Perspective

Autonomic dysregulation and the Window of Tolerance model of the effects of complex emotional trauma

FM Corrigan¹, JJ Fisher² and DJ Nutt³

Abstract
This paper reviews the Window of Tolerance model of the long-term effects of the severe emotional trauma associated with childhood abuse, a model which can also be applied to adult trauma of sufficient severity to cause post-traumatic stress disorder, chronic dysthymic disorders and chronic anxiety disorders. Dysfunctional behaviours such as deliberate self-harm and substance abuse are seen as efforts to regulate an autonomic nervous system which is readily triggered into extreme states by reminders of the original traumatic events. While midbrain areas such as the periaqueductal gray mediate instant defence responses to traumatic events and their memory triggers it is proposed that ascending monoaminergic tracts are implicated in longer-term changes in mood and arousal. An imbalance of ascending dopaminergic tracts may drive rapid fluctuations in level of arousal and in the associated mood, drive and motivation. Animal models of depression frequently use traumatic experiences of pain, isolation or social defeat to induce changes in mesolimbic and mesocortical dopamine systems which may alter prefrontal cortical control of midbrain defence responses. A focus on the pharmacology of the Window of Tolerance could provide advances in drug treatments for promoting emotional regulation in those who are suffering from the chronic sequelae of traumatic experiences.

Keywords
Ascending dopamine systems, autonomic dysregulation, dysfunctional behaviours, trauma, window of tolerance

The psychophysiology of traumatic experience

It has been established that exposure to threat or trauma stimulates the autonomic nervous system (ANS), resulting in sympathetic hyperarousal and parasympathetic (dorsal-vagal-mediated) hypoarousal states accompanying animal defence survival responses such as fight, flight, submission and freeze (LeDoux, 2002; Ogden et al., 2006; Porges, 2003; Van der Kolk, 1996a, 1996b). Following cessation of the threat, many victims continue to suffer from autonomic sensitivity to stimuli directly or indirectly related to the traumatic events. Thus, threatening and traumatic experiences result in a bewildering array of cognitive, emotional and physiological symptoms: emotions of fear, shame and rage; numbing of feelings and body sensations; overactivity of the stress response system; and painful, negative beliefs about the self that serve to intensify the distressing feelings and body responses. With a dysregulated nervous system that cannot modulate either heightened emotional states or states of depression and numbing, patients often report difficulty in tolerating emotional and physiological arousal without becoming overwhelmed, as well as problems in recovering from experiences of intense activation or depression (Ogden et al., 2006; Van der Kolk, 1996a). In addition, they report strong somatic responses in which the body tends to become frozen, collapsed or driven: action becomes either impossible or impulsive. Non-threatening situational cues often activate sympathetic nervous system (SNS) activity and flight–flight responses, while dangerous situations instead elicit parasympathetic non-responsiveness or submission–compliance responses.

Physiological arousal and the Window of Tolerance

One model for understanding and explaining the fluctuations in clinical features that can occur unpredictably and rapidly in the disorders that arise from the effects of severe trauma (Ogden et al., 2006) is the ‘Window of Tolerance’ model of autonomic arousal (Siegel, 1999). Siegel (1999) proposes that between the extremes of sympathetic hyperarousal and parasympathetic hypoarousal is a ‘window’ or range of optimal arousal states in which emotions can be experienced as tolerable and experience can be integrated (Figure 1). Although it has not yet been validated experimentally, the pleomorphic complex trauma disorders that are the result of childhood abuse become more comprehensible within this framework and there is evidence that different emotions are accompanied by distinct patterns of ANS response with sympathetic

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activation accompanied by varying degrees of parasympathetic deactivation (Rainville et al., 2006). Other studies have observed that trauma-related symptoms and emotions may be accompanied by more extreme autonomic effects (Lanius, 2005; Perry et al., 1995). In a study of individuals with borderline personality disorder, a diagnosis that has been correlated with childhood trauma (Herman et al., 1989; Ogata et al., 1990; Zanarini et al., 1989) subjects demonstrated sympathetically-driven active defence responses to social interaction with a stranger, in contrast with controls who were more able to readily engage the ‘vagal brake’ (the ventral vagal complex) for rapid attunement with the other person (Austin et al., 2007). While emotional dysregulation driving maladaptive efforts to diminish distress has provided a useful model for treating borderline personality disorder with dialectical behaviour therapy (Linehan, 1993), and can be adapted to many situations in which harmful actions occur in response to distress, the autonomic dysregulation model allows additional hypotheses about the associated psychophysiology of involuntary somatic responses to triggers that evoke some component of a trauma memory.

Trauma, negative cognitions and affective states outside the Window of Tolerance

When a traumatic event is overwhelming and inescapable, the associated high arousal emotional state may not be easily modulated, leading to inhibition of cortical activity (LeDoux, 2002; Ogden et al., 2006), a loss of cognitive witnessing, and perhaps even to states of speechless rage or blind terror (Van der Kolk, 1996b). Alternatively, the dorsal vagal branch of the parasympathetic nervous system (PNS) may become activated (Porges, 1995) leading to a state of total submission characterized by numbing, collapse, dissociation or even ‘feigned death’ (Porges, 2003), a state from which the prospect of dying can seem a welcome release. The PNS-dominant state of near death is accompanied by flaccidity of the muscles and is therefore distinguishable from the tonic immobilization state (‘scared stiff’ or catatonic) (Moskowitz, 2004), in which high physiological arousal is combined with an inability to engage in voluntary movement of the body, a peritraumatic orienting and defence response postulated to be secondary to simultaneous SNS and PNS co-activation (Ogden et al., 2006). Peritraumatic tonic immobilization has been associated with severe psychological sequelae of depression and anxiety years after the childhood sexual abuse in which it was experienced, when fear and helplessness were combined with an inability to escape from the horrifying situation (Bovin et al., 2008; Heidt et al., 2005). More recently the occurrence of tonic immobility in male victims of urban violence has been associated with a poor response to drug therapy (Fisman et al., 2008).

This Window of Tolerance model (Ogden et al., 2006; Siegel, 1999) describes all these animal defensive states (Figure 1): the hyperarousal connected to sympathetic activation, the autonomic hypoarousal characteristic of parasympathetically mediated dorsal vagal responses, and the ‘deer in the headlights’ frozen flight response connected to high SNS and PNS co-activation. In addition, the Window of Tolerance as an explanatory conceptualization also prescribes a treatment approach: that of regulating autonomic arousal within a Window of Tolerance in which affect and cognition can be tolerated so that patients can both think and feel (Fisher and Ogden, 2007). When patients with trauma-related disorders, such as post-traumatic stress disorder (PTSD) and borderline personality disorder, develop greater ability to self-regulate autonomic arousal, symptoms tend to diminish or ameliorate, and they are able to engage more effectively in well-established treatments for trauma. In addition, use of a

<table>
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<tr>
<th>Sympathetic-dominant Hyperarousal:</th>
<th>Freeze</th>
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<tr>
<td>Emotionally flooded, reactive, impulsive, hypervigilant, fearful, angry.</td>
<td>Mute, terrified, frozen</td>
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<tr>
<td>Intrusive imagery and affects, racing thoughts</td>
<td>defence responses.</td>
</tr>
<tr>
<td>Flashbacks, nightmares, high-risk behaviour</td>
<td>High arousal coupled</td>
</tr>
<tr>
<td>Efforts to reduce this state may include suicide planning, self harm, compulsive cleaning, abuse of alcohol or opiates</td>
<td>with physical immobility*</td>
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<tr>
<th>Parasympathetic-dominant Hypoarousal:</th>
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<tr>
<td>Flat affect, numb, “empty” or “dead”</td>
<td></td>
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<td>Cognitively dissociated, inability to think</td>
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<td>Collapsed, disabled defensive responses</td>
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<td>Helplessly and hopeless</td>
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<td>Efforts to reduce may include suicide planning, self-harm, compulsive</td>
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**Figure 1.** Autonomic arousal in the wake of trauma: sympathetic hyperarousal and parasympathetic hypoarousal states drive emotional and autonomic dysregulation. Also shown is the frozen fear state in which both extremes may be present. States of optimal arousal and emotional regulation are relatively rare or difficult to maintain. Some examples are included of how dysfunctional behaviours can be utilised in the service of emotional regulation: both to reduce the intensity of the high arousal states and the depth of the low arousal states. Adapted from Ogden et al (2006) and Siegel (1999).
model that emphasizes the role of the ANS in perpetuating post-traumatic symptoms addresses both physiological hyperarousal symptoms (high-risk behaviour, suicidal impulses, self-injury) and hypoarousal symptoms (shame, dysthymia, depression, loss of energy, self-loathing) (Figure 1).

Emotions, defence responses and the midbrain periaqueductal grey

One hypothesis offering an explanatory model for these effects of traumatic experiences on arousal levels involves the midbrain periaqueductal grey (PAG), which is a key structure for mediating the physiological effects of defence responses. Dorsolateral columns are involved in active, sympathetically driven fight or flight behaviours while ventrolateral areas are engaged in parasympathetically dominant freeze reactions (Bandler and Shipley, 1994; Watt, 2000). Recently it has been proposed that the dorsomedial column has specificity for the modulation of aversive, avoidant states with corticotrophin-releasing factor (CRF) exerting an excitatory influence on this region (Borelli and Brandao, 2007). It will be of interest to see whether more precise techniques for imaging the brainstem reveal an association of the dorsomedial column with trauma-related avoidant responses of disgust and shame as activation of the dorsomedial column leads to conditioned place aversion (Zanoveli et al., 2007). The Window of Tolerance model displayed in Figure 1 sees freeze responses as the result of co-activation of sympathetic and parasympathetic components of the ANS and this, in PAG terms, would mean co-activation of dorsolateral and ventrolateral columns. However, dorsomedial PAG stimulation for conditioned place aversion is associated with increased open field freezing, possibly of the attentive, information-gathering type (Zanoveli et al., 2007), and there are two other types of freezing (stimulus bound and non-stimulus bound) produced by activation of dorsal aspects of PAG (Brandao et al., 2008). Thus it is possible that there are several different types of freeze response depending on which dorsal PAG columns are co-activated with the low-arousal, opioid-mediated ventrolateral area responsible for conditioned freeze with its bradycardia, hypotension and energy-conservation functions. The PAG activation of other brainstem structures mediates the autonomic changes required by emotions and defence responses and the resulting changes in the physiological state of the body are fed back through the thalamus to insular and anterior cingulate cortices (Craig, 2005). Distressing emotions associated with the sympathetic arousal of trauma, such as fear, anger and disgust, are also dependent on activation of the right anterior insular cortex. The concomitant opponent deactivation of the left insular cortex (Craig, 2005) may lead to loss of feelings of comfort and safety and difficulties in articulating the experience. During treatment with a safe, empathic therapist encouraging non-judgemental mindfulness, and through training in skills for soothing self-regulation (e.g. Fay, 2007), the balance of insula activation could move to left-dominance.

Motor aspects of defence responses will require subcortical circuits through the PAG similar to those described by McHaffie et al. (2005). The behaviours associated with fight or flight have sufficient similarity in different people to suggest that there are intrinsic tendencies to activate particular muscle groups when the situation requires specific actions to ensure survival. Grillner et al. (2005) describe a toolbox of motor programs which is kept under tonic inhibition by gamma aminobutyric acid (GABA)ergic pallidal neurons (including those of the substantia nigra pars reticulata) until a selection is made in the striatum. A failure of selection from two disinhibited programs would lead to the state of frozen flight or frozen fight accompanying the ANS co-activation. The neurochemistry of PAG activation is complex, involving, to select a few examples, 5-hydroxytryptamine (5HT)-activated inputs from the basolateral amygdala (Martinez et al., 2007), cholinergic stimulation of the central amygdala (Leite-Panissi et al., 2003), GABA-A modulated 5HT activation of the ventrolateral orbital prefrontal cortex (Huo et al., 2008) and intrinsic acetylcholine (Kroes et al., 2007), GABA (De Menezes et al., 2006; Reimer et al., 2008), cytokines (Bhatt et al., 2008), opioids (Kishimoto et al., 2001), cannabinoids (Terzian et al., 2008), CRF (Carvalho-Netto et al., 2007), glutamate and 5HT (Moraes et al., 2008).

Affect regulation and the Window of Tolerance

During multiple or prolonged exposures to childhood traumatic events (including sexual abuse, physical abuse, exposure to domestic violence, and trauma related to medical treatments or accidents), hyper- and hypoarousal states occur not only in response to threatening events but also to their anticipation. After repeated SNS/PNS activation during formative years, the adult in later life may have difficulties in regulating affect (Ogden et al., 2006; Schore, 2003; Van der Kolk, 1996a), resulting in prolonged states of fear and anger (SNS-dominance) or despair and depression (PNS-dominance). In the affectively flattened hypoaroused state, the trauma survivor may feel that life is not worth living, that nothing matters, that death would be a relief. There is a lack of energy and enthusiasm, and a reported absence of distress may coexist with the matter-of-fact suicidal thinking. This presentation may mimic, or coexist with, a major depressive episode, and prescription of antidepressants is the obvious choice for the clinician. If antidepressant use leads to an increase in anxiety and arousal, there can be a switch to a hyperaroused state (in which the energy for a suicide attempt is available) or a rapid alteration between the extremes. If suicidal thinking is initially a way of soothing the empty nihilism and despair of the hypoaroused state (Herman, 1992), antidepressant-related autonomic activation may result in the ideas taking on fresh urgency as a way to end intense suffering. Similarly, a temporary intensification of the hypoaroused state would increase suicidal thinking, which, if followed by increased energy, could result in impulsive acting out. The converse may also occur when suicidal thinking is initially a way of soothing intense activation, unbearable impulses and overwhelming emotions. Increased focus and autonomic stability as a result of increased serotonin reuptake inhibition may result in more ability to plan and implement actions.
Ascending tracts and levels of arousal

Although the acute physiological effects of traumatic events and post-traumatic triggers can be attributed to the SNS/PNS accompaniments of defence responses, the sustained effects on cognition and emotion require an alternative explanation for the alteration of the ‘torque’ (Watt, 2000) of the thalamocortical mantle. Key areas are the intralaminar nuclei, the nucleus reticularis thalami, the superior colliculi, the core monoamine nuclei in the brainstem, and the midbrain reticular formation, with PAG outputs having modulatory influences on these significant structures (Watt, 2000). Ascending dopaminergic tracts such as the mesocortical, nigrostriatal and mesolimbic systems are good candidates for this role. The innervation from the midbrain ventral tegmental area (VTA) reaches not only the nucleus accumbens and ventral pallidum but also areas involved in the memory of emotional experiences and learning of fear responses, such as the basolateral nucleus of the amygdala (McGaugh, 2004). Also, the mesodiencephalic areas involved in the generation of emotions and defence responses have bilateral projections to the thalamus that are separate from the nigrostriatal, mesolimbic and mesocortical dopamine systems (Sanchez-Gonzalez et al., 2005) and have more diverse origins. The PAG projections to the mediadorsal nucleus, the principal thalamic input to the orbitomedial prefrontal cortex, are likely to be significant for affectively loaded mood states and behaviours but a circuit involving the laterodorsal nucleus of the thalamus, the basolateral amygdala and the dorsal PAG has also been proposed for panic disorder (Zanovelli et al., 2007).

Long-term administration of antidepressant drugs attenuates the footshock stress response of mesocortical dopamine neurons in the rat (Dazzi et al., 2001). The atypical antipsychotics olanzapine and clozapine have a similar effect (Dazzi et al., 2004), which may help to explain why drugs such as quetiapine and olanzapine are often clinically useful for widening the Window of Tolerance in complex trauma patients. The persistent state of behavioural depression following a prolonged period of repeated immersion stress which is accompanied by reduced dopamine transmission in the rat prefrontal cortex (Mizoguchi et al., 2008) may serve as a model for the hypoarousal state.

Stimulation of dopamine D2 receptors in the prefrontal cortex reduces, whereas N-methyl D-aspartate (NMDA) antagonism in the prefrontal cortex increases, the release of dopamine in the nucleus accumbens and the spontaneous motor activity of the rat (Del Arco and Mora, 2008), supporting the hypothesis that an imbalance of dopamine transmission in mesocortical and mesolimbic systems would have effects on motor activation and arousal.

Dysfunctional behaviours and the Window of Tolerance

Illicit drugs that activate the mesolimbic dopamine (ML-DA) system and provide reward through activation of the shell of the nucleus accumbens include cocaine and amphetamine (Alcaro et al., 2007). One explanatory hypothesis for the development of substance abuse, self-destructive behaviour and other dysfunctional behaviours in patients with a history of trauma is that these substances and the associated compulsive activities seek to regulate low- and high-arousal states. The use of alcohol and cannabis to reduce high activation states is more difficult to explain if the only relevant neurobiology relates to the rewarding stimulation in the nucleus accumbens shell. However, alcohol and benzodiazepines would reduce arousal through a GABAergic inhibition of the ML-DA system, and GABA interneurons are responsible for different degrees of activation of the PAG columns (Watt, 2000).

Suicide planning is used by trauma patients to both activate and deactivate arousal, depending on the baseline state (Perry and Szalavitz, 2007). This soothing or activating scenario-construction is likely to require imagery circuitry in the visual cortex, precuneus and posterior cingulate cortex but also important may be the dopaminergic projections to the prefrontal cortex which, according to Alcaro et al. (2007), facilitate information processing without the affective aspects of Seeking, potentially an increase in arousal without positive affect. Given that these mesocortical projections can inhibit dopamine release in the nucleus accumbens (Alcaro et al., 2007) so the prefrontal areas will be critical to the direction of the modulation.

Bathing, washing and cleaning are often used by complex trauma survivors to avoid the dysphoria associated with hyper-arousal states. The association between childhood trauma and adult obsessive-compulsive symptoms has recently been documented from a large study of college students (Mathews et al., 2008) and an affective orbitofrontal–striatal circuit has been implicated in obsessive-compulsive disorder (Menzies et al., 2008). A wide range of obsessive-compulsive behaviour functions to either increase cortical activity (as in counting and checking) or regulate arousal (as in bathing, washing and cleaning rituals).

The valence of the hyperarousal state is also subject to fluctuations and dysfunctional behaviours may be attempts to convert a fearful, negatively valenced hyperarousal to a more positive appetitive state. Reynolds and Berridge (2008) have demonstrated that the shell of the rat nucleus accumbens is highly sensitive to environmental influences such as bright light and loud music, and the behaviours generated by disruption of glutamate transmission there are readily converted from appetitive to fearful. There is preliminary evidence from functional magnetic resonance imaging (fMRI) studies of altered processing of rewards in the nucleus accumbens and prefrontal cortex in PTSD (Saider et al., 2008).

Rapid oscillation between extremes of arousal state and frantic efforts to achieve regulation, even by way of dysfunctional behaviours, can lead to a ‘biphasic rollercoaster’ of experience which is chaotic and disturbing to the sufferer (Figure 2).

Trauma and animal models of depression

Animal models of depression that have highlighted the importance of dopaminergic tracts have relied on the traumas of pain, isolation or defeat. Rearing rat pups in social isolation induces hyperfunction of ML-DA systems and hypofunction of mesocortical dopamine (Fone and Porkess, 2008). Similar
observations are made when tail pressure is used as the stressor: dopamine depletion in the medial prefrontal cortex potentiates the stress-induced increase in extracellular dopamine in the nucleus accumbens shell (King et al., 1997).

Rats that repeatedly demonstrated defensive or submissive behaviour when placed in the cage of an aggressive resident rat were found to have increased dopamine levels in the nucleus accumbens and prefrontal cortex when they were again exposed to the threat of social defeat (Tidey and Miczek, 1996), providing support for the hypothesis that the hypervigilant, hyperaroused state is associated with increased extracellular dopamine in the nucleus accumbens and prefrontal cortex. However, rats that were returned to the safety of their home cage (not in sight of the aggressor) were found to have higher dopamine concentrations while being behaviourally predominantly inactive, suggesting that they were in a state of aroused vigilance rather than in a post-traumatic hypoarousal condition. The aversion to social contact of socially defeated mice is normalized by chronic administration of antidepressant (Berton et al., 2006), supporting the use of this animal trauma response model in modelling depression and in the discovery of new antidepressants.

Thus, trauma can lead to increased mesolimbic dopamine and reduced or increased mesocortical dopamine. Also, the dopaminergic tracts from PAG through the dorsomedial thalamus to prefrontal cortex which have been demonstrated in the macaque monkey (Sanchez-Gonzalez et al., 2005) would warrant further study in the traumatized human.

Prefrontal cortex and the autonomic nervous system

The orbitomedial prefrontal cortex has projections, presumably regulatory, to the mesodiencephalic areas necessary for the generation of core emotions and defence responses (Ongur and Price, 2000). Animal studies suggest that in some species parasympathetic responses, with bradycardia and respiratory inhibition, are elicited from the anterior cingulate cortex while sympathetic responses are elicited from more ventral regions of subcallosal and orbital prefrontal cortex (Buchanan and Powell, 1993). Sympathetic responses can also be elicited by stimulation of midline and mediadorsal thalamic nuclei and these structures may therefore be able to counteract parasympathetic changes mediated by the anterior cingulate and orbital prefrontal cortex (Buchanan and Powell, 1993). In the rat there are direct projections from the anterior cingulate and orbitofrontal cortex to the dorsal motor nucleus of the vagus, the solitary nucleus and the nucleus ambiguus of the medulla. In the rabbit there are also projections to the mediodorsal, midline and intralaminar nuclei of the thalamus. Given that a direct pathway exists from areas 32 and 25 to the autonomic regulatory nuclei in the medulla it has been proposed that prefrontal cortex and thalamic activity is associated not with reflex homeostatic changes in autonomic activity but with the more complex changes involved in associative learning. The anterior cingulate cortex, the orbitofrontal cortex and the mediadorsal nucleus of the thalamus all have reciprocal connections with the basolateral nucleus of the amygdala (Buchanan and Powell, 1993).

Functional brain imaging in the human confirms the role of both the anterior cingulate cortex and the ventral prefrontal cortex in control of autonomic responses. Stimulation of the sympathetic system with exercise or arithmetic is accompanied by activation in the dorsal anterior cingulate cortex (Critchley et al., 2000), while parasympathetic modulation is accompanied by activation in the ventromedial prefrontal cortex (Nagai et al., 2004; Wong et al., 2007). The vagal brake (Porges, 1995) may have its hardwiring in the human brain in the ventromedial prefrontal cortex rather than the anterior cingulate cortex as would be expected from the animal studies referred to above. It is not yet possible to attribute these prefrontal activations unequivocally to specific autonomic effects or to identified neurotransmitter systems.

However, Bergmann (2008), echoing and developing the work of Schore (1994), has proposed that post-traumatic hyperarousal states are mediated by a dopaminergic circuit involving a ventral sympathetic area of orbitofrontal cortex that has reciprocal dopaminergic connections with the ventral tegmental area and projections to the nucleus accumbens. This system is often involved in positively valenced states of appetitive behaviour, motivational reward and active coping, but could be negatively valenced under conditions of threat (Reynolds and Berridge, 2008). The post-traumatic hypoorousal state, in contrast, is considered by Bergmann (2008) to be mediated by a noradrenergic circuit involving lateral regions of orbitofrontal cortex that have reciprocal connections with, amongst others, parasympathetic autonomic areas

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**Figure 2.** An example of how dysfunctional behaviours can be efforts to regulate distress by a person striving to be within the Window of Tolerance. Eating for comfort to soothe the terror of a flashback is initially helpful but then leads to feelings of shame, self-loathing and worthlessness. This gives rise to suicidal thinking but also to withdrawal and social isolation which make intrusive memories more disturbing. The next flashback is accompanied by rage then by shame at the rage, leading to alcohol intoxication to promote oblivion. Withdrawal from the alcohol leads to a high arousal state in which triggers to further flashbacks with dominant fear or rage will occur, continuing the cycle.
of the lateral hypothalamus and arousal-regulating neurons in brainstem vagal centres. This lateral segmental limbic forebrain–midbrain circuit down-regulates negative affect by activating the onset of a parasympathetic inhibitory state which can be positively valenced with soothing and calming or negatively valenced with apathy and shame.

**Brain imaging in complex trauma and in depression**

Preliminary findings suggest that patients with complex trauma and dissociative disorders have smaller hippocampal volumes than controls and that the degree of reduction in hippocampal volume is correlated both with the clinical severity of the disorder and the extent of early trauma (Ehling et al., 2008). Similar findings were reported in a study of women with borderline personality disorder and a history of early life trauma (Driessen et al., 2000). Despite these findings, imaging studies of hippocampal volume in depression are often conducted with no recording of the trauma history of the participants and this is acknowledged to be a possible confounding variable in efforts to link volume changes with depressive subtype (Greenberg et al., 2008). Brain research by Lanius et al. (cited in Ogden et al., 2006) demonstrated reduced thalamic activation in subjects with histories of trauma relative to controls but this has not yet been studied in relation to arousal level.

**The immediacy of hopelessness and chronic depression**

In some cases, depressive episodes appear to be linked to years of bullying, neglect or other abuse. Psychodynamic theorists considered internalized anger to be capable of transformation into depressed mood but they provided no account of how this might be mediated physiologically. If there are repeated situations in which a fight response is obstructed, thoughts of hopelessness, helplessness and worthlessness accompanying the parasympathetic down-regulation of the fight response would be associated with low mood – and a mental state that is biologically determined for a brief and immediate response to attack can then become chronic. During an attack by a predator there is a need for a focus on immediate response rather than on long-term planning. The function of hopelessness, the belief that ‘this is never going to get better’, may be the disconnection of the situationally redundant fight and flight responses. This outlook conserves energy, through avoidance, hiding or other appropriate behavioural responses, and also facilitates submission if there is a clear imbalance of power.

The physiological experience of helplessness (loss of energy and tone, collapse, slowed cognitive processing), accompanied by the cognition ‘there is nothing I can do: no action of mine will be helpful’ promotes resignation and energy conservation. Like hopelessness and worthlessness (‘I deserve this because I’m bad’) it reinforces submission responses and passive compliance or acceptance. Thus, symptoms of depression and hopelessness reflect the experience of incomplete and/or obstructed fight responses automatically followed by parasympathetically mediated ‘total submission’ (Porges, 1995) responses. Energy conservation allows individuals to sustain such states for lengthy periods of time. Subsequently, the patient’s subjective experience is one of depression, hopelessness and worthlessness, which is often exacerbated in the context of anger or self-assertion.

Energy conservation can be seen in the DSM-IV (APA, 1994) criteria for major depressive episode of reduced energy and fatigue. Low mood is described as feeling sad or empty, and feelings of worthlessness or inappropriate guilt may be present. Feelings of hopelessness feature in the DSM-IV criteria for dysthymic disorder, along with other features of a low arousal state such as low energy and low self-esteem. Concurrent experience of anxiety and depression then would not be a question of co-morbidity but of activated fear simultaneous with the incomplete fight or flight responses. When these are constantly present, rather than available briefly for situations of danger, the short-term perspective remains and obviates the possibility of optimism. How can there be enjoyment, interest, energy or pleasure when the outlook rises from a state of frozen submission? This result of social defeat stress, as in the rat model of Berton et al. (2006), is a chronic depressive condition reflecting the survival need for dorsal vagal and parasympathetic dominance.

Because trauma-related stimuli continue to evoke sympathetically mediated hyperarousal responses and the ‘vagal brake’ to inhibit or truncate fight or flight responses, trauma patients often experience characteristic fluctuations of state described in the ‘distress dipole’ model. If fight or flight responses chronically coexist with a hypoarousal state that down-regulates to truncate active defensive responses, patients may become trapped in the ‘distress dipole’ and become unable to access any positive affective state. Some examples are given in Figure 3.

**Summary: psychopharmacology and the Window of Tolerance**

We are arguing that while arousal states outside the window of tolerance are initially associated with SNS or PNS activation, the psychological effects that persist beyond the acute change in heart rate and respiratory rate appear to be mediated – at least in part – by ascending dopaminergic tracts from the midbrain to the thalamus and the mesocortical, nigrostriatal and mesolimbic dopaminergic systems. Evidence from animal studies supports the view that trauma induces excessive dopamine release in mesolimbic systems, but the role of reduced dopaminergic activity in mesocortical tracts is less clear. It may be an imbalance between mesocortical and mesolimbic dopamine transmission that facilitates rapid switching between high and low arousal states in those with a history of severe trauma. The nucleus accumbens is sensitive to environmental factors (Reynolds and Berridge, 2008) and the experience of the arousal state as positively or negatively valenced may relate to whether it is in fearful/defensive or appetitive mode.
High arousal states that are aversive can be modulated by suicide planning, starvation, abuse of alcohol and cannabis, bathing, grooming and compulsive cleaning, and by self-harm. Low arousal states can be modified by compulsive activities involving grooming and cleaning, suicide planning, risk-taking (such as driving too fast), self-harm, and abuse of alcohol, amphetamine, ecstasy or cocaine. Treatment approaches need to involve patient education about these states and their role in symptom perpetuation and exacerbation. In addition to pharmacological approaches, the substitution of more effective and less harmful behaviours to regulate autonomic states must be emphasized. For both hyperarousal and hypoarousal, mindfull curiosity is regulating, as is psychoeducation. In high arousal, soothing strategies may be useful, as well as exercise, yoga and other physical activities requiring focused attention. Low arousal benefits from gentle activity, movement, humour and increased cortical activity. In suicidal patients with both low and high arousal patterns, treatment with antidepressants and atypical antipsychotics needs to be monitored carefully from the perspective of autonomic arousal and the ‘Window of Tolerance’ to maximize the psychopharmacological benefits in this population and reduce the possibility of an increase in suicidal behaviour.

References


