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The Stress-System Model for Functional Somatic Symptoms

Abstract This chapter introduces the reader to the stress-system model for functional somatic symptoms through the personal journey of the first author. The stress-system model provides clinicians with a framework for thinking about the neurobiology of functional somatic symptoms and for explaining them to children and their families. The components of the brain-body stress system—the neurobiological systems that regulate body state—include the circadian clock, hypothalamic-pituitary-adrenal axis, autonomic nervous system, immune-inflammatory system, and brain stress systems that underpin salience detection, arousal, pain, and emotional states. All components of the stress system are interconnected and form part of a larger, integrated system that ensures effective energy regulation, promotes health and survival, and protects the individual from a broad range of threats. When the stress system—or one or more components of the stress system—is activated too much, too little, too long,

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or in aberrant ways, or when it fails to return to baseline function, then functional somatic symptoms may arise.

As every mental health clinician knows, a good clinical assessment requires one to listen carefully to the child (including the adolescent) and family, and to piece together the story behind the clinical presentation. After listening to patients' stories for some years, I (the first author, KK) realized that my own observations of children with functional somatic symptoms ran contrary to the assumptions and myths that shaped clinical thinking and practice in the late 1990s, which is when I began my clinical practice as a child psychiatrist. I also realized that my observations of the child and her functioning in the family rarely matched those of the family. Over the years, as I puzzled about these recurring discrepancies, conducted my own research, and read countless research and clinical articles about patients with functional somatic symptoms, I came to recognize the central importance of *stress*. All of this clinical work and research comes together in the stress-system model for functional somatic symptoms, the focus of this book.

The easiest way to understand this model is to retrace my path and to review the discrepancies, puzzles, and clinical phenomena that led me both to recognize the centrality of stress and to use it as a foundation for understanding functional somatic symptoms. This retracing takes us through the first half of the chapter; the shared work of the three authors (KK, SS, HH) begins again with the section 'Embodied Family History'. Additional references for this chapter are available in Online Supplement 1.3.

Clinical Observations About the Role of Stress

The Consistent Presence of Stress in the Family Story

When I first learnt about functional somatic symptoms, they were seen as a reflection of stress and distress (Taylor 1986; Maisami and Freeman 1987), which is actually how I see them now. But importantly, there was also a lingering belief, dating to the work of Sigmund Freud, that unusually adverse life events—such as abuse, maltreatment, or incidents involving serious trauma—were the main factors contributing to and triggering the

symptoms (see Online Supplement 1.3). A product of this belief was that clinicians spent a lot of time probing for, and asking about, the existence of such events. As might be expected, this process often made the family uncomfortable—and also reluctant to engage in treatment. For example, in the story of Samantha in Chapter 2, engagement with the mental health team and Samantha failed because the team was intent on looking for a history of sexual abuse—and they kept asking questions about potential sexual abuse—when sexual abuse was not, in fact, part of Samantha's story.

Recent research has presented a more complicated picture of how functional somatic symptoms emerge. As originally thought, there *is* an association between functional somatic symptoms and maltreatment early in life or exposure to serious trauma (Afari et al. 2014). Children who have been sexually abused have a higher lifetime prevalence of somatic symptoms or syndromes (see studies listed in Online Supplement 1.3). Likewise, individuals traumatized by war have higher rates of functional somatic symptoms. For example, Holocaust survivors from World War II—who suffered from a combination of intense stress, severe physical deprivation, and loss of loved ones when they were children or young adults—have a higher prevalence of functional gastrointestinal symptoms, fibromyalgia, chronic/complex pain, and other nonspecific somatic symptoms (dizziness, exhaustion, and weakness), often comorbid with depression and post-traumatic stress disorder (see studies listed in Online Supplement 1.3). Finally, adolescent Cambodian refugees—fleeing from the more than two decades of ongoing strife in that country—also experienced high rates of somatic symptoms, with headache and dizziness being the most common (Mollica et al. 1997). Interestingly, orthostatic symptoms, including dizziness, were some of the most common functional somatic symptoms experienced by soldiers from the American Civil War (1861–1864) (see Online Supplement 1.1).

Nevertheless, my clinical experience with children presenting with functional somatic symptoms, as well as my own research and that of others over the past 20 years, indicated that exposure to extreme stress was not actually necessary—or even common. Most of the children and families that I saw had stories that were full of relatively common, but also surely adverse, life events—such as physical illness, death of a grandparent, especially intense athletic training, or conflict in the family or at school (including bullying)—that had occurred in relatively

close proximity to one another and that seemed to have had a cumulative effect on the child over time. Very often a minor physical event—viral illness, minor fall or twisting injury, knock on the head by a ball, or medical intervention or illness—or a relatively minor psychological event had precipitated the functional presentation. A small handful of children and families *did* report maltreatment (physical or sexual abuse, or serious neglect), family conflict that had gotten out of control (domestic violence), or some other especially traumatic event, but these circumstances were uncommon. The typical pattern that came up time and again was that of cumulative, normative stress events. The family and child reported that the child had coped with event 1, had coped with event 2, had coped with event 3, but had then, following event 4, suddenly developed debilitating functional somatic symptoms that had had precipitated the presentation to hospital.

After hearing many, many stories, it became clear to me that the origin of the functional somatic symptoms was associated with the overall burden of *chronic* or *repeated* stress—whether physical or emotional. It also seemed that the brain did not adhere to mind-body dualism and that physical stress events could trigger the illness just as easily as emotional events. As we got better at documenting trigger events in our studies, we found that about half our patients presented with physical triggers and half with emotional triggers, usually in the context of chronic or repeated stress (Kozłowska et al. 2011).

Research over the last 20 years has highlighted the important role of commonplace adverse life events. In particular, results from the Adverse Childhood Experiences Study (ACE Study) (Redding 2003; Felitti et al. 1998) showed that *household dysfunction*—situations such as the child's mother being treated violently, mental illness of a family member, substance abuse, parental separation or divorce, and imprisonment of a household member—played a central role in health and disease. Early research using this broader framework focused on the association between adverse childhood experiences and common physical health (ischaemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease) and mental health (alcoholism, drug abuse, depression, and suicide attempts) conditions (see studies listed in Online Supplement 1.3). More recent studies have confirmed the long-observed association between adverse childhood experiences and

functional somatic symptoms and syndromes (see studies listed in Online Supplement 1.3). In our own studies of children with functional neurological disorder (FND) and chronic/complex pain, antecedent illness or injury, family conflict, and bullying in the school and peer contexts have also consistently emerged as additional important antecedents (Kozłowska et al. 2011; McInnis et al. 2020).

The Parents Said ‘Our Child Is Fine’, but the Child’s Body Did Not Agree

When telling their story, the parents and the child reported that, even though the child had experienced one difficulty after another, the child had coped and seemed to be *fine*. I found, however, that when the child’s story was tracked via the child’s body—the response of the body being used as the beacon by which the child’s wellness was gauged—a different picture emerged (Kozłowska et al. 2013). The child’s body had been signalling stress and distress for some time, but these signals had not been heeded. Common signals included the following: a disturbance in sleep (difficulties getting to sleep, waking up in the middle of the night, or waking unrefreshed and fatigued); difficulties eating because food felt like a lump in the child’s tummy; increased frequency of abdominal pain, headache, or pain associated with muscle tension elsewhere in the body; a story of viral illnesses that the child found difficult to recover from and that had been followed by prolonged fatigue; and sometimes even the odd panic attack with a racing heart, sweatiness, and difficulty breathing.

The body’s signals had not been heeded; the connection between the symptoms and the events in the child’s life had not been made; and help for the child to manage her distress, her *dis-ease*, had not been provided (for a discussion of *dis-ease* vs. *disease*, see Online Supplement 1.1). Instead, the child had continued to struggle valiantly onward; she had continued to smile to reassure her parents that she was fine; and when anyone asked, she told them that she was fine. Her symptoms were, in effect, masked, and everyone carried on as always, secure in the belief that the child was resilient, that the child was doing well. But, of course, the child’s body was not fine. The child’s body told a different story. The body’s story suggested that each stress had switched on the child’s stress

system. With each new stress, the stress system had been activated more and more, and was less and less able to turn itself off. The story that had begun with one functional somatic symptom was now a story of many different symptoms (see, e.g., the story of Paula in Chapter 2).

Translating Clinical Insights into a Research Program

Although the children and their parents typically told me that they were psychologically and emotionally unmarked by the adverse life events that they had experienced, I felt unconvinced. Likewise, although the paediatricians who referred children for treatment of functional somatic symptoms always confirmed that the physical examination was normal, that there was nothing wrong with the children's physical health and no evidence of disease, my impression was that their bodies had activated in response to stress and had not settled back down. It was common for the child's respiratory rate to be elevated—a sign of motor activation, possibly coupled with sympathetic activation. Another such sign was the child's response—with pain—to palpation of their postural muscles, the neck and back muscles that maintain posture and that activate when the body prepares itself for action; this response suggested that those muscles were activated or braced as they would be if the children were readying themselves for self-protective action.

To examine the questions raised by these encounters with patients and families, I was able to use research methodologies developed by two important mentors: the developmental psychologist and attachment researcher Patricia (Pat) Crittenden, and the neuroscientist Leanne (Lea) Williams. For many years (since 1996), alongside other clinicians, I had contributed to Pat's efforts to develop clinical tools to identify patterns of attachment in school-age children and adolescents within her Dynamic-Maturational Model of attachment and adaptation (DMM) (Crittenden 1999; Crittenden et al. 2010; Farnfield et al. 2010). Patterns of attachment—also known as attachment strategies—evolve from infancy through adolescence via one's experience with close others. Attachment strategies function to maximize safety, comfort, and the biological drive

for survival and reproduction. Importantly for us, attachment figures also function, across development, as psychobiological regulators. On a daily basis, during playful interactions, attachment figures activate the child's stress system in a moderate way. Likewise, on a daily basis, attachment figures use a range of soothing strategies to help settle the stress system back down again. These repeating interactions with the attachment figure(s) function to regulate, either effectively or ineffectively, the child's developing stress system (see studies listed in Online Supplement 1.3). These early interactions of children are the building blocks of each person's self-regulatory capacities later in life. But when families are stressed—because of commonplace adverse life events, loss events, or trauma—the caregiver's capacity to function as a psychobiological regulator may be compromised.

A key strength of the DMM methodology for assessing attachment is its emphasis on procedural (i.e., memory of past action patterns), affective, and imaged evidence to help coders identify patterns of self-protective organization. For example, in assessing attachment in young children, the focus is on observed behaviour, and in older children, the focus is on the structure of language rather than its content per se. In this way, by going beyond words, the DMM clinical tools allow babies, as well as young children who are not yet verbal or who do not have the cognitive and emotional capacity to articulate their predicaments, to have a voice. And since stress is, for us in this book, embodied, the DMM methodology thus allows the body to *speak*.

I met Lea Williams—now Professor of Psychiatry and Behavioral Sciences at Stanford University and founding director of the Stanford Center for Precision Mental Health and Wellness—in 2005. Lea took me under her wing as my PhD supervisor, and in her lab I was able to do a series of studies that examined biomarkers, or biological markers, (in both the body and brain) of stress-system activation. The cohort included children with FND (and other somatic symptoms) and an equal number of age- and sex-matched healthy controls. Seventy-six children with FND participated in the attachment component of the study, and 57 of those also attended the testing in Lea's lab. Because many of the children were functionally impaired—they could not walk at the time of testing or had non-epileptic seizures (NES)—I made many trips with various wheelchairs to get the children to the lab.

Fig. 4.1 Attachment strategies used by children with functional neurological disorder (vs. healthy controls). The strategies used by children and adolescents with FND are depicted by red dots, and by healthy controls, green dots. The attachment strategies at the top of the circle (A1-2, B1-5, and C1-2) represent the normative attachment strategies. The attachment strategies at the bottom of the circle (A3-4, A5-6, C3-4, and C5-6) represent the at-risk attachment strategies (© Patricia Crittenden. Reprinted with permission)

Identifying Stress and Distress Using Assessments of Attachment

The development of the DMM structured interviews to assess attachment in school-age children and adolescents enabled me to use them in my PhD research program with children presenting with FND (Kozłowska et al. 2011). Blinded coders classified these children with FND as predominantly using at-risk attachment strategies: the Type A+ strategies or the Type C+ strategies (Fig. 4.1). Via linguistic markers, coders also identified unresolved loss or trauma in 75 percent of children with FND versus 12 percent in healthy controls. In a later study, children who had presented to our hospital disabled by chronic/complex pain also predominantly used at-risk strategies (Ratnamohan and Kozłowska 2017). Two large, prospective studies have highlighted the

association between the quality of the attachment relationship in early childhood and functional somatic symptoms later in life (Rask et al. 2013; Maunder et al. 2017). For an explanation of the different attachment strategies, see Crittenden (1999) and Online Supplement 4.1.

The overall message from the attachment studies is loud and clear. Children who presented to our hospital for the treatment of functional somatic symptoms—and associated functional impairment—had a long-standing history of relational stress, and they organized self-protectively in ways that maximized safety and comfort in their attachment relationships. For our purposes, given that parents and, more generally, attachment relationships function as the foundation for effective psychobiological regulation, the disruption of attachment relationships evident across studies suggests that these children's stress systems will continue to be more easily and strongly activated in response to any future stress.

Identifying Stress-System Activation Using Biomarkers and Brain Measures

The studies from my PhD research program, which looked at stress-system activation on a group level of analysis, confirmed my clinical impression that children with FND presented in a state of neurophysiological activation/arousal. The group level of analysis—looking at a larger group of children with functional somatic symptoms compared to sex- and age-matched healthy controls—allowed me to identify differences that would not be evident to the paediatrician looking at the test results of a single patient. For references to research articles from my PhD research program, see Online Supplement 1.3.

Autonomic Nervous System

Our studies looking at the autonomic nervous system showed that it was activated too much. Our patients had elevated heart rates (decreased parasympathetic/vagal tone $\pm$ sympathetic activation), lower heart rate variability (decreased parasympathetic/vagal tone), and increased skin conductance (sympathetic activation). How dysregulation of the autonomic

nervous system contributes to the generation of functional somatic symptoms is discussed in Chapter 6 and in Online Supplement 7.1.

Motor System

Our studies looking at the motor system showed that it was also activated too much. Our patients (with FND) had faster reaction times to emotion faces, reflecting increased vigilance and motor readiness in response to emotional signals. Our patients with NES (a subset of FND) showed that many of these children were also breathing too fast. In other words, they had increased activation of the respiratory motor system, with the consequence that they were hypocapnic at rest: they had lower levels of arterial carbon dioxide because they had exhaled too much carbon dioxide. How hyperventilation and hypocapnia contributes to the generation of functional somatic symptoms is discussed in Chapter 7 and in Online Supplement 7.1.

Immune-Inflammatory System

Our studies looking at the immune-inflammatory system suggested a shift toward a state of low-grade inflammation. What this means is that the children showed a *small* increase in a common marker of inflammation, suggesting that the immune-inflammatory system had been activated by stress—physical or emotional—alongside other components of the stress system. This finding is in contrast to rheumatologic diseases or infections, which show a *large* increase in immune-inflammatory markers. How activation of the immune-inflammatory system contributes to the generation of functional somatic symptoms is discussed in Chapter 9.

Pain

Pain was also documented in all our studies. The term *chronic/complex pain* refers to pain for which available medical explanations either do not explain, or fail to account for the severity of, the child's impairment. In one set of studies, chronic/complex pain was the primary presentation. But when children presented other functional somatic symptoms—for

example, FND—pain was also present in 60–84 percent of the children. For more information about chronic/complex pain, see Chapter 9.

Fatigue

Fatigue was also documented in all our studies. Fatigue was present in 33–58 percent of patients even when functional neurological symptoms or chronic complex pain was their primary presenting symptom. For more information about fatigue, see Chapters 9 and 11.

Activation of Brain Systems

We also looked at stress-system activation—and activation of motor-processing regions—on the brain system level. A study looking at cortical arousal using the electroencephalogram (EEG) showed that children with FND showed increased activity in midline regions both in the resting state and in response to an auditory stimulus. These midline regions are involved in salience detection, arousal, pain, and emotional states, and are part of the brain stress systems. Stimuli and body sensations that the brain tags as being *salient* are those that have particular importance for the individual because they signal that the body or the self needs protection from threats to its physical or psychological integrity.

One of the midline regions that we found to be overactivated—the supplementary motor area—is known to have dual role. It functions both as part of the brain stress systems and as a motor-processing region that is involved in motor preparation. Consequently, when the brain stress systems activate, motor function can be affected. How activation of the brain stress systems contributes to the generation of functional somatic symptoms is discussed in Chapter 11.

Brain Structure

Finally, we looked at brain structure using high-resolution MRI to see whether changes in brain function were also associated with subtle changes in brain structure. Importantly, all our patients had clinically normal

scans, with no disease or lesions to explain their presentation with functional somatic symptoms. But other structural changes were detected. We found increased grey matter volume—the layers in the brain that contain neuron cell bodies and glial cells—in the supplementary motor area (the same motor area that was overactivated in the EEG study; see above), right superior temporal gyrus (which is involved in face processing), and dorso-medial prefrontal cortex (a region that is part of the brain stress systems). We also found that greater volumes of the supplementary motor area (responsible for motor preparation) correlated with faster reaction times in identifying emotions. These various changes in brain structure (with increased grey matter volume) were likely to reflect experience-dependent plasticity changes that made the children susceptible to the development of functional neurological symptoms (e.g., motor symptoms). For a discussion of plasticity changes, see Chapter 8 and Online Supplement 8.2.

To summarize this section: in line with clinical observations suggesting that children with functional somatic symptoms present in a state of stress-related *activation*, our studies looking at attachment patterns, biomarkers of stress-system activation, and brain function and structure showed activation of multiple components of the stress system and concomitant activation of the motor-processing regions and regions involved in pain, salience detection, arousal, and emotion processing. From the stories that the children and their families told, it seemed that the children's stress systems had been previously activated and sensitized (primed) by previous stress, had then been *switched on* by a recent trigger event, but had then somehow failed to *switch off*, the result being the emergence, in these particular children, of functional somatic symptoms.

Embodied Family History

The Family-of-Origin Story

The family-of-origin story—understood as encompassing the lives of previous generations, not all still living—has always held an important place for clinicians who work with children and their families (Kerr and Bowen

1988). In one way or another, stress and perturbations in the lives of previous generations seem to reverberate in each family's problems in the here and now. Many tribal cultures conceptualize healing as involving the healing of the ancestral line (Artlandish Aboriginal Art Gallery 2019).

The importance of the family-of-origin story in children with functional somatic symptoms was first raised by Wencke Seltzer, who worked with families of children presenting with FND (Seltzer 1985). Seltzer noticed that while the families perceived the sick child as 'well-equipped intellectually, well-adjusted socially, and free of psychological or emotional complications' (p. 267), the experiences of the majority of the parents in their own families-of-origin were marked by 'themes of extreme poverty, social humiliation, and family disintegration' (p. 269).

Interest in the effects of family-of-origin history have been rekindled in the last decade as animal and human studies have demonstrated that stress exposure can result in epigenetic alterations that can be transmitted to subsequent generations, increasing the offspring's vulnerability to, among other things, stress-related symptoms, even if these subsequent generations were not exposed to the initial traumatic event (for more, see following section on epigenetics).

Epigenetics: How Stress Weaves Its Way into the Body

Epi comes from the Greek meaning over, above, outer, or around; and *epigenetic* processes are those that influence gene expression without modifying the genetic code itself—typically by increasing or decreasing how the gene is expressed. Epigenetic modifications, the patterns of gene expression that control the body's biological processes, are not themselves static; they are modulated by life experiences and environmental factors in an ongoing way. The epigenetic changes that are the product of adverse life events potentially enhance the responsivity of the child's stress system by changing the expression of genes that are central to stress regulation (e.g., the glucocorticoid receptor gene) (Hyman 2009). The field of epigenetics helps us to understand how stress that occurred in previous generations, during pregnancy, in response to parental stress or poor parental care, or during the child's development 'weaves its

way into the neural and biological infrastructure of the child', affecting stress-system function, health, and well-being (Nelson 2013, p. 1098).

In Online Supplement 1.2—Historical Context: The Emerging Science of the Stress System—we discuss how researchers in the 1980s began to recognize that a person's life experiences, especially early-life experiences, actually become biologically embedded in the brain and body.

In Online Supplement 4.2 we list some of the different terms that researchers have used to refer to biological processes through which life experiences alter the function and structure of the brain and body. Many of these terms came into use before we knew anything about epigenetics.

In Online Supplement 4.3 we provide additional information about epigenetic modifications, the biological mechanisms that enable stress-related epigenetic changes to affect health and well-being. We also provide references to the handful of studies that have documented epigenetic changes in patients with functional somatic symptoms, including those with fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome, FND, and chronic/complex pain.

The emerging themes from this body of work is that epigenetic changes—changes in gene expression—are one of the mechanisms by which adverse life experiences weave their way into the brain and body. Although the research in this area is still in its infancy, it appears that changes in gene expression can lead to changes both in stress-system function (e.g., increased activation) and in tissue structure in both brain and body tissues.

The Stress-System Model for Functional Somatic Symptoms

In the final section of this chapter, building on all the information discussed above, we present the stress-system model for functional somatic symptoms. The stress system is made up of multiple interconnected brain-body systems—the autonomic nervous system, hypothalamic-pituitary-adrenal (HPA) axis, immune-inflammatory system, and brain stress systems underpinning salience detection, arousal, pain, and emotional states. These systems form part of a larger, integrated system that protects the individual from a broad range of threats (Chrousos and Gold 1992; Chrousos 2009;

Fig. 4.2 Circles metaphor of the stress-system model for functional somatic symptoms. The overlap between the different components of the stress system—the HPA axis, autonomic nervous system, immune-inflammatory system, and brain stress systems—is presented by the overlap between the circles. The circadian clock is placed within the top circle because the master clock is found in the hypothalamus, a small region located in the base of the brain. The motor system, which includes central and peripheral components, is represented by the pink ball. The placement of the pink ball in the overlap between the brain stress systems and autonomic system reflects that activation of these systems can be accompanied by changes in motor function. The pain system, which also includes central and peripheral components, is represented by the spiky oval. The placement of pain in the overlap between the brain stress systems and immune-inflammatory system reflects that activation of these systems maintains chronic pain. Online Supplement 4.4 includes a version of the circles metaphor that can be printed out (© Kasia Kozłowska [2013](#))

Kozłowska [2013](#)) (see Fig. 4.2). Activation of any single part of the system, whether by emotional stress, pain, injury, infection, or psychological trauma, can activate or dysregulate other components within the system. When the stress system—or one or more components of the stress system—is activated too much, too little, for too long, or in aberrant ways, or when it fails to return to baseline function, then functional somatic symptoms may arise.

The Stress System in Maintenance and Restorative Mode

In the normal course of events, when the child goes about her daily activities, the brain-body systems that make up the stress system regulate the body: they keep the body functioning within normative physiological limits and ensure that the body has access to sufficient energy resources to face the challenges of daily life. For most children (and most adults), whose lives are full of minor and occasional stress, rapid mobilization and timely termination of stress-system activation occur as the challenges of life are met and addressed, with the body (and stress system) then returning to its baseline function (see Fig. 4.3). When the stress system is functioning in this flexible and healthy way, we refer to it as being in *maintenance and restorative mode*—*restorative mode*, for short.

Restorative mode is a state of neurophysiological regulation characterized by the easy flow of life processes, an efficient utilization of energy, and the capacity to respond to environmental demands and to the need for tissue regeneration and repair. Restorative mode is associated with what McCraty and colleagues have called *physiological coherence*: the ‘degree of order, harmony, stability in’, and ‘synchronization between’, the body’s ‘various rhythmic activities over any given time period’, which in humans involves the near-24-hour period of the human circadian clock (McCraty and Childre 2010, p. 11; McCraty and Zayas 2014). In this way, restorative mode involves *flexibility* in response to environmental needs, *harmony* and *physiological coherence* between its various components, and *efficient energy use*—a flow of life processes that is associated with health, well-being, connectedness, and a subjective sense of comfort or ease.

The Stress System Stuck in Defensive Mode

Unfortunately, when stress is chronic, uncontrollable, unpredictable, cumulative, recurrent, or overwhelming—and the stress system is activated too much, too long, or too frequently—the stress system can get *stuck* in defensive mode (see Fig. 4.3, Frame B). When that happens, the stress system remains activated or, as it were, *switched on*. In this

Fig. 4.3 Visual representation of restorative mode and defensive mode. In the normal course of events, the components of the stress system activate to address the challenge presented (denoted in red). They may stay activated for days or even weeks, but then the body returns to *restorative mode* (denoted in blue), its original baseline level of function (see Frame A). The problem is that in the case of many children, the child's body may not return to baseline functioning. In this scenario, even though the challenge or threat has passed, the child remains stuck in *defensive mode* (denoted in red)—and her brain and body may continue to respond as if the threat, whether psychological or physical, were still occurring (see Frame B) (© Kasia Kozłowska 2017)

scenario, biomarkers that mark stress-system activation or dysregulation can be found on a group level of analysis (see earlier section 'Identifying Stress-System Activation Using Biomarkers and Brain Measures').

Not only does the child's body continue to work harder than it needs to, but the body is missing out on the energy renewal, tissue regeneration, and repair functions that take place in restorative mode. *A stress system stuck in defensive mode*—or with one or more of its components stuck in defensive mode—is a system that has lost the ease and flow of life processes, along with the efficient use of energy resources. A stress system stuck in defensive mode is associated with the loss of health, well-being, and connectedness, and with a subjective sense of discomfort or dis-ease. And it can also lead to the production of functional somatic symptoms.

Fig. 4.4 Visual representation of the change in set-points over time in the context of chronic or repeated stress. With repeated stress the set-point—that is, the baseline to which the stress system returns—can change over time. The blue parts of the lines represent the stress system at baseline activation, and the red parts of the lines represent the stress system in an activated state (© Kasia Kozłowska 2017)

Perhaps the most intuitive way of understanding what happens over time—when the stress system is stuck in defensive mode—is that the baseline, or *set-point*, to which the stress system returns, and from which it reacts to new stress, changes over time (see Fig. 4.4). The technical name for the change in set-points is *allostasis*, and the technical term for the long-term biological cost of chronic activation, with a change in set-points, is *allostatic load* (see Online Supplement 1.2). As the set-point moves to higher levels, defensive mode is progressively more engaged even in a ‘resting’ state, and progressively fewer resources are consequently available, even in that resting state, for repair and maintenance. By the same token, because fewer resources are available for repair and maintenance, the process of restoration is compromised, and recovery from each new stress is difficult and often incomplete.

Visual Metaphors of the Stress-System

Children enjoy looking at pictures, and when we talk to children and their families about the stress system and stress-system activation, we like to draw pictures as we talk. With very young children, we

sometimes call the stress system the *danger system*, because the word *danger* is one that even young children understand.

The Circles Metaphor of the Stress System

As discussed above, the circles metaphor provides a simple framework that clinicians can use to organize and make sense of a large—and ever-increasing—body of literature about the way in which the body responds to stress and about the neurobiology of functional somatic symptoms. The model is easily translated into the lay language of daily clinical practice; children and families find it a helpful framework for understanding what is happening to the child's body and why (see case of Paula in Chapter 3).

The overlapping circles highlight the way in which the components are interconnected and interrelated (see Fig. 4.2). In the conversation with the child and family, the overlapping circles help to highlight that when one component of the stress system is activated or dysregulated, other components are also likely to be activated or dysregulated *to some degree*. Very often the child will say something like, 'I see, it is switched on, so now we need to switch it off.'

Online Supplement 4.4 includes a version of the circles metaphor that can be printed out.

The Castle-Fortress Metaphor of the Stress System

The castle-fortress metaphor provides an alternative visual representation of the stress system (see Fig. 4.5). According to this metaphor the stress system is like a castle-fortress. When everything is calm, the castle-fortress (specifically the castle, the place for living) is a calm and welcoming place, with the gates wide open, a place where the tasks of daily life are carried out in a rhythmic and predictable manner (=restorative mode). When the castle-fortress comes under threat, however, the gates of the castle-fortress are shut, the alarm is raised, and the defence towers (specifically those of the fortress) are manned, as needed, to protect the castle-fortress as a whole (=defensive mode). In this metaphor, the stress system, like a castle-fortress, is designed to activate, when necessary, its defence

Fig. 4.5 Castle-fortress metaphor of the stress system model for functional somatic symptoms. In this metaphor, each castle tower and the walls surrounding the castle-fortress represent a component of the stress system. Online Supplement 4.4 includes a version of the castle-fortress metaphor that can be printed out (and filled in) (© Kasia Kozłowska 2017)

systems—all of them, if necessary, to maximize protection. Some children, families, and even clinicians find the castle-fortress metaphor of the stress system easier to use than the circles metaphor. In the castle-fortress metaphor, activation of a particular stress-system component can be depicted by shading in the appropriate tower—each of which represents a different component of the stress system. In clinical practice we colour in the towers with red, which, in all the metaphors used in this book, denotes activation into defensive mode (Fig. 4.6).

Online Supplement 4.4 includes a version of the castle-fortress metaphor that can be printed out (and filled in).

The Blue, Red, and Purple Metaphor of the Stress System

The third metaphor used in our clinical practice involves colour coding. Blue always represents baseline restorative, healthy mode. Red and purple represent a shift into defensive mode. For example, in the

Fig. 4.6 Paula's castle-fortress. Paula—whom we met in Chapters 2 and 3—had a complex history of functional somatic symptoms. In discussions with Paula and the family, we mentioned every component of her stress system as being activated or dysregulated. The symptom of chronic pain began following an injury (colour in the immune-inflammatory tower and pain tower). That injury was followed by sleep disturbance (colour in the clock tower) and functional neurological symptoms (colour in the brain stress systems) in the context of significant bullying. Finally, as Paula became immobile and more and more deconditioned, she developed symptoms related to dysregulation of the autonomic system: panic attacks accompanied by hyperventilation and symptoms of postural orthostatic tachycardia (colour in the autonomic tower [which also includes the respiratory motor system that activates alongside]). Because HPA-axis dysregulation has been documented in studies of women with NES, and because the HPA axis was also likely to be dysregulated due to Paula's reversed sleep pattern, it could also have been coloured in (© Kasia Kozłowska 2017)

autonomic nervous system (see Fig. 4.2), the restorative parasympathetic system is depicted by a light blue line, the sympathetic system by a red line, and the defensive parasympathetic system by a purple line (see also Fig. 6.1). As another example, in the immune-inflammatory system, a macrophage (cell that cleans up debris and is involved in chronic/complex pain) depicted in restorative mode (anti-inflammatory mode) is coloured blue. By contrast, a macrophage depicted in defensive mode (pro-inflammatory mode) is coloured red and purple (see Fig. 9.1).

The Role of Sex Hormones

Stress has a central role in the emergence of functional somatic symptoms in both men and women, but the threshold for developing such symptoms is different for the two sexes. Some female sex hormones—for example, oestrogen—potentiate HPA-axis function and glucocorticoid secretion from the adrenal cortex, accentuate the action of catecholamines in the brain, activate the immune-inflammatory response, and work alongside glucocorticoids to modulate changes in gene expression (Chrousos 2010) (see Fig. 4.7). In this context, chronic or cumulative stress has a more deleterious impact on post-pubertal females than on men and boys. Likewise, this additive engagement of female sex hormones in the stress response, as mediated by the HPA axis, helps to explain why, in civilian settings, women and post-pubertal girls have always been more susceptible to stress-related illnesses and

Fig. 4.7 The role of sex hormones in activating the stress response. This figure represents the fact that female hormones (specifically, oestrogen) up-regulate the stress system (see text for description) and that male sex hormones (specifically, testosterone) down-regulate it (© Kasia Kozłowska 2017)

functional somatic symptoms than men and boys. It seems that it takes higher levels of stress—as created, for example, in the context of military combat—to trigger the same symptom presentations in men and boys (see Online Supplement 1.1).

Sex hormones have many diverse roles within the body that are unrelated to their role in reproduction. An emerging body of work looks at the way that sex steroids modulate the expression of immune-inflammatory cells and molecules within the central and peripheral nervous systems, along with the effects of these processes on chronic/complex pain. For example, recent studies suggest that progesterone and testosterone may down-regulate the immune-inflammatory system—shifting it away from an inflammatory state. The implications of these discoveries for the treatment of chronic pain—which involves activation of the immune-inflammatory system on the tissue, spinal, and brain system levels (see Chapter 9)—are the focus of current research (for references see Online Supplement 1.3).

Chapter Summary

In this chapter, and in an effort to make this important scientific material about the stress system a bit more intuitive, we have retraced the first author's steps in developing the stress-system model for functional somatic symptoms. We have also taken time to look at the model itself.

When working with children it is important to be able to explain complex ideas in simple, visual form—and, if possible, in a form that can be drawn in the clinic on a piece of paper and then taken home by the child and her family. The stress-system model for functional somatic symptoms is a simple way of putting together complex information about how the body, brain, mind, and relational environment interact to make a child vulnerable to functional somatic symptoms. In the upcoming chapters we briefly summarize the neurobiology for each component of the stress system in order to provide clinicians who work with children and families a basic understanding of the biology underpinning the stress-system model. In those chapters we try to present the information in a clear, succinct form and to use visual

metaphors to summarize large chunks of information. In Chapter 5 we discuss the circadian clock; in Chapter 6, the autonomic nervous system; in Chapter 7, the close coupling between the autonomic and skeletomotor systems; in Chapter 8, the HPA axis; in Chapter 9, the immune/inflammatory system; and in Chapter 10, the important role of the microbiota-gut-brain axis in regulating human health and disease. We complete our discussion of neurobiology in Chapters 11 and 12, which discuss the role of the brain itself and, more broadly, the role of brain systems and the mind in producing functional somatic symptoms.

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