11

The Brain Stress Systems I: The Implicit Level of Brain Operations

Abstract In this chapter we continue our exploration of the neurobiology of functional somatic symptoms by considering the role of the brain. The brain plays a key role in regulation, in coordinating the stress response, and in helping the child adapt to the circumstances of living over time. Every component of the body stress system—the HPA axis, autonomic nervous system, and immune-inflammatory system—is regulated by the brain or connected to it, or communicating with it, in some way. When a child is exposed to stress that is chronic, uncontrollable, unpredictable, cumulative, recurrent, or overwhelming, it leads to activation of brain systems that are involved in managing stress and in stress-related adaptations. Because these regions interact with and modulate motor-, sensory-, pain-, and fatigue-processing regions, the sustained activation of the brain stress systems changes patterns of neural activation and connectivity across and between these systems, and sets up the necessary conditions for generating functional

Electronic supplementary material The online version of this chapter (https://doi.org/10.1007/978-3-030-46184-3_11) contains supplementary material, which is available to authorized users.

somatic symptoms. All the processes discussed in this chapter are non-conscious—the implicit level of brain operations—and involve processes that the brain engages in spontaneously, by itself, without conscious control or conscious awareness.

The neuroscientist Bruce McEwen has called the human brain ‘the central organ of stress and adaptation’ (McEwen 2009, p. 911), and the neuroscientist Christof Koch has described the brain as ‘the most complicated object we know of in the universe’ (Koch 1993, p. 13). All functional somatic symptoms depend upon implicit—that is, automatic and unconscious—processes that involve the brain and its response to threat or perceived threat. But somehow, in talking with children (including adolescents) about their functional somatic symptoms, we need to bring that complexity down to earth. How is the clinician to do that?

In the stress-system model, we use the metaphor of the stress system as depicted by overlapping circles. The brain stress systems—the implicit processes that involve and occur in the brain—are represented by the top circle (see Fig. 4.2). This circle represents all the brain regions that are involved in stress regulation and the stress response, including the brain regions that underpin salience detection (stimuli and body sensations that have particular importance for the individual), arousal, pain, and emotional states. The brain stress systems play a key role in initiating, amplifying, and maintaining functional somatic symptoms.

The top circle and even the term *brain stress systems* are simple metaphors that we can use to communicate with children and their families about the brain’s role in functional somatic symptoms. For readers interested in the details of the neuroscience, including basic science articles and the many different expressions used in the neuroscience literature to denote the brain stress systems, see Online Supplement 11.1.

The Brain in Maintenance and Restorative Mode

As we have seen throughout this book, body regulation is a never-ending task, much of which is framed within repeating patterns across the circadian cycle. In the normal course of events, when things

are safe and going well, the brain stress systems maintain body function within normative physiological limits (homeostasis) and ensure that the child's body has access to sufficient energy resources to face the challenges of daily life (allostasis) (see Online Supplement 1.2). But in the face of threat or perceived threat, the brain stress systems can shift from maintenance and restorative mode—*restorative mode*, for short—into defensive mode. Rapid mobilization into *defensive mode* and, in turn, timely termination, with a consequent return to restorative mode, are adaptive responses to the challenges of daily life, to stressful experiences, and to situations that threaten the child's safety or well-being (see also Chapter 4).

The Brain in Defensive Mode

When events pose a threat to the body's internal environment or to the well-being of the child, the brain stress systems activate into defensive mode: this means that the brain shifts gears (organization) into a mode that prioritizes automatic (unconscious) responses and switches off the capacity for reflective (conscious) processes (Arnsten 2015). The activation of the brain stress systems is an implicit process that occurs automatically and without any conscious control. Differences in the intensity and pattern of activation are thought to reflect individual genetic and epigenetic variations as well as the degree to which the child's stress system has been primed—activated by stressful events—in the child's own lifetime.

In that initial, threshold step of tagging the event as *salient*, the brain, which is continuously anticipating the body's energy needs, begins activating the stress system to meet those needs (Kleckner et al. 2017; Picard et al. 2018). All these processes occur without conscious awareness. Activation of the brain into defensive mode occurs in tandem with activation of the stress system as a whole. The brain secretes neurotransmitters (the brain's messenger molecules), including noradrenalin in the locus coeruleus (in the brain stem) and corticotropin-releasing hormone (CRH) in the hypothalamus, to facilitate processing in the brain, to change the pattern of neural activation and connectivity, and to activate the broader

stress system (Chrousos and Gold 1998; Pervanidou and Chrousos 2018; Arnsten 2015). At the same time, the HPA axis is switched on (via the hypothalamus) to mobilize energy resources throughout the body (see Chapter 8); the sympathetic system is switched on (via the brain's autonomic centres) to increase arousal in the body (see Chapter 6); and the immune-inflammatory system is switched on (via immune-inflammatory cells that reside in the brain) to work with neurons to support the brain's response to stress (see Chapter 9).

Along with the change into defensive mode is a change in how information is processed and also how risk is assessed (for different terminologies in the neuroscience literature, see Online Supplement 11.1). States of calm and safety facilitate certain patterns of processing, and states of threat facilitate (and necessitate) others. An example from the animal kingdom will illustrate the point here.

In the Canadian Rockies, the second author (SS) was, from a very safe distance, observing a grizzly bear eating dandelions (a dietary staple), seemingly without a care in the world and without taking much into account except the location of the next dandelion. But then, the bear stumbled, likely because of some unpredicted unevenness in the ground. With a suddenness that was actually frightening, the bear's body tensed, and he seemed to grow in size. He jerked his head around, looked to the rear, scanned the environment for potential threats, and gave every appearance of being the dangerous, aggressive predator that one hears so much about (whether true or not). In that instant, everything about the bear's stress system and how the bear processed information had changed. While focused on dandelions, information from the environment—noises, smells, colours—was presumably scanned only for major or surprising changes. But after the bear stumbled, many of the previously disregarded details suddenly became salient. All the bear's energy was now focused on identifying and assessing potential threats.

What we see here is a dramatic (and frightening) change in the bear's brain-body state, moving from restorative mode (while eating dandelions) to defensive mode (prepared to defend itself from potential danger). And what we see in the bear is basically what we see when humans encounter threats. The relevant systems have a long evolutionary

history. From the particular perspective of the stress system, we are no more than just another mammalian species.

Innate Defence Responses and Functional Somatic Symptoms

One potential manifestation of the brain in defensive mode is activation of innate defence responses. Evolution has endowed all humans with a continuum of innate, hard-wired, automatically activated defence behaviours triggered by extreme danger or threat to self (Kozłowska et al. 2015). These very primitive responses involve activation of evolutionarily old regions in the brain: the brain stem and amygdala. *Flight or fight* is an active defence response for dealing with threat; *freezing* is a flight-or-fight response put on hold; *tonic immobility* and *collapsed immobility* are responses of last resort to inescapable threat, when active defence responses have failed; and *quiescent immobility* is a state of quiescence that promotes rest and healing. Arousal is the first step in activating any of these automatic defence responses. Each response has a distinctive neural pattern mediated by a common neural pathway: activation or inhibition of particular functional components within the brain stress systems (the amygdala, hypothalamus, periaqueductal grey, and sympathetic and vagal nuclei [the brain component of the autonomic nervous system]).

Innate defence responses are usually time-limited; they are switched on in response to extreme threat and then switched off when the threat has passed. We mention them briefly here because a small percentage of children who present with functional somatic symptoms present with innate defence responses that are being activated frequently or that fail to resolve in a timely manner.

For example, children who frequently activate the tonic immobility defence response (long periods of immobility and non-responsiveness) or the collapsed immobility defence response (episodes of collapse or fainting) are often referred for neurological assessment. The neurologist will typically diagnose non-epileptic seizures (NES), a subtype of functional neurological disorder (FND). In our own clinical practice, most

Fig. 11.1 Opossum in collapsed immobility. The opossum's trunk and limbs are limp and immobile. The animal has the appearance of being dead. The terms *death feint* and *playing dead* have been used to describe collapsed immobility in animals. In actual fact, the animals are not playing at anything. Collapsed immobility in animals and humans is totally automatic (unconscious) (Source This figure was first published in Kozłowska and colleagues [2015]. © Kasia Kozłowska 2015)

of the children who have presented in this way have a past history of maltreatment or brain pathology that compromises their capacity, in a neurological sense, to respond to stress. See, for example, the case of BJ, a 16-year-old adolescent who manifests a range of innate defence responses in the context of a history of childhood maltreatment, as discussed in Ratnamohan and colleagues (2018), or the vignette of Danae, a 14-year-old adolescent with left cerebral atrophy of unknown origin, as discussed in Kozłowska and colleagues (2015).

When explaining tonic immobility and collapsed immobility to children and their families, we often use videos of animals—for example, the American opossum, which uses the collapsed immobility defence response to protect itself from predators (Fig. 11.1).

We can see the same sort of collapsed immobility in the following vignette of a young boy.

Frank was an 11-year-old boy who lived with his mother. Frank had been exposed to significant domestic violence that had occurred between his mother and one of her previous partners, Don. Frank described one episode of domestic violence in the following words:

Then mum like hit him. Then Don pushed her, then they started hitting each other and slapping each other and hitting. And Don held her around here (pointing to neck) and smashed her into a shelf and walked off and all my stuff fell down on top of her. So then Don, they went to the lounge room and Don, and mum came back in and got the coffee table lid like since it opened up had all this stuff in pulled it back so it smashed down on top of Don's laptop. Then I could hear lots of smashing and lots of stuff being thrown around. Then my mum screamed out 'let go' 'cause she was getting literally pushed down like up against the couch, pushed down in a lock so she couldn't get away. And then um last when Don was about to leave, he had a bleeding lip and mum had bruises all up her arm and stuff. And um we [Frank and his siblings] were just standing there crying.

In the years following the domestic violence, when Frank got stressed, he experienced intrusive memories of the violence. At those times he suffered from disrupted sleep, headaches, vomiting attacks, and bouts of hyperventilation, and sometimes he would collapse to the ground and remain inert for a long period of time. His mother would find him lying collapsed in some part of the house or yard, sometimes in a pool of blood, from a cut on the head or face.

Finally, as noted in Chapter 9, it is possible that children, or at least some children, presenting with fatigue that is unrelenting and completely debilitating have activated the *quiescent immobility* defence response—a biologically ancient response to stress or injury—and have been unable to switch it off (see Chapter 9 for a discussion of chronic fatigue as a homeostatic alarm and for a clinical case scenario). In animals, 'quiescent immobility involves the cessation of all ongoing spontaneous activity, hypo-reactivity (absence of orientation, startle response, and vocalization), hypotension, and bradycardia' (Kozłowska et al. 2015, p. 275). Patients who meet criteria for chronic fatigue syndrome may likewise manifest cessation of spontaneous activity, enter a hypo-metabolic state (Komaroff 2019; Naviaux et al. 2016), and experience autonomic dysregulation that manifests as difficulties in appropriately adjusting blood pressure and heart rate when standing upright or when exercising (see Online Supplement 6.1).

For a detailed description of the way that the innate defence responses present in clinical practice, see ‘Fear and the Defense Cascade’ (Kozłowska et al. 2015).

The Brain Stuck in Defensive Mode and the Generation of Functional Somatic Symptoms

More commonly, functional somatic symptoms do not involve activation of innate defence responses. Instead, they are generated when the brain stress systems get stuck in defensive mode, setting in motion a range of processes, involving other brain regions, that are maladaptive and that enable functional somatic symptoms to occur. These brain processes are interrelated, interact in non-linear ways, and contribute to changes in brain function and, on a cellular and molecular level, also in brain structure. In this section we briefly discuss some of these interrelated processes. For additional information and references to basic science articles pertaining to each of these subsections, see Online Supplement 11.1.

Aberrant Changes in Neural Activation and Connectivity

A recurring theme from neuroscience studies of patients with functional somatic symptoms is that when the brain stress systems become overactive and over-dominant—that is, get stuck in defensive mode—they over-connect with and disrupt brain regions for motor, sensory, pain, and fatigue processing (Pick et al. 2019; Blakemore et al. 2016; Vachon-Preseu et al. 2016; Sun et al. 2020). Disrupted or aberrant processing within these regions is, in turn, expressed in the individual’s *body* as aberrant motor patterns or in her *subjective experience* as aberrant sensory experiences or as feelings of persisting pain or fatigue. Because this aspect of the neuroscience research is easily depicted in visual metaphors, we use it as a foundation for our explanations to children and their families (see later section, ‘Metaphors for Explaining Changes in Brain Function to Children with Functional Somatic Symptoms’).

Dysregulated Immune-Inflammatory Mechanisms That Amplify and Perpetuate Pain

As we have seen in the clinical vignettes peppered throughout this book, children can present with pain either as the primary presenting symptom or as one among other functional somatic symptoms. When the brain stress systems are stuck in defensive mode, they can maintain activation of the brain's pain maps and the subjective experience of pain (Vachon-Pressseau et al. 2016; Ji et al. 2018; Li et al. 2019). Because the brain's immune-inflammatory cells and immune-inflammatory signaling molecules work in tandem with neurons on all levels of the nervous system to activate the pain system, these processes are referred to as *central sensitization* or *neuroimmune dysregulation* on the brain and spinal cord levels, as *neurogenic inflammation* on the tissue level, or simply as *neuroinflammation* within the pain system as a whole (see Chapter 9). Activation of the immune-inflammatory processes at all these levels is implicated in the initiation, amplification, and maintenance of musculoskeletal pain and chronic/complex pain felt in the viscera (abdominal or pelvic cavity).

Plasticity Changes in the Brain and Epigenetics

In Chapter 8 (about the HPA axis), we discussed how cortisol, the end product of the HPA axis, was involved in coordinating plasticity changes—via changes in gene expression (epigenetic mechanisms)—to help the brain and body adapt to stress during the individual's lifetime and across generations. Here we remind the reader that when a child is exposed to stress that is cumulative, recurrent, or overwhelming, the brain itself begins to change in order to make sure that it is adapting to the child's actual life experience and that it is ready to respond to future stress in a robust way. This process, called *experience-dependent plasticity*, involves functional and structural changes of neurons, glial cells, and neuronal circuits that occur in response to experience. It is also part of the brain's adaptive response to chronic stress. Although plasticity changes are occurring in the brain all the time in everyone—which is how cell differentiation, development, and learning take

place—plasticity changes acquired in the context of extreme stress can become maladaptive by continuing to affect brain function even when the level of threat has abated. When that happens, the brain stress systems are sensitized to stress and remain ready to respond robustly to each new threat that arises. Even seemingly minor stress, such as a minor injury, an illness, or an event associated with negative emotions, can trigger a stress response far in excess to what is required. In this manner, plasticity changes can contribute to and help maintain maladaptive activation of the brain stress systems, thereby setting the stage for the generation of functional somatic symptoms (Bègue et al. 2019; Ji et al. 2018).

Inefficient Use of Energy Resources

Energy underpins all life processes. *Defensive mode* involves increased utilization of energy resources and a decreased capacity for energy renewal, tissue regeneration, and repair (see also Chapter 4). The use of energy is even greater (and under the circumstances, excessive) when defensive mode persists beyond the presence of the immediate threat. The continuing activation of the brain stress systems requires excess energy, and the patterns of information processing characteristic of defensive mode (think about the grizzly, above) are also associated with increased energy use. Contemporary researchers propose that the brain is well equipped to perform non-conscious analyses pertaining to the energy-related costs and benefits of behaviour. These researchers suggest that the information that an action is not worth performing—that the energy costs involved outweigh benefits—is signalled as the feeling of fatigue (Boksem and Tops 2008, p. 130). In this context, fatigue functions as an adaptive signal—and as an *alarm* signal. When the brain is stuck in defensive mode, and when functional somatic symptoms are being generated, feelings of fatigue may serve as an adaptive signal—an alarm signal (Pedersen 2019) or homeostatic alarm (Wyller 2019) (see Chapter 9)—that activation of the stress system into defensive mode is depleting energy resources and is no longer adaptive.

Aberrant Predictive Representations

The processes of energy regulation and allostasis—the ongoing changes of stress-system activation in response to the challenges of daily living—require the brain to assess information about the external environment and the state of the body, and to predict what is likely to happen next. In the science literature, these initial predictions—which the brain generates automatically without any conscious awareness—are often referred to as *predictive representations*, and the process of generating these representations, as *predictive coding* (Kleckner et al. 2017). This process of predictive coding enables the brain to work efficiently and to conserve energy resources, and the predictive representations generated by this process are continually (and non-consciously) adjusted as the brain compares them to real-time sensory and interoceptive inputs from the world and the body, respectively. By identifying when something new or different or unexpected has occurred, these representations enable the brain to make appropriate adjustments.

Predictive representations contribute to the regulation of, and ongoing changes in, body state. They also contribute to the child's subjective experience of body state, including the homeostatic emotions of pain and fatigue. But like all biological processes, predictive coding can go awry. If the predictions of body state been made by the brain are erroneous—because, for example, they are tailored for a threat-related context that is no longer present—then these erroneous representations will hold priority over afferent inputs, the actual sensory and interoceptive information coming from the body. This priority will hold even when there is a significant mismatch between the erroneous predictive representations and actual body state. Threat-related information is always prioritized by the brain because the consequences of failing to respond to threat may be irreversible—and include the death of the organism.

Although the predictive-coding framework involves predictions that are made by the brain without conscious awareness, the mismatch of the brain's erroneous representations and actual body state sometimes comes into conscious awareness, as we see in the following vignette.

Jai, the 14-year-old boy whom we met in Chapter 5, presented with painful fixed dystonia in the neck, motor weakness and lack of coordination in the legs, and a pain-related curve of the body to the left. He consequently both sat and slept in a C-shape. He could not walk, sit up straight in the wheelchair, or toilet or shower himself. After the clinical team determined that Jai was highly hypnotizable—he could enter the trance state easily—hypnosis was integrated into his occupational therapy and physiotherapy sessions. While Jai was in a trance state, his psychotherapist made suggestions to Jai about his body state—that his body was deeply relaxed, that he could disconnect from the pain, that he could image that his body was bendable like a reed, or that his body could sway like a tree. These suggestions enabled the physiotherapist and occupational therapists to straighten and reposition Jai in the wheelchair. At the end of each session, when Jai was guided out of the trance state, he would suddenly find himself in the non-C-shaped position, and he would panic. He reported that he perceived his body—temporarily straight in the wheelchair—as being bent and wrong. By contrast, his internal perception of the C-shaped position was that his body was straight. Jai was initially unable to utilize any interventions to manage his panic—including suggestions during the trance state that he stay calm—but the length and intensity of the panic gradually settled as he habituated himself to the process of emerging from a trance.

As Jai got better, his subjective experience of his body shape—when straight or bent—progressively normalized. For additional reading material about predictive coding, see Online Supplements 1.3 and 11.1. For a full description of Jai’s treatment, see Khachane and colleagues (2019).

Stress-Related Wear and Tear

Stress-related wear and tear is best documented in stress-related conditions such as post-traumatic stress disorder (PTSD) (Miller et al. 2018). Because functional somatic symptoms also involve activation of the brain stress systems into defensive mode over significant periods of time, and because chronic activation of the brain (and body) uses considerably more energy than the brain (and body) in restorative mode,

the brain's opportunities for energy renewal, tissue regeneration, and repair are also likely to be restricted. The long-term cost of this activation is known as *wear and tear*, and scientifically as *allostatic load* (see Online Supplement 1.2). Major contributors to this wear and tear in the brain are the adrenal cortisol secreted by the HPA axis in response to prolonged stress (Miller et al. 2018) and the free radicals that are the natural byproduct of energy metabolism in the brain (Salim 2017). These free radicals are more difficult to neutralize when energy use remains high and restorative processes are compromised. Other interrelated processes will no doubt be identified. What is already known and clear, however, is that in the short term, stress-related plasticity changes increase the brain's implicit (non-conscious and automatic) processing capacity, enabling it respond to stress more effectively. If defensive mode is maintained over long periods of time, however, wear and tear may occur, compromising the brain's capacity to regulate body state and to respond to stress in the future.

Key Lessons from This Body of Work

A fundamental lesson from this body of work is that the brain—both brain function and brain structure on the micro level—can change in the context of both positive and adverse experiences. Positive experiences promote good regulation, health, and learning. Adverse experiences—excessive physical or psychological stress—activate changes that are adaptive in the short term but can become maladaptive in the long term, especially if the brain stress systems become stuck in defensive mode. What this means from a practical point of view is that clinicians need to support interventions that will help the child's stress system, including the brain stress systems, shift from defensive mode back to restorative mode. Such interventions may involve the body system level (promoting body states that mobilize restorative and repair processes; see Chapter 14), the mind system level (interventions that use the mind to mobilize restorative and repair processes; see Chapter 15), or the relational system level (interventions that use co-regulation between the child and her

caregivers and siblings to mobilize restorative and repair processes; see Chapter 16).

Metaphors for Explaining Changes in Brain Function to Children with Functional Somatic Symptoms

In this section we present some of the visual metaphors that we use with children and their families to communicate key themes from the neuroscience literature concerning the changes in brain function that are associated with functional somatic symptoms. In this context, we discuss three types of functional neurological symptoms (motor symptoms, sensory symptoms, and NES), chronic/complex pain (including syndromes such as fibromyalgia and chronic tension headache), and symptoms of persisting fatigue that accompany other functional somatic symptoms. Our visual metaphors are simple: they try to capture key themes in a way that is, at least in general terms, clinically and scientifically accurate, that is useful for clinicians in their discussions with patients and families, but that avoids details that would likely muddy that communication with unneeded complexities. The goal is to keep one's eye on the ball, and in this context the challenge is to promote shared understandings that enable clinicians, patients, and families to work together and to promote healing. For further reading and basic science articles pertaining to each subsection, see Online Supplement 11.1.

Activation of Brain Stress Systems and Functional *Motor* Symptoms

Functional motor symptoms include limb paralysis, limb weakness, tremor, tic-like movements, functional cough, and dystonia. They fall under the umbrella of FND. When talking to children who have presented with functional motor symptoms, we use the visual metaphor in Fig. 11.2 to discuss research findings from neuroscience and to provide

an explanation of what is happening in the brain. The key message for children and families is that functional motor symptoms emerge when the brain stress systems are overactive and over-dominant, and when they over-connect with and disrupt—hijack—motor-processing regions and motor function. Neuroscientist Valerie Voon and colleagues first used the term *hijack* in her wonderful study of motor preparation in patients with functional motor symptoms (Voon et al. 2011). Other references that underpin this visual metaphor are available in Online Supplement 11.1.

Our conversation—in effect, a step-by-step commentary on Fig. 11.2, with the details filled in as we draw—proceeds along the following lines:

Fig. 11.2 Overactive brain stress systems and motor function. *Frame A.* The red ball represents the brain regions that underpin salience detection, arousal, pain, and emotional states—the *brain stress systems*, for short. The pink ball represents brain areas involved in motor processing—*motor-processing regions*, for short. When all is well, the brain stress systems get on with their job, as do the motor-processing regions, and they interact together in a balanced way (see Online Supplement 11.1 for the brain regions that lie at the intersection of the *brain stress systems* and motor processing). *Frame B.* In functional motor symptoms, the relationship between the brain stress systems and motor-processing regions changes and becomes unbalanced, disrupting or hijacking motor function and activating aberrant motor patterns (functional motor symptoms) (© Kasia Kozłowska 2017)

When everything is going well, the brain stress systems and motor-processing regions in the brain work together in a balanced equal way [draw Frame A]. Sometimes, however, illness, injury, emotional stress, or trauma can *switch on* the brain stress systems and make them bigger and stronger. When this happens, they take over and disrupt the motor-processing regions, and they disrupt motor function and cause all sorts of motor symptoms [draw Frame B]. In your case, the brain stress systems were switched on by [event or series of events from child's history]. They are still switched on now, and they are disrupting your [describe the motor function]. They should have *switched off* when the [trigger or other recent stress] had passed, but they didn't. They have stayed *switched on*. So, we need to do that ourselves, using different types of interventions: *mind-body* interventions help to *switch off* the brain stress systems; *physiotherapy* interventions help your [arms or legs] start working normally again; and *psychological*, *family*, and *school* interventions help to address the stress in your life.

Activation of Brain Stress Systems and Functional Sensory Symptoms

Functional sensory symptoms include functional blindness (or changes in vision), functional deafness (or tinnitus or changes in hearing), and loss of touch sensation in the limbs. Like functional motor symptoms, they fall under the umbrella of FND. The key message for children and families is that functional sensory symptoms emerge when the brain stress systems are overactive and over-dominant, and when they over-connect with and disrupt sensory-processing regions and sensory function (see Fig. 11.3). When using this metaphor, the reader can adapt the language that we set forth above in our example for functional motor symptoms.

Loss of Top-Down Executive Control in Non-epileptic Seizures

NES also fall under the umbrella of FND. Other names for NES are *psychogenic non-epileptic seizures*, *functional seizures*, and *dissociative*

Fig. 11.3 Overactive brain stress systems and sensory function. *Frame A.* The red ball represents the brain stress systems. The yellow ball represents brain areas involved in sensory processing—*sensory-processing regions*, for short. When all is well, the brain stress systems get on with their job, as do the sensory-processing regions, and they interact together in a balanced way. *Frame B.* In functional sensory symptoms, the relationship between the brain stress systems and sensory-processing regions changes and becomes unbalanced, disrupting or hijacking sensory function and activating aberrant sensory patterns (functional sensory symptoms) (© Kasia Kozłowska 2019)

seizures (Asadi-Pooya et al. 2020). NES can occur alongside motor and sensory neurological symptoms, or they may be the sole presenting symptom. NES are paroxysmal: they occur suddenly, in time-limited episodes. Many children are able to identify the approaching onset of NES because they can feel somatic sensations that reflect sudden increases in arousal, what we call their *warning signs*. Common warning signs include increased heat in the chest, sweatiness, nausea, butterflies in the abdomen, feelings of tension or sudden pain in the muscles of the head (or elsewhere), buzzing in the head, muscle twitching or motor agitation (jiggling legs), breathing too fast, dizziness, blurry vision, visual blackout, wobbly legs, being unable to think clearly, an altered state of consciousness (e.g., feeling fuzzy, foggy, disconnected, or floaty, or ‘spacing’ or ‘vagueing out’). Because children can learn to identify interoceptive sensations associated with mounting arousal/motor activation and can then implement arousal-decreasing interventions—before the specific mechanisms that generate their NES are activated—they are able to avert most potential episodes of NES.

In this context, the working hypothesis of the first author (KK) is that sudden increases in arousal disrupt normal brain processes in the prefrontal cortex and also the connectivity between the prefrontal cortex and subcortical regions, and that these disruptions result in the release of motor programs in the basal ganglia, midbrain, and brain stem, resulting in the body movements, changes in tone, and time-limited alterations in consciousness that present as NES (Kozłowska et al. 2018a). For details about the various mechanisms that are thought to contribute to disruption of brain function in NES, see Kozłowska and colleagues (2018a, b) and Szaflarski and LaFrance (2018).

When talking to children who have presented with NES, we use the visual metaphor in Fig. 11.4 to discuss the above-described, hypothetical explanation of what is happening in the brain. For a summary of different types of NES presentations, see Kozłowska and colleagues (2018a).

Fig. 11.4 Visual representation of the hypothesized mechanism underpinning non-epileptic seizures. *Frame A.* The mother figure represents the prefrontal cortex, the control area of the brain. The child figures represent motor programs in the basal ganglia, midbrain, and brain stem. When all is well, the mother (prefrontal cortex) maintains control over the children (the motor programs). *Frame B.* In NES, the mother (prefrontal cortex) goes offline in the context of stress-related changes, and the children (motor programs) activate and present as NES (© Kasia Kozłowska 2017)

Our conversation proceeds along the following lines:

In this cartoon the mother figure represents the prefrontal cortex—the control centre of the brain—and the child figures represent motor programs in the lower regions of the brain: the basal ganglia, midbrain, and brain stem. When things are going well, the mother keeps control of the children; that is, the prefrontal cortex maintains control over the motor programs in the basal ganglia, midbrain, and brain stem. But in NES, the mother figure—the prefrontal cortex—gets really stressed, gets overwhelmed, cannot function, and goes *offline*. When this happens, the mother loses control of the children; the motor programs in the basal ganglia, midbrain, and brain stem are out of control. They activate and produce NES. There are lots of things that stress out the prefrontal cortex. In your case, [Here insert the presentation that is relevant for the child. Possibilities include the following: breathing too fast in response to stress (hyperventilating); worrying or recalling bad memories or feelings; sudden pain; or closing vocal cords and shutting off the air passage in response to stress (causing hypoxia).] The team will help you work on catching the warning signs that an NES is coming and on making your brain and body calm, so that you can prevent the NES from happening.

Activation of Brain Stress Systems and Chronic/Complex Pain

The neurobiology of chronic/complex pain that occurs in the absence of tissue injury is complex. Pain is a homeostatic emotion (Craig 2003), an alarm (Wyller 2019) that signals, whether accurately or erroneously, that the body or the self needs protection from threats to its physical or psychological integrity (Moseley and Butler 2015; Brodal 2017). Pain signals are carried by afferent nerves from the body to the spinal cord and by special pain pathways within the spinal cord to the brain. In the brain, pain processing involves a widely distributed network of regions that, in our work with children, we refer to as *pain maps* (for other terminology see Online Supplement 11.1). Pain maps function as an alarm signal. They can be activated by pain signals from the body and by signals from the brain itself—from the brain stress systems. Because of their role as an alarm signal, they are often activated alongside other

components of the stress system to signal that the body or the self needs protection from threat. For basic science references about pain-related processes on the brain system level, see Online Supplement 1.3.

Complex/chronic pain is maintained by a number of different interacting processes. As we saw, for example, in Chapter 9, chronic/complex pain is maintained when the immune-inflammatory system keeps the pain system activated, across multiple levels of the body system. This process is also known as *neuroimmune dysregulation* because the nervous system and the immune-inflammatory system activate together to maintain a vicious cycle of changes that maintain chronic/complex pain.

Chronic/complex pain is also maintained by (non-conscious) activation of the brain stress systems: when these systems become overactive and over-dominant—that is, get stuck in defensive mode—they over-connect with and activate brain regions involved in pain processing. In this way, the subjective experience of pain is both maintained and amplified.

Finally, chronic/complex pain can also be maintained by factors on the mind level of operations—attention to pain, catastrophizing, and negative emotions—because these processes operate in a top-down manner to activate the brain stress systems, which, in turn, maintain activation of pain maps (see Chapter 12).

When talking to children who present with chronic/complex pain, we use the visual metaphor depicted in Fig. 11.5.

Our conversation proceeds along the following lines:

When everything is going well, the pain maps in the brain, the parts of the brain that allow us to feel pain, are switched off. When everything is going well, the brain stress systems, the parts of the brain that switch on with stress, are also switched off. When I say *stress*, I mean anything that is stressful for the body, including illness, injury, emotional stress, or trauma. But when we experience stress, we *switch on* the brain stress systems. They become active, big and strong. And then after the stress has gone, the brain stress systems should switch off. But sometimes they fail to switch off, and because they have a close relationship with the pain maps, they can switch them on, too (or keep them switched on)—even when your body has healed or is not injured at all. And the pain maps make you feel pain. From the story you told me, it seems that in your

Fig. 11.5 Overactive brain stress systems and the subjective experience of pain. The red ball represents the brain stress systems. The spiky ball represents pain-processing regions—*pain maps*, for short. The overlap between the balls represents what the pain literature sometimes refers to as the emotional, affective, or aversive dimension of pain (see Online Supplement 11.1). In chronic/complex pain the brain stress systems become overactive and over-dominant, and they drive and amplify the pain experience (© Kasia Kozłowska 2019)

case the brain stress systems were switched on by [event or series of events from child's history]. They are still switched on now, and they are keeping your pain maps activated and signalling pain: like a pain-alarm system that cannot be switched off. So, treatment involves *mind-body* interventions that help to *switch off* the brain stress systems, because they are keeping the pain maps switched on; *physiotherapy* interventions that help you to keep up your level of fitness and to assist your body in fighting—switching off—the pain maps [see discussion of macrophages in Chapter 9]; *psychological* interventions that help switch off the pain maps and help to address the stress in your life; and family and school interventions that help support you in the best way possible.

Activation of Brain Stress Systems and Fatigue

Fatigue is a common comorbid symptom in children presenting with functional somatic symptoms. For example, in the clinical practice of the first author, fatigue is also reported by a quarter to half of the children

presenting with FND and two-thirds of children presenting with chronic/complex pain. The term *chronic fatigue syndrome* is used when fatigue is the primary presenting symptom, and when the child meets the available symptom-based criteria (of which there are several versions) (Gluckman 2018; Knight et al. 2019). In this section we discuss fatigue in a general way and not chronic fatigue syndrome per se (see Chapter 9 for a discussion of persisting fatigue and chronic fatigue syndrome).

In the brain, fatigue processing involves a widely distributed network of regions (Boksem and Tops 2008; Noakes 2012), which, in our work with children, we refer to as the *fatigue alarm system* or the *fatigue alarm*. Fatigue, like pain, is a homeostatic alarm (Wyller 2019) that signals, whether accurately or erroneously, either an urgent homeostatic imbalance (Hilty et al. 2011, p. 2151) or an urgent need to protect the body's energy resources (Boksem and Tops 2008). In the context of stress, whether physical or psychological, and when the brain stress systems shift into and get *stuck* in defensive mode, the fatigue alarm is frequently activated. The fatigue alarm signals the loss of physiological coherence: the easy flow of life processes, harmony between body systems, and efficient utilization of energy are all lost when the stress system shifts from restorative mode and gets stuck in defensive mode. In this way, the fatigue alarm signals that the brain stress systems have been activated too much, for too long, or too frequently and that they need assistance to help them shift back into restorative mode and regain physiological coherence (as described above). For other metaphors for discussing persisting fatigue, see Chapter 9.

When talking to children who present with comorbid fatigue, we use the visual metaphor depicted in Fig. 11.6.

Our conversation proceeds along the following lines:

The biology of fatigue is very complicated, and scientists are still trying to work it out. The current thinking is that fatigue—like pain—is one of the body's alarm systems. The fatigue alarm allows us to feel fatigue. And the feeling of fatigue tells us many things. Sometimes the fatigue alarm tells us when the body has used up too much energy and it is time to stop. Sometimes the fatigue alarm tells us that it is time to go to sleep—to rest and to make energy for the next day. Sometimes the fatigue alarm tells us that our brain stress systems and our body stress systems have been

Fig. 11.6 Overactive brain stress systems and the fatigue alarm. The red ball represents the brain stress systems. The green ball represents the fatigue alarm. When the brain stress systems (and other components of the stress system) are activated by infection, illness, injury, or emotional stress, and when they get stuck in defensive mode, the fatigue alarm activates to signal the loss of physiological coherence—the loss of easy flow of life processes, harmony between body systems, and efficient utilization of energy—that occurs when the stress system shifts from restorative mode and gets stuck in defensive mode (© Kasia Kozłowska 2019)

activated too much and too long. As you already know, the brain stress systems and body stress systems include all the parts of the brain and body that activate with physical or emotional stress—illness, injury, emotional stress, or trauma. The stress system uses a lot of energy. That's why, when the stress system is switched on, the fatigue alarm is often switched on, too. The fatigue alarm signals that the stress system is hard at work (and maybe even a bit too hard at work) and that we need to take care of the stress and also to help the stress system switch off. This is why fatigue is so common in children who have [put in child's presentation, such as FND, chronic/complex pain, autonomic activation/dysregulation]. The treatment for your fatigue involves *mind-body* interventions that help to *switch off* the brain-body stress systems; *physiotherapy* interventions that help you keep up your level of fitness, that switch off pain, and that promote health and well-being; *psychological* interventions that help address the stress in your life; and family and school interventions that help support you in the best way possible. Once the brain-body stress systems have switched off,

and your body has returned to a healthy way of being, your fatigue alarm will also switch off, and your feelings of fatigue will go away, too.

Combining Metaphors

In the previous subsections we have provided metaphors for different types of functional somatic symptoms. In real life, however, children present with multiple somatic symptoms. It may therefore be necessary to combine metaphors or even to use two different types of metaphor together—for example, the circles metaphor of the stress system, together with one of the metaphors specific to FND, pain, or fatigue. Figure 11.7 shows the combination of metaphors for a child presenting

Fig. 11.7 Overactive brain stress systems, disrupted motor and sensory function, and the subjective experience of pain. The red ball represents the *brain stress systems*. The pink ball represents *motor-processing regions*; the yellow ball represents *sensory-processing regions*; and the spiky ball represents *pain maps*. When the *brain stress systems* are activated by infection, illness, injury, or emotional stress, they become overactive and over-dominant, disrupt motor and sensory processing, and amplify pain processing, causing functional motor and sensory symptoms and amplifying feelings of pain (© Kasia Kozłowska 2019)

with functional motor symptoms, functional sensory symptoms, and chronic/complex pain.

Problems with Memory and Concentration

Many patients with functional somatic symptoms report problems with memory and concentration, and families frequently ask about these symptoms. For example, in our study cohorts of children with FND, approximately one-fifth of children present with some sort of memory loss—failing to recognize their parents, siblings, or friends—or showing a sudden loss in some aspect of their academic function, as in speaking, reading, or writing. Likewise, memory and concentration difficulties are a key element in children whose main presenting symptom is persistent fatigue.

When talking to children whose presentations include difficulties with memory and concentration, we discuss the many different ways in which an activated stress system can interfere with cognitive function. We also tell families that this is an area of current research. Factors that are known to contribute to cognitive difficulties include the following:

- disturbed sleep (see Chapter 5)
- increased cortisol levels secondary to HPA-axis activation (high cortisol levels disturb functioning in the executive regions of the brain) (see Chapter 8)
- increased levels of stress hormones (noradrenalin, endogenous opioids, endogenous cannabinoids, and other anaesthetic neurochemicals) that are secreted as part of the brain's stress response during states of high arousal (these stress hormones likewise disturb functioning in the executive regions of the brain) (Lanius et al. 2014)
- chronic or episodic hyperventilation (see Chapter 7).

For additional reading materials pertaining to the impact of stress on cognitive function, see Online Supplement 11.1.

* * *

In this chapter we have highlighted that all functional somatic symptoms involve activation or dysregulation of the brain stress systems. The brain stress systems play a key role in initiating, amplifying, and maintaining functional somatic symptoms. We have also provided clinicians working with children and families with simple metaphors to discuss research findings from neuroscience and to provide an explanation of what is happening in the brain. All the processes discussed in this chapter have been non-conscious—the implicit level of brain operations—and have involved processes that the brain engages in spontaneously, by itself. Humans also have the capacity, however, to generate conscious representations that affect body state and that contribute to the generation of functional somatic symptoms. We look at this mind level of brain operations—psychological factors—in the next chapter.

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