has led to the description here of two types of shock – and of course there may be more depending on the type of horror encountered. A high-energy impact shock which occurs before the affective response is hypothesised to arise from the innate alarm system [73,74] and therefore to be mediated by the locus coeruleus and its widespread noradrenergic innervation of spinal cord, thalamus, and cortex. The second type of shock occurs with sudden and overwhelming affect and is hypothesised to be mediated by the structures of the defensive system, the PAG and hypothalamus, and may be the precursor to neurochemical dissociation.

The SC constitute a fundamental component of the innate alarm system [73,74] which rapidly responds to threatening stimuli and relational adversities so severe as to be experienced as horrifying or shocking. The enhanced response to direct gaze in complex PTSD [75] may indicate not only a brainstem response to threat but a sensitisation of an innate self-other connection system mediating shock and horror. The two types of shock described here, pre-affective and affective, share a thoroughly unpleasant activation which is sudden in onset, carries a deep repugnance towards the originating stimulus, and implies the presence of something which is to be turned away from for relief even as it fixes attention. The attentional capture of the pre-affective shock involves a hgh level of tension and a physiological activation which is disturbing without any specific affect such as fear or loathing being identifiable. In the second, the affective, type of shock, there is an experience of an overwhelmingly distressing state in which affects such as terror and horrified repugnance dominate. Sometimes the activation is felt as a frantic restlessness which may indicate an excessive stimulation of the SC/PAG. Horror which feels frozen may then be filtered through secondary affective perspectives of fear, rage, grief or shame. Overall it is clear that the anatomical substrates of the innate systems for connection, alarm, and defensive responding are closely linked for rapidity of response and can have aspects of their function overlap under conditions of adversity.

The locus coeruleus (LC) has been implicated in the arousal of orienting to a novel stimulus, (some of this research was summarised in Corrigan et al. [76]), and Scaer [77] has emphasised the LC in the physiological origins of traumatic experiences that fail to resolve spontaneously. When there are shock and horror involved it would be expected that the ascending tracts to the thalamus and cortex prime the brain to focus attentional capabilities on the most salient danger. The LC receives direct inputs from the medulla and hypothalamus but also from adjacent regions that have inputs from prefrontal cortex, amygdala and dorsal raphe [78], suggesting a capacity for integration of exteroceptive, sensory, and interoceptive, visceral, information essential in the learning of emotional memories [79]. There is also a functional adjustment of the levels at which sensory stimuli are attended to, important for determining which are to be remembered, and for the overall level of alertness and arousal. Some authors differentiate alerting as a readiness to respond from orienting to a stimulus, and both of these involve the LC [80].The projections from the LC to the amygdala and prefrontal cortex promote flexibility in behavioural responses to fluctuating levels of threat [81]: when the threat is severe and LC discharge is increased then the function of the prefrontal cortex is impaired in favour of more posterior areas, including the primary motor cortex. People under severe stress are then less able to think clearly but more able to react with action – until the LC activation is so high that behaviour is completely arrested [82,83]. The pedunculopontine tegmental nucleus, which receives inputs from the SC and the LC, may be a critical structure in preventing impulsive responding that could be damaging [84]. When following fight and flight impulses, by the release of subcortical circuits through the basal ganglia [61], could reduce the risk of survival the pedunculopontine may be the brake within the basal ganglia circuitry [84]. Action-outcome learning can occur at the pedunculopontine level – well below the level of the limbic system [84].

Activation of the Innate Alarm System (IAS, [85]) following a shocking stimulus engages the pulvinar and the amygdala as there is no direct projection from the SC to the LC. There are motor projections from the LC to the spinal cord so some of the tension seen in response to an attachment or threat shock could be initiated here rather than in the deep layers of the SC. There are projections from the LC to autonomic nuclei which enhance sympathetic and decrease parasympathetic responses so there can be an immediate automic nervous system impact before involvement of the PAG. The response to a subliminal visual stimulus demonstrates that the IAS [73] is sensitised in PTSD [74,85], an important demonstration of brainstem learning. Some of this sensitisation by adversity can be expressed in projections from the LC to the SC as mice exposed to repeated stress show enhanced responses to looming stimuli [86]. Stress activates LC-SC projections involving adrenergic receptors and is associated with anxiety-like behaviours in addition to those increased reactions to looming [86]. Curiously, those looming-evoked responses can be weakened by gentle handling of the laboratory mice over the week before the presentation of the overhead threat [87]. Perhaps this functions as a stress-relieving massage which modifies the perception of the degree of threat/safety of the environment. The LC has receptors for corticotropin-releasing factor (CRF) which may mediate the impact of stress on receptor sensitivity and neurotransmitter function in human PTSD [88].

Aloneness, helplessness, hopelessness and worthlessness are experienced to varying degress and in varying combinations with most trauma that does not resolve spontaneously so it is noteworthy that as we track a stimulus anatomically down through the layers of the SC, through the active defensive response areas of the dorsal/lateral PAG, through the passive defensive response areas of the ventrolateral PAG, we arrive at the dorsal raphe nucleus (DRN) which is situated in the ventral part of the PAG and receives afferents from the ventrolateral PAG in addition to those from other brainstem areas, lateral habenula, hypothalamus and medial prefrontal cortex. Efferents from the DRN project to other brainstem areas and to many areas of cortex, nucleus accumbens, amygdala, hippocampus and thalamus [89]. The serotonergic projections influence the sensitivity of structures engaged in social interactions, as well as in defensive responses, and social deficits can be overcome by stimulation of DRN neurons projecting to 5-HT receptors in the nucleus accumbens in a mouse model of autism [90]. The serotoninergic projections of the DRN also modify the defensive respone to overhead looming [91] discussed above.

However it is dopaminergic neurons of the DRN that have been specifically linked with loneliness in a mouse model [92]. While activation of the dopamine neurons of the ventral tegmental area is involved in socially rewarding interactions, activation of the DRN dopamine neurons, in the absence of a target for such rewarding interaction, mediates an aversive state [92]. Perhaps the dopaminergic projections of the DRN contribute to the agonising loneliness which is at the heart of many traumatic experiences. Different experiences of painful aloneness and abandonment may be derived from different activations within the ascending systems of the brainstem.

The zona incerta (ZI) as a critical hub for information processing

While the authors have been greatly influenced by the concept of the efference cascade [68], the effector output of a huge number of cortical neurons being enacted through a relatively small group of brainstem neurons, there is the possibility of areas additional to the SC also being instrumental in the stored deep-brain response to a trauma memory. One such area is the zona incerta (ZI) which can integrate exteroceptive and interoceptive experience [93] through its extensive connectivity with cortical, subcortical, brainstem and spinal cord areas. The ZI has the widespread connectivity through different levels of the nervous system to allow it to be a hub for the integration of responses to aversive stimuli [94], including those arising from a trauma memory or disturbing attachment experience. More specifically, the ZI modifies the manifest active defensive behaviours of the PAG [95] and is implicated in conditioned fear memory [96]. The ZI has four sectors defined according to the neurochemistry of their different cell structures: rostral, caudal, dorsal and ventral [93]. When the contents of consciousness are sufficiently activating that they provoke a continuing autonomic, affective, cognitive and motor response it is possible that the ZI provides an integrative function for the disparate elements. The ventral ZI projects to the intermediate and deep motor output layers of the SC associated with gaze direction [97] so the integrative capacity may extend to therapies reliant on gaze fixation such as Brainspotting [76] and the Comprehensive Resource Model [34]. The connectivity of the ZI with frontal eye fields and collicular areas for saccadic eye movements may also make it of relevance to Eye Movement Desensitization and Reprocessing [98] which, in its original form, relied on the induction of eye movements for the reprocessing of trauma memories. Selective optogenetic activation of the ZI can lead to immediate binge eating [99] which is of interest when binge eating is sometimes used as an affect regulator in post-traumatic disorders.

The neomammalian brain

The concept of the triune brain with a paleomammalian limbic system inserted between a reptilian basal ganglia responsible for species-typical behavioural routines and a neomammalian cortex which can question the structure and function of the cosmos was developed by MacLean in the 1950s [57]. The model is often used in trauma therapy to explain the disparity between what can be held “in the body” and what can be readily articulated in words and descriptive concepts. The brainstem is frequently presented as a component of the reptilian brain even though that was not part of MacLean’s original proposal. In fact, MacLean [100] includes brainstem and neocerebellar structures *connected to the neocortex* as part of the neomammalian brain capable of problem solving and learning.

Brain imaging studies of emotion demonstrate the importance of a specific area of medial prefrontal cortex incorporating parts of Brodmann’s areas 9 and 32 which is co-activated with the hypothalamus and PAG [101]. However, anatomical work demonstrates that BA25 also has significant projections to PAG and hypothalamus and to brainstem autonomic regulatory nuclei [102]. It is interesting to note that BA 32, like BA9, is an isocortical area [103] while Brodmann area 25 is a periarchicortical area (a transition between allocortex and proisocortex). Even if the human PAG does not have major structural differences when compared with other primate brains the connectivity with neocortical areas 9 and 32 [104] would place it in the neomammalian brain as defined by MacLean [51,90]. Projections from BA 25 in the limbic cingulate cortex would provide the PAG with additional modulators – but also with potential conflicts between the rational and sensible (from BA 32) and the emotionally-charged (from BA 25), life dilemmas not confined to psychotherapy sessions.

A similar case could be argued for the SC and their connections with neocortical eye fields and would better accord with the view of Panksepp [6] that the SC is where “we begin to get a glimmer of the first evolutionary appearance of a sophisticated representation of self" (10; page 77). The brainstem origins of the highly evolved self of the human brain can still be regarded as neomammalian in triune brain terms because of the neocortical connections. Bringing central executive monitoring [80], and other prefrontal functioning, to limbic system and brainstem responses residual from relational and other adversity is bypassing the reptilian brain for reasons of efficiency while remaining fully neomammalian in scope.

Deep Brain Reorienting: clinical applications of the innate connection, alarm, and defensive systems model in orienting-tension-affect-seeking (OTAS) sequences for trauma memories and maladaptive relational responses

This paper has outlined the theoretical basis for a psychotherapeutic approach termed Deep Brain Reorienting (DBR). It is not possible to give here a full description of the treatment process and there is as yet no clinical evidence to support its use. Therefore, what follows is a brief outline intended to demonstrate how the theory has been applied in clinical situations rather than being a "how to" guide. Underlying principles are similar to those of some other body-based apporoaches. For example, Kurtz [105] stresses the importance of mindfulness of the body in accessing core states; the organic nature of human emotional healing; the healing interaction of therapist and client; the tracking of the flow of the body's responses during processing; and the attention to evoked, spontaneous experience as a guide to underlying conflict. The difference with DBR is that the aim is to use a present-day trigger to evoke a specific sequence, hypothesised to be based in the brainstem structures outlined above, and to bring focused, mindful attention to it. Also, in DBR, it is very important to identify the orienting tension, which is often fleeting and transitory unless specifically sought, to use as an anchor in the present day to avoid overwhelm and dissociation. Attention to the likely physiological sequencing in the brainstem of the components of self-other connection, alarm, and defensive responses allows transformation of responses that have been established many years previously, perhaps even before there were words available to describe them. The early ontogenetic maturation of the brainstem confers the ability for complex orienting and affective responding – and for the learning of interactional templates – long before there is an advanced cortical capacity for emotion regulation or, indeed, before there are words for concept construction and analysis. The templates are accessed clinically, even decades later, through subtle body responses to specific cues in interactions – or through states of body activation triggered by mnemonic cues. Mindfully attending to the template sequences allows spontaneous re-orienting to aspects that have become dysfunctional and clears patterns of response that no longer serve, having been learned in an early attachment that had specific affective characteristics or in a traumatic situation.

We define OTAS sequences on the basis of the neuroanatomy and neurophysiology outlined above. First there is orienting (O); this can be to an external stimulus such as the presence of a significant other person, or it can be to an internal cascade relating to the contents of consciousness. For the latter the OTAS sequence can be initiated by inviting the client or patient to attend to the internal image of the person to whom there is a conflicted attachment. Avoiding the tendency to get into the narrative around the person or to get into "upper level" thinking about the situation allows the deeper sequences to be accessed. This can be achieved by using a remembered instance of a facial expression, a gesture or posture, or a way of expressing verbally, that immediately captures the attention. The resulting tension (T) in the face and neck is carefully tracked, in ultra-slow-motion, as the orienting tension provides not only the next part of the sequence but also provides grounding sufficient to avoid affective overwhelm and/or dissociation. Particular attention is paid to the neck muscles as these are found to express tension, often fleetingly, in accordance with the animal work of Corneil [106]. There then emerges the tension conferred by the incipient approach (for connection) or defensive response; bracing in certain muscle groups. This deep attention to tension states provides information on the pre-affective components of the trauma memory, the parts that are otherwise readily swamped by the affect, especially when it is highly distressing. Respiratory changes may also be observed before the emotional change occurs and these are presumed to be secondary to PAG activation of relevant brainstem nuclei [107]. When the O and T parts of the sequence are clarified then the affect (A) provoked by the person (or by the trauma memory) and associated with that specific orienting-tension pattern is identified. Here it will usually become clear if there are parallel sequences holding conflicting tendencies, for example, approach and defend urges occurring simultaneously and with different affective colouring, perhaps care/nurturing and fear. Reaching movements in attachment interactions have many cortical and subcortical substrates but the fundamental activation of these, especially when they are not tightly controlled through conscious awareness, is in the deep layers of the SC [108,109]. Shock and horror expressions, as are seen with some trauma memories, also occur before and after the affect comes into awareness and can be identified before emergence of the valenced SEEKING (S) state. Finally, the affectively-charged cognition, assumed to be dependent on cortical processing, emerges; this may form the start of a separate sequence in the brainstem or may contribute to the processing of the entire OTAS information file.

Only this brief outline is supplied here as a full account of the intricacies and complexities of individual human responses is beyond the scope of this article. Deep Brain Reorienting does not require alternating bilateral stimulation (ABS) such as that used in EMDR [98] but sometimes the processing is deepened by the use of tactile, auditory, or photic ABS. Experimental evidence in support of ABS working at the collicular level has recently emerged [110] and supports its use in DBR. Careful processing of OTAS sequences allows attention to pre-affective and affective shock and promotes a thorough resolution of hitherto unresolved adverse experiences stored in the nervous system. The change in the self's perspective on the self has a different quality when the the processing of past traumatic events and relational conflicts is carried out from a "collicular" (i.e. circuits hypothesised to be based in the "where am I in relation to the world around me?") perspective. This spontaneously emerging new perspective is what instantiates the deep brain reorienting arising from the processing. The clinical separation of components of sequences established early in life in response to attachment stimuli, and a similar decatenation of unresolved trauma response sequences, promotes flexibility in responding and allows healing of deep emotional woumds.

Deep Brain Reorienting: the clinical sequences identified in triggered trauma and attachment memories (with putative key brain regions sequentially involved in parentheses).

- Orienting: to what is activating (Superior Colliculi (SC) - superficial layers).
- Tension: in face and neck area in response to that orienting (SC – intermediate/deep layers).
- Shock: pre-affective – innate alarm system (SC – amygdala – locus coeruleus (LC)).
- Respiration: sudden change in breathing (Periaqueductal Gray (PAG)).
- Tension: pre-defensive (SC – deep layers; PAG).
- Affect: visceral, respiratory and emotional components (PAG/hypothalamus).
- Shock: affective; when the response is sudden and overwhelming (PAG/hypothalamus).
- Dissociation: high or low arousal dissociative response to overwhelming affect (PAG/hypothalamus).
- Abandonment/isolation pain (VLPAG/DRN).
- Seeking: drive and motivational changes – and their valence (ML-DA).

- Cognition: thoughts relevant to the activation (Cortex).
- Perspective: the way in which the self sees its self (Subcortical-cortical midline systems of the self, including a deep SC-PAG-thalamus-cortex axis).

Hypotheses are designed to be tested and those that have a bearing on clinical practice are most in need of careful evaluation. Notwithstanding the difficulties in researching new, non-cognitive, non-behavioural approaches [1,2], it is hoped that the treatment approach outlined here will be studied in terms of clinical outcomes and in terms of changes identifiable through neuroimaging. The clinical evaluation of a treatment approach which does not rely on meaning-making, although that may occur spontaneously, and which is based on mindful tracking of sequences of evoked responses thought to be held in circuits through the brainstem, is important conceptually and in terms of effective health care provisions.

Declaration of Competing Interest

Funding sources: none. However, both authors have received fees and/or expenses for providing training in the clinical approach Deep Brain Reorienting which is outlined at the end of the paper.

References

[1] Corrigan FM, Hull AM. The emerging psychological trauma paradigm: an overview of the challenge to current models of mental disorder and their treatment. Int J Cogn Analytic Therapy Relational Mental Health 2018;2:121–46.
[2] Corrigan FM, Hull AM. Recognition of the neuobiological insults imosed by complex trauma and the implications for psychotherapeutic interventions. BJPsych Bull 2015;39:79–86.
[3] Solms M. The scientific understanding of psychoanalysis. BJPsych Int 2018;15:5–8.
[4] Guskjolen A, Kenney JW, de la Parra J, Yeung BA, Josselyn SA, Frankland PW. Curr Biol 2018;28:2283–90.
[5] Triplett JW. Molecular guidance of retinotopic map development in the midbrain. Curr Opin Neurobiol 2014;24:7–12.
[6] Shang S, Liu Z, Chen Z, Shi Y, Wang Q, Liu S, et al. A parvalbumin-positive excitatory visual pathway to trigger fear responses in mice. Science 2015:1472–7.
[7] Yuan, T-F., Su, H. Fear learning through the two visual systems, a commentary on: “A parvalbumin-positive excitatory visual pathway to trigger fear responses in mice”. Front Neural Circuits, 9, 1-3.
[8] Davis KL, Panksepp J. The emotional foundations of personality. New York: WW Norton; 2018.
[9] Lyons-Ruth K, Dutra L, Schuder MR, Bianchi I. From infant attachment disorganization to adult dissociation: relational adaptations or traumatic experiences? Psychiat Clin North Am 2006;29:63–86.
[10] Panksepp J. Affective Neuroscience: the foundations of human and animal emotions. New York: Oxford University Press; 1998.
[11] Corrigan FM. Shame and the vestigial midbrain urge to withdraw pp. In: Lanius UF, Paulsen S, Corrigan FM, editors. Neurobiology and treatment of trau matic dissociation: towards an embodied self. New York: Springer; 2014. p. 173–92.
[12] Corrigan FM, Elkin-Cleary E. Shame as an evolved basic affect – approaches to it within the Comprehensive Resource Model (CRM). Med Hypotheses 2018;119:91–7.
[13] Bowlby J. Attachment and loss. Vol. 1: Attachment. Basic Books, New York, 1969.
[14] Bowlby J. Attachment and loss. Vol. 2: Separation, anxiety and anger. Basic Books, New York, 1973.
[15] Bowlby J. Attachment and Loss. Vol. 3: Loss, Sadness and Depression. Basic Books, New York, 1981.
[16] Stern D. The first relationship: infant and mother. Cambridge, MA: Harvard University Press; 2002.
[17] Stern D. The interpersonal world of the infant. London: Karnac; 1998.
[18] Stern D. Diary of a baby. New York: Basic Books; 1990.
[19] Malloch S, Trevarthen C. Communicative musicality: exploring the basis of human companionship. New York: Oxford University Press; 2009.
[20] Trevarthen C, Dellafield-Butt J. The child’s curriculum. Oxford: Oxford University Press; 2018.
[21] Trevarthen C. The affectionate, intersubjective intelligence of the infant and its innate motives for relational mental health. Int J CAT RMH 2017;1(1):11–52.
[22] Panksepp J, Trevarthen C. The neuroscience of emotion. In S. Malloch and C. Trevarthen, Communicative Musicality, pp. 105–146. Oxford University Press: New York, 2009.
[23] Schore AN. Affect regulation and the repair of the self. New York: WW Norton; 2003.
[24] Perry B, Szalavitz M. The Boy Who Was Raised as a Dog: And Other Stories from a Child Psychiatrist’s Notebook Revised and Updated. 3rd Edition. Basic Books: New York, 2017.
[25] Schore AN. Affect regulation and the origin of the self: the neurobiology of emotional development. New Jersey: Lawrence Erlbaum Associates; 1994.
[26] Perry BD. Child Maltreatment: a neurodevelopmental perspective on the role of trauma and neglect in psychopathology. In: T. Beauchaine, S. Hinshaw, eds., Child and Adolescent Psychopathology, pp.93–129, John Wiley & Sons, 2008.
[27] Perry BD. The Neurosequential Model: a developmentally-sensitive, neuroscience informed approach to clinical problem solving. In: J. Mitchell, J. Tucci, E. Tronick, eds., For: The Handbook of Therapeutic Child Care: Evidence-Informed Approaches to Working with Traumatised Children in Foster, Relative and Adoptive Care. Jessica Kingsley, London, 2019.
[28] Braithwaite EC, Pickles A, Sharp H, et al. Maternal prenatal cortisol predicts infant negative emotionality in a sex-dependent manner. Physiol Behav 2017;175:31–6.
[29] Zhang W, Finik J, Dana K, Glover V, Ham J, Nomura Y. Prenatal depression and infant temperament: the moderating role of placental gene expression. Infancy 2018;23:211–31.
[30] Jure R. Autism pathogenesis: the superior colliculus. Front Neurosci 2019;12:1029.
[31] Trevarthen C. Action and emotion in the development of the human self, its sociability and cultural intelligence: why infants have feelings like ours. In: Nadel J, Muir D, editors. Emotional development. Oxford: Oxford University Press; 2005. p. 61–91.
[32] Alcaro A, Panksepp J. The SEEKING mind: primal neuro-affective substrates for appetitive incentive states and their pathological dynamics in addictions and depression. Neurosci Behav Rev 2011;35:1805–20.
[33] Corrigan FM, Wilson A, Fay D. Attachment and attachment repair. In: Lanius UF, Paulsen S, Corrigan FM, editors. Neurobiology and Treatment of Traumatic Dissociation: Towards an Embodied Self. New York: Springer; 2014. p. 193–212.
[34] Schwarz L, Corrigan FM, Hull A, Raju R. The comprehensive resource model: effective therapeutic techniques for the healing of complex trauma. Abingdon, Oxon: Routledge; 2016.
[35] Delafield-Butt JT, Gangopadhyay N. Sensorimotor intentionality: the origins of intentionality in prospective agent action. Dev Rev 2013;33:399–425.
[36] Marx V, Nagy E. Fetal behaviour responses to maternal touch. PLoS ONE 2015 June;10(6):8. https://doi.org/10.1371/journal.pone.0129118. Online Publication.
[37] Moon CM, Fifer WP. The Fetus: Evidence of transnatal learning. J Perinatol 2000;20:S36–43.
[38] Meredith MA, Wallace MT, Stein BE. Visual, auditory and somatosensory convergence in output neurons of the cat superior colliculus: multisensory properties of the tecto-reticulo-spinal projection. Exp Brain Res 1992;88:181–6.
[39] Polan HJ, Hofer MA. Psychobiological origins of infant attachment and separation responses. In: Cassidy J, Shaver PR, editors. Handbook of attachment: theory, research, and clinical applications. New York: The Guilford Press; 1999. p. 162–80.
[40] Brazelton T, Sparrow D. Touchpoints: birth to three: your child’s emotional and behavioural development. Cambridge, MA: Da Capo Press; 2006.
[41] Brazelton T, Cramer BG. The Earliest Relationships: Parent, Infants and the Drama of Early Attachment, Da Capo Press: Reprint Eds., Cambridge, MA, 1991.
[42] Tronick E, Als H, Adamson L, Wise S, Brazelton TB. The infant’s response to entrapment between contradictory messages in face-to-face interaction. J Am Acad Child Adolesc Psychiatry 1978;17:1–13.
[43] Dean P, Redgrave P, Westby GW. Event or emergency? Two response systems in the mammalian superior colliculus. Trends Neurosci 1989;12:137–47.
[44] Evans DA, Stempel AV, Vale R, Ruehle S, Lefler Y, Branco T. A synaptic threshold mechanism for computing escape decisions. Nature 2018;558:590–4.
[45] Comoli, E. das Neves Favaro, P., Vautrelle, N., Leriche, M., Overton, P.G., Redgrave, P. Segregated anatomical input to sub-regions of the rodent superior colliculus associated with approach and defense. Front Neuroanatomy, 2012, 6, 1–19.
[46] Corrigan FM, Holstege G. Tremor and trauma: the brainstem emotional motor system and recovery from traumatic experience. In: Berceli D, Scaer R. (Eds.), Shake it off naturally: reduce stress, anxiety, and tension with (TRE). CreateSpace Independent Publishing Platform, 2015, pp. 36–54.
[47] Olive I, Tempelmann C, Berthoz A, Heinze H-J. Increased functional connectivity between superior colliculus and brain regions implicated in bodily self-consciousness during the rubber hand illusion. Hum Brain Mapp 2015;36:717–30.
[48] Bandler R, Keay K, Floyd N, Price J. Central circuits mediating patterned autonomic activity during active vs. passive emotional coping. Brain Res Bull 2000;53:95–104.
[49] Trevarthen C, Schaffer HR. Descriptive analyses of infant communication behaviour. Studies in mother-infant interaction. London: Academic Press; 1977. p. 227–70.
[50] Ammaniti M, Ferrari P. Vitality affects in Daniel Stern’s thinking-a psychological and neurobiological perspective. Infant Mental Health J 2013;34:367–75.
[51] Holmes J. John Bowlby and attachment theory. London: Routledge; 2014.
[52] Watt D, Panksepp J. Depression: an evolutionarily conserved mechanism to terminate separation distress? A review of aminergic, peptidergic, and neural network perspectives. Neuropsychoanalysis 2009;11:7–51.
[53] Ikemoto S. Brain reward circuitry beyond the mesolimbic dopamine system: a neurobiological theory. Neurosci Biobehav Rev 2010;35:129–50.
[54] Feldman R. The neurobiology of human attachments. Trends Cogn Sci 2017;21:80–99.
[55] Geva R, Sopher K, Kurtzmann L, Galili G, Feldman R, Kuint J. Neonatal brainstem dysfunction risks infant social engagement. Social Cogn Affective Neurosci 2013;8:158–64.
[56] Miller SM, Marcotulli D, Shen A, Zweifel LS. Divergent medial amygdala projections regulate approach-avoidance conflict behavior. Nat Neurosci 2019;22:565–75.
[57] MacLean PD. Introduction: perspectives on cingulate cortex in the limbic system.

In: Vogt B, Gabriel M, editors. Neurobiology of cingulate cortex and limbic thalamus. Boston: Birkhauser; 1993. p. 1–18.
[58] Aldridge JW, Berridge KC, Rosen AR. Basal ganglia neural mechanisms of natural movement sequences. Can J Physiol Pharmacol 2004;82:732–9.
[59] Li B, Mody M. Cortico-striato-thalamo-cortical circuitry, working memory, and obsessive-compulsive disorder. Front Psychiatry 2016;7:1–3.
[60] Alexander GE, Crutcher MD, DeLong MR. Basal ganglia-thalamocortical circuits: Parallel substrates for motor, oculomotor, "prefrontal" and "limbic" functions. Prog Brain Res 1990;85:119–46.
[61] McHaffie JG, Stanford TR, Stein BE, Coizet V, Redgrave P. Subcortical loops through the basal ganglia. Trends Neurosci 2005;28:401–7.
[62] Reynolds SB, Berridge KC. Emotional environments retune the valence of appetitive versus fearful functions in nucleus accumbens. Nat Neurosci 2008;11:423–5.
[63] Gilbert P. The compassionate mind. London: Constable; 2009.
[64] Ashar YK, Andrews-Hanna JR, Dimidjian S, Wager TD. Empathic care and distress: predictive brain markers and dissociable brain systems. Neuron 2017;94:1263–73.
[65] Immordino-Yang MH, McColl A, Damasio H, Damasio A. Neural correlates of admiration and compassion. PNAS 2009;106:8021–6.
[66] Panksepp J, Northoff G. The trans-species core SELF: the emergence of active cultural and neuro-ecological agents through self-related processing within subcortical-cortical midline networks. Conscious Cogn 2008;18:193–215.
[67] Gilbert P. Introducing compassion-focused therapy. Adv Psychiatr Treat 2009;15:199–208.
[68] Merker B. The efference cascade, consciousness, and its self: naturalizing the first person pivot of action control. Front Psychol 2013;4:501.
[69] Meredith MA, Stein BE. Visual, auditory, and somatosensory convergence on cells in superior colliculus results in multisensory integration. J Neurophysiol 1986;56:640–62.
[70] Cuppini C, Stein BE, Rowland BA. development of the mechanisms governing midbrain multisensory integration. J Neurosci 2018;38:3453–65.
[71] Dendrinos G, Hemelt M, Keller A. Prenatal VPA exposure and changes in sensory processing by the superior colliculus. Front Integr Neurosci 2011;5:68.
[72] Pitti A, Kuniyoshi Y, Quoy M, Gaussier P. Modelling the minimal newborn's intersubjective mind: the visuotopic-somatotopic alignment hypothesis in the superior colliculus. PLoS ONE 2013. https://doi.org/10.1371/journal.pone.0069474.
[73] Liddell BJ, Brown KJ, Kemp AH, Barton MJ, Das P, Peduto A, et al. A direct brainstem-amygdala-cortical 'alarm' system for subliminal signals of fear. NeuroImage 2005;24:235–43.
[74] Lanius RA, Rabellino D, Boyd JE, Harricharan S, Frewen PA, McKinnon MC. The innate alarm system in PTSD: conscious and subconscious processing of threat. Curr Opinion Psychol 2017;14:109–15.
[75] Steuwe C, Daniels JK, Frewen PA, Densmore M, Pannasch S, Beblo T, et al. Effect of direct eye contact in PTSD related to interpersonal trauma: an fMRI study of activation of an innate alarm system. Soc Cognit Affect Neurosci 2014;9:88–97.
[76] Corrigan FM, Grand D, Raju R. Brainspotting: sustained attention, spinothalamic tracts, thalamocortical processing, and the healing of adaptive orientation truncated by traumatic experience. Med Hypotheses 2015;84:384–94.
[77] Scaer R. The trauma spectrum: hidden wounds and human resiliency. New York: W.W. Norton; 2005.
[78] Aston-Jones G, Waterhouse B. Locus coeruleus: from global projection system to adaptive regulation of behavior. Brain Res 2016;1645:75–8.
[79] Venkatraman A, Edlow BL, Immordino-Yang MH. The brainstem in emotion: a review. Front Neuroanat 2017;11:15.
[80] Geva R, Zivan M, Warsha A, Olchik D. Alerting, orienting or executive attention networks: differential pattern of pupil dilations. Front Behav Neurosci 2013;7:1–11.
[81] Uematsu A, Tan BZ, Ycu EA, et al. Modular organization of the brainstem noradrenaline system coordinates opposing learning states. Nat Neurosci 2017;20:1602–11.
[82] Chandler DJ. Evidence for a specialized role of the locus coeruleus noradrenergic system in cortical circuitries and behavioral operations. Brain Res 2016;1641:197–206.
[83] Carter ME, Yizhar O, Chikahisa, et al. Tuning arousal with optogenetic modulation of locus coeruleus neurons. Nat Neurosci 2010;13:1526–33.
[84] Gut NK, Winn P. The pedunculopontine tegmental nucleus – a functional hypothesis from the comparative literature. Mov Disord 2016;31:615–24.
[85] Terpou BA, Densmore M, Thome J, Frewen P, McKinnon MC, Lanius RA. The innate alarm system and subliminal threat presentation in posttraumatic stress disorder: neuroimaging of the midbrain and cerebellum. Chronic Stress 2019;3:1–13.
[86] Li L, Feng X, Zhou Z, et al. Stress accelerates defensive responses to looming in mice and involves a locus-coeruleus-superior colliculus projection. Curr Biol 2018;28:859–71.
[87] Liu X, Chen C, Liu Y, et al. Gentle handling attenuates innate defensive responses to visual threats. Front Behav Neurosci 2018;12:1–10.
[88] Borodovitsyna O, Joshi N, Chandler D. Persistent stress-induced neuroplastic changes in the locus coeruleus/norepinephrine system. Hindawi Neural plasticity, 2018, Article ID 1892570.
[89] Hornung, J-P. Raphe nuclei In: Mai JK, Paxinos G (Eds.), The human nervous system, 3rd ed., Elsevier, Amsterdam, 2012, pp. 401–424.
[90] Walsh JJ, Christoffel DJ, Heifets BD, et al. 5-HT release in nucleus accumbens rescues social deficits in mouse autism model. Nature 2018;560:589–94.
[91] Huang L, Yuan T, Tan M, et al. A retinoraphe projection regulates serotonergic activity and looming-evoked defensive behaviour. Nat Commun 2017;8:14908.
[92] Matthews GA, Nieh EH, Van der Weele CM, et al. Dorsal raphe dopamine neurons represent the experience of social isolation. Cell 2016;164:617–31.
[93] Mitrofanis J. Some certainty for the "zone of uncertainty"? Exploring the function of the zona incerta. Neuroscience 2005;130:1–15.
[94] Essig J, Felsen G. Warning! Dopaminergic modulation of the superior colliculus. Trends Neurosci 2016;39:2–4.
[95] Chou XL, Wang X, Zhang ZG, et al. Inhibitory gain modulation of defense behaviors by zona incerta. Nat Commun 2018;9:1151.
[96] Zhou M, Liu Z, Melin MD, Ng Y, Xu W, Sudhof TC. A central amygdala to zona incerta projection is required for acquisition and remote recall of conditioned fear memory. Nature Neurosci 2018;21:1515–9.
[97] May PJ, Basso MA. Connections between the zona incerta and superior colliculus in the monkey and squirrel. Brain Struct Funct 2018;223:371–90.
[98] Shapiro F. Eye movement desensitization and reprocessing (EMDR) therapy. New York: The Guilford Press; 2018.
[99] Zhang X, van den Pol AN. Rapid binge-like eating and body weight gain driven by zona incerta GABA neuron activation. Science 2017;356:853–9.
[100] MacLean PD. Evolutionary psychiatry and the triune brain. Psychol Med 1985;15:219–21.
[101] Kober H, Barrett LF, Joseph J, Bliss-Moreau E, Lindquist K, Wager TD. Functional grouping and cortical-subcortical interactions in emotion: a meta-analysis of neuroimaging studies. Neuroimage 2008;42:998–1031.
[102] Buchanan SL, Powell DA. Cingulothalamic and prefrontal control of autonomic function. In: Vogt BA, Gabriel M, editors. Neurobiology of cingulate cortex and limbic thalamus. Boston: Birkhauser; 1993. p. 381–414.
[103] Zilles K, Amunts K. Architecture of the cerebral cortex. In: Mai JK, Paxinos G, editors. The human nervous system. 3rd ed.Amsterdam: Elsevier; 2012. p. 836–95.
[104] Price JL. Connections of orbital cortex. In: Zald DH, Rauch SL, editors. The orbitofrontal cortex. Oxford: Oxford University Press; 2006. p. 39–56.
[105] Kurtz R. Body-centered psychotherapy: the Hakomi method. LifeRhythm, Mendocin, CA.
[106] Corneil BD, Munoz DP, Chapman BB, Admans T, Cushing SL. Neuromuscular consequences of reflexive covert orienting. Nat Neurosci 2008;11:13–5.
[107] Subramanian HH, Holstege G. Periaqueductal gray control of breathing. Adv Exp Med Biol 2010;669:353–8.
[108] Linzenbold W, Himmelbach M. Signals from the deep: reach-related activity in the human superior colliculus. J Neurosci 2012;32:13881–8.
[109] Himmelbach M, Linzenbold W, Ilg UJ. Dissociation of reach-related and visual signals in the human superior colliculus. NeuroImage 2013;82:61–7.
[110] Baek J, Lee S, Cho T, Kim SW, Kim M, Yoon Y, et al. Neural circuits underlying a psychotherapeutic regimen for fear disorders. Nature 2019;566:339–43.