5

The Circadian Clock and Functional Somatic Symptoms

Abstract We begin our exploration of the neurobiology of functional somatic symptoms with the circadian clock because every organ, tissue, and cell in our body has a circadian rhythm—and all components of the stress system are regulated by the circadian clock. The integrity of the circadian clock is important in health and dis-ease, and is often dysregulated in children and adolescents with functional somatic symptoms. We examine the healing functions of sleep and why good sleep is important for subjective well-being, facilitating physiological coherence within the stress system and the body as a whole. We then consider sleep interventions as a good starting place for the treatment of functional somatic symptoms. Improvements in sleep can act as a circuit breaker, the first step in the process of healing, the first step in the process of shifting the body from a dysregulated to a more regulated state.

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The Circadian Clock

In our hospital-based Mind-Body Program for functional somatic symptoms, we (the first author [KK] and her clinical team) noticed that many of the children (including adolescents) admitted to the program were bleary-eyed in the morning and that they reported that they had not slept well during the night. The children also reported—and we observed—that after a night of bad sleep, their pain was worse, they felt more nauseous, their fatigue was more pervasive, or they felt more *off* and *icky* in general. And if the child presented with non-epileptic seizures (NES), we noticed that she was more likely to have one following a night of bad sleep. A bleary-eyed child on ward rounds meant a hard day for everyone. The child would struggle with the Mind-Body Program—to attend the hospital school, to do her physiotherapy, to implement her mind-body strategies to manage arousal and pain—and the multidisciplinary team would struggle to support the ailing child in all these tasks.

Because of these clinical observations, we came to pay the circadian clock a great deal of attention. Regulation of the child's circadian cycle became a priority—the intervention that we implemented first—with all our patients who presented with functional somatic symptoms. As the years went by, we became convinced that regulating the circadian clock made a real difference. It seemed to activate the body's own healing powers, and the patients who slept better in the right phase of the circadian cycle—and not too little or too much—seemed to do better. In the stress-system model for somatic symptoms, the circadian clock is prominently represented within the top circle, which depicts the brain stress systems (see Fig. 4.2). Although the healing powers of sleep have long been recognized (Adam and Oswald 1984), new information about the circadian clock and the restorative functions of sleep have continued to emerge over the last decades. The awarding of the 2017 Nobel Prize in Physiology or Medicine to three scientists—Jeffrey Hall, Michael Rosbash, and Michael Young—for their work on circadian biology has highlighted the overarching role of the circadian rhythm in understanding health and illness (see Fig. 5.1).

Fig. 5.1 The circadian clock system. The large clock in the brain symbolizes the master clock in the brain's suprachiasmatic nucleus that synchronizes all the secondary clocks in every tissue and every cell of the body (represented by the clocks situated in the body of the figure) (© Kasia Kozłowska 2019)

Evolution

All plants, animals, and humans that live on planet earth have internal biological rhythms that are synchronized with the earth's revolutions as it orbits the sun. From an evolutionary perspective, these inbuilt day and night rhythms—circadian rhythms—have enabled organisms living on our planet to predict when it will be hot and cold, light and dark, and when predators are likely to be out hunting, thereby facilitating adaptations that increase the probability of survival (Smarr 2017). In humans, circadian clocks are genetically inbuilt into all the cells of the body; cells that work together tend to work in harmony and to share a circadian rhythm. In this way, all organs and tissues have their own circadian rhythms.

The central circadian rhythm is generated by the master circadian clock, which lies in the suprachiasmatic nucleus of the hypothalamus (Zelinski et al. 2014). The master clock, along with the genes that drive it, is reset on a daily basis by exposure to morning light via the eyes. The peripheral circadian rhythms present in cells, organs, and organ systems are also regulated by their own gene-based mechanisms. To maintain harmony across and between body systems, the master and peripheral clocks maintain constant communication via a complex system of neuronal and messenger pathways—the autonomic nervous system, neurotransmitters, and neuropeptide and hormone messengers—that are expressed throughout the brain and body (Zelinski et al. 2014). Information from the body is used by the master clock to help synchronize the peripheral circadian clocks (Nader et al. 2010). Synchronization between different clock rhythms facilitates *physiological coherence*. This notion of coherence can be understood as the ‘degree of order, harmony, stability’ and the ‘degree of synchronization’ between different body systems in the ‘various rhythmic activities’ within the body over each near-24-hour period of the human circadian rhythm (McCraty and Childre 2010, p. 11) (see Chapter 4).

The Reciprocal Relationship Between the Circadian Clock and the Stress System

The circadian clock system and the stress system communicate with and regulate each other in many different ways (Nicolaidis et al. 2017). Each component of the stress system has its own diurnal rhythm, and synchronization between components facilitates coherence and well-being in a well-regulated body. The master clock regulates the hypothalamic-pituitary-adrenal (HPA) axis, whose end product is cortisol (a glucocorticoid) (see Chapter 8). It activates the axis in the early hours of the morning to facilitate cortisol production and an increase in energy consumption, and deactivates it in the afternoon to decrease cortisol production and energy consumption as the body begins to wind down for the night (see Fig. 5.2). The autonomic system also follows a circadian rhythm (see Chapter 6). Within the autonomic system, the sympathetic system activates in the early hours of the morning—alongside

Fig. 5.2 Diurnal rhythms. This figure shows the normal, healthy diurnal rhythms of cortisol, melatonin, lymphocytes (white blood cells), and interleukin-6 (a cytokine) (© Kasia Kozłowska 2019)

the HPA axis—and deactivates at night, when the restorative parasympathetic system activates to support biological processes associated with energy renewal and with healing and repair functions (Buijs et al. 2013). Immune-inflammatory cells, which are found throughout the body and brain, likewise follow a diurnal pattern, regulated by the circadian clock (Labrecque and Cermakian 2015) (see Chapter 9). As noted above, feedback and modulation from all these systems influence circadian clock activity and the setting of diurnal rhythms within the body; these ongoing adjustments to the body's circadian rhythms ensure that the individual is prepared, and at the right times, to respond to challenges, stress, or threat.

Because of the close relationship between the circadian clock and the stress system, dysregulation of one system can lead to dysregulation of the other. Dysregulation of the circadian clock system (e.g., by night shiftwork [in adults] or late-night study routines [in children] or internet surfing throughout the night) can lead to activation of the HPA axis and elevated levels of cortisol (a glucocorticoid). These processes can, in turn, reset the expression of peripheral clock genes and induce additional epigenetic modifications in other body systems. Moving from the opposite direction, when stress leads to activation of the HPA axis and,

in turn, to elevated levels of cortisol, the rhythm of the master circadian clock is disrupted, and as described above, peripheral clocks are reset, in this case in order to promote a state of wakefulness and high energy consumption. While this resetting of the peripheral clocks is adaptive in the short term—during periods of stress—because it enables the child to adjust the circadian rhythm—linked activity of her brain and body to properly respond to stress, it is maladaptive in the long term because it adversely affects sleep. Likewise, because of the close relationship between the circadian clock and the autonomic system, dysregulation of one system can lead to dysregulation of the other. For additional references about these interactions, see Online Supplement 1.3.

We can see many of the above processes at work in the following vignette:

David was a 15-year-old boy who lived with his mother and older brothers. As a baby and toddler, David had lived in a household dominated by strain, conflict, and domestic violence. During primary school David often missed school because of asthma, recurrent abdominal pain, and frequent viral illnesses. After his parents separated (at the beginning of high school), he became depressed. He was treated with a selective serotonin reuptake inhibitor (SSRI) by his family doctor, which helped regulate his mood, but he then stopped taking it. His relationship with his father continued to be strained. As he got older and wanted to spend more time with his friends, his father became jealous of them and complained that David should prioritize time with him. His father's demands were a source of ongoing stress. In high school, David began to suffer from pain that started in his head but then migrated around his body, with an especially painful locus in his lower back. Because of this back pain, David exercised less and less, became physically deconditioned, and missed progressively more school. He began to feel lightheaded on standing up due to an exaggerated heart rate response (orthostatic intolerance, see Chapter 6). At night the pain in his back was at its worst, and David reported that his spine moved and shifted, causing bulging and pain. Unable to sleep at night, David went to bed later and later, and slept into the day. He stopped going to school, stopped seeing the physiotherapist, and became housebound. His mood dropped; he was constantly fatigued; and he began to suffer from suicidal ideation. He then developed functional

neurological symptoms—weakness in the right leg, a turned-in right foot, loss of sensation in the right leg, and an abnormal gait in which he dragged his right leg behind him—and became very depressed. By this time his sleep cycle was entirely reversed.

The above vignette is typical of children with functional somatic symptoms in one crucially important way: children with such symptoms typically present at a point that multiple systems are dysregulated, often with the problems of one exacerbating the problems with another. Another element worth emphasizing is that problems with sleep are typically intertwined with the expression—and exacerbation—of functional somatic symptoms. The first intervention with David was, indeed, to regulate his sleep cycle, thereby correcting his problem of *circadian misalignment*, to which we now turn.

The Health Consequences of Circadian Misalignment

The term *circadian misalignment* refers to a disruption in any of the body's near-24-hour circadian rhythms, including 'inappropriately timed sleep and wake, misalignment of sleep/wake with feeding rhythms, or misaligned central and peripheral rhythms' (Baron and Reid 2014, p. 139). The health consequences of circadian misalignment are substantial.

Jet lag, the misalignment of the circadian clock due to travel across multiple time zones, is probably the commonest example of circadian clock misalignment. It is associated with diverse, but transient, functional somatic symptoms. In addition to daytime sleepiness, fatigue, and a general feeling of not being well and difficulty concentrating, jet lag commonly involves symptoms that reflect disruption of the gut's circadian rhythms: indigestion, nausea, constipation, diarrhoea, and off-schedule defecation.

Shiftwork likewise disrupts light/dark exposure, sleep/wakefulness, rest/activity, or feeding/fasting cycles, all of which are important in maintaining healthy circadian rhythms. After three days of a shiftwork schedule, many metabolites—products of cell metabolism that mark body-system function—show a change in their circadian rhythms and a loss of

synchrony with the master circadian clock (Skene et al. 2018). The gut's circadian clock shows circadian rhythm reversal. The body experiences shiftwork as a chronic stress. The chronic circadian misalignment leads to activation and dysregulation of the stress system—autonomic dysregulation and activation of the immune-inflammatory system—along with changes in eating patterns, appetite regulation, glucose regulation, and mood. Chronic dysregulation contributes to an increased risk of medical disorders (e.g., cardiovascular disease), mental health disorders (e.g., depression), and functional somatic symptoms and disorders (e.g., irritable bowel syndrome) (for references see Online Supplement 1.3).

Patterns of Circadian Clock Dysregulation in Children with Functional Somatic Symptoms

Patterns of circadian clock dysregulation can be identified in children with functional somatic symptoms by taking a careful clinical history. As we saw with David, functional somatic symptoms will often result, over time, in difficulties with sleep, but the direction of causality can also go the other way. Difficulties with sleep or disturbed sleep—whether the result of illness, anxiety, depression, academic demands, or lifestyle factors—may contribute to the factors that trigger or maintain the child's functional somatic symptoms.

Kim was a 14-year-old girl who lived with her parents and an older sister. Because Kim's parents were immigrants, they wanted Kim to do well at school and go to university to become a lawyer or a doctor. They had provided Kim—then 12 years old—with tutoring to help her pass exams for a selective school, and the pressure to keep up good grades was relentless. When Kim failed to perform up to expectations, her mother would lose her temper and yell at Kim. Her father said nothing, but Kim could see the disappointment and anger in his face. During the first year of high school, Kim—now 13 years old—had begun to study late into the night. During the school day she was fatigued, and she started to suffer from headaches and bouts of abdominal pain. Whenever Kim's friends suffered from a cold, Kim seemed to catch it and become sick. By the second year of high school, Kim's sleep was very disturbed. She found it difficult

to get to sleep; she woke during the night; and she never felt refreshed. She began to experience fainting episodes and had frequent visits to the school nurse. When she began to experience non-epileptic seizures, or NES, the neurology team involved in her care referred her and the family for an assessment with the mind-body team. A subsequent cognitive assessment suggested that Kim was an average student and that the expectations that her parents had from her were way above her capacity.

Sleep problems often interact with other functional somatic symptoms, leading to the following sort of clinical presentation.

Abigail, a 17-year-old girl in the final year of high school, presented following the sudden onset of functional neurological symptoms (functional tremor, gait disturbance, and fluctuating visual disturbances). Her history included the following: four years of unrefreshing sleep, fatigue, and gut symptoms (nausea, plus diarrhoea alternating with constipation), all in the wake of a hospital admission for severe gastritis; and two years of mixed anxiety and low mood. She reported that, after the hospital admission for gastritis, her gut function had never returned to normal, that her sleep had lost the sense of rejuvenation and renewal associated with a good night's sleep, and that, as a consequence, her energy levels had never been the same. For a period of four years she had woken unrefreshed and had struggled, day to day, to meet the challenges of daily living. The additional demands of the final year of high school had proved too much for Abigail. In addition to the symptoms described above, her body had responded to the academic stress with new symptoms of chronic pain in her head and back (of six months duration) along with the functional neurological symptoms that triggered her presentation to hospital.

What is important from the perspective of the stress-system model is the idea of a vicious cycle in which the dysregulated stress system affects the functioning of the circadian clock, and the dysregulated circadian clock affects the functioning of the stress system. As time passes, if the systems are unable to reset themselves back to a healthy pattern, the dysregulation within the body can become self-reinforcing: stress-system activation will continue to disrupt sleep and the physiological coherence of the circadian clock, and disrupted sleep and dysregulation of the circadian clock will maintain dysregulation within the stress system.

The Restorative Functions of Sleep

A dysregulated circadian clock manifesting as a disrupted sleep rhythm is important because it powerfully influences the child's sense of well-being and of physical ease or *dis-ease* (for a discussion of disease vs. dis-ease, see Online Supplement 1.1). When sleep is disrupted, so are the vital restorative functions that occur at night—cleaning up, resetting the homeostatic system, and regeneration and repair—resulting in a loss of well-being. We list some of the restorative functions of sleep below. Clinicians can use this information to engage families in sleep interventions and in the treatment process more generally. For references about each of these processes, see Online Supplement 1.3.

Restorative System 1: Sleep Cleaning by the Glymphatic System

The *glymphatic system* is like a layer of piping that exists in the space between the brain's blood vessels and the feet of glial cells—the brain's immune-inflammatory cells—and that allows waste products from brain cell metabolism to drain out into cerebrospinal fluid. During sleep, when the brain stress systems are switched off (sympathetic tone and catecholamine levels are low), the glymphatic system expands and works at maximum efficiency. In this way, each night as we sleep, the glymphatic system gives the brain a sleep clean.

Restorative System 2: Brain Reboot by Synaptic Shrinking and Resetting

Nerve cells within the brain reboot and reset during sleep. In the sleeping brain the synapses between neurons shrink, which allows new synapses to be made the next day. The nightly process of *synapse shrinking* and *resetting* may facilitate brain health and physical well-being by resetting homeostatic set-points across brain-body systems. Synapse shrinking and resetting allows new learning to take place the next day and facilitates

‘*smart forgetting*’ (Tononi and Cirelli 2014, p. 24). It may also help in the process of processing, dulling, and putting behind painful memories that follow in the wake of adverse life events.

Restorative System 3: Slow-Wave (Deep) Sleep Switches Off Arousal and Inflammation

Slow-wave sleep occurs during the first half of the night, is greatest in young children, and lessens with age (Harvard Medical School, Division of Sleep Medicine 2007). Among other things, the HPA axis and sympathetic system are generally switched off. In addition, in a process sometimes referred to as the *anti-inflammatory reflex* or *cholinergic anti-inflammatory pathway*, the restorative parasympathetic system (vagal nerve) (see Chapter 6) up-regulates and facilitates restoration and repair. The vagal nerve also dampens the production of inflammatory proteins, including cytokines, in the spleen and other body tissues, and it inhibits macrophage activity throughout the body, effectively shutting down the body’s inflammatory processes.

Restorative System 4: Sleep Resets Daytime Pain Thresholds

In animal studies, disturbed sleep has been found to increase *pain sensitivity*—a pattern that is also clinically evident in children with functional somatic symptoms. Pain sensitivity may increase for any of the following reasons: improperly reset pain thresholds (see Restorative System 2); increased inflammation or increased sympathetic activation (which activates inflammatory cells) (see Restorative System 3); psychologically depleted coping resources; or multiple interacting processes.

Restorative System 5: Clean-Up and Repair Molecules

During sleep the body secretes hormones and other molecules—including melatonin and growth hormone—that are involved in cell

reproduction, tissue regeneration, DNA repair, and radical scavenging. Melatonin secretion is inhibited with the onset of daylight. Regular sleep and maintenance of synchronized circadian rhythms across and between body systems appear to be critical for fine-tuning cell cycles and sleep-related restorative processes that maximize healing, health, and well-being.

Addressing Sleep as a Therapeutic Intervention

As we saw in the section above, all the mechanisms associated with sleep work together to maintain restoration and repair processes, and they contribute in a substantive way to the child's subjective feeling of refreshment and well-being following a good night's sleep. From a clinical perspective, sleep interventions provide the clinician with a starting point for achieving significant changes within a complicated biological system (see Fig. 4.2). Sleep interventions are, when needed, a vital first step in helping the child's body shift from its current, dysregulated state to a state of better regulation, health, and well-being. Given that most children and families intuitively understand that a good night's sleep is important for health and well-being, the clinician has an opportunity to use a sleep intervention as establishing common ground with the child and family. Moreover, because the circadian clock and stress system are so interrelated, failure to normalize the circadian clock makes it much more difficult for the clinician to treat the child's functional somatic symptoms. A dysregulated circadian clock will continue to drive stress-system activation, and stress-system activation will, in turn, continue to drive the production of functional somatic symptoms. By contrast, a better-regulated circadian clock helps harness the body's intrinsic healing functions (see above). And when sleep is stabilized, some of the child's functional somatic symptoms might become less intense or even just melt away, resulting in a much less complicated clinical picture. In any event, the sleep intervention shifts the brain-body system to a more regulated state and increases the probability that other, more focused interventions will actually help to reduce or even resolve the functional somatic symptoms.

In the following vignettes we provide some clinical examples of the types of sleep issues that are part of our clinical practice with children

with functional somatic symptoms. The interventions fall along a spectrum. Simple interventions involving sleep hygiene measures are always implemented first and are appropriate for all patients and all clinical settings (Owens et al. 2019).

When the simple interventions fail (or are reasonably expected to fail) to establish restorative sleep, a more assertive intervention is required. These mixed interventions combine sleep hygiene measures with simple medication regimes that are widely used because of their safe profiles—they are well tolerated—or because they have a reasonable evidence base in paediatric practice. Nonetheless, the use of medication requires ongoing monitoring by a medical professional to ensure that medications are used on an interim, short-term basis and discontinued once a healthy circadian cycle and restorative sleep have been re-established.

Finally, still more assertive interventions are reserved for situations characterized by significant functional impairment, where the risk of chronic illness and disability are key concerns. Such presentations may also be complicated by severe anxiety, depression, pain, or opiate/benzodiazepine addiction. These assertive, complex interventions, which are typically undertaken only after other approaches have been trialed, combine sleep hygiene measures with off-label medications, together with withdrawal from opiates/benzodiazepines and the treatment of anxiety and depression. Complex interventions are sometimes seen as controversial because of concerns pertaining to the potential for adverse side effects from medications and long-term misuse of medications by patients (for references discussing the controversy, see Online Supplement 1.3). Such interventions require careful assessment and monitoring, and they need to be limited to inpatient, tertiary care settings or the equivalent, where the patient's clinical response to the intervention can be monitored closely, and where the risks and benefits of the pharmacotherapeutic intervention can be assessed in an ongoing manner.

Three of the following vignettes involve adolescents whom we met earlier in this chapter. The fourth vignette describes a complex intervention implemented in the first author's inpatient setting.

Fifteen-year-old David was very distressed by his functional somatic symptoms—migrating pain worse in the back, and right leg weakness

and loss of sensation—and he was highly motivated to be accepted into the inpatient Mind-Body Program. In establishing a treatment contract with David and his mother, the team explained that the program was hard work and that before beginning the program, David needed to engage in some preliminary interventions. First, he needed to return his sleep cycle to a normal rhythm. He could do this over a two-week period by going to bed two hours later each day, until he got to his previous healthy bedtime of 10 p.m. (see Text Box 5.1). Once he reached that point, the team wanted him to take melatonin, a natural substance that the brain secretes to help with sleep, so that his sleep cycle stayed regulated. They also wanted him to eat breakfast in a sunny spot in the house, making sure he got a good dose of morning light. Second, David needed to eat three healthy meals a day—including sufficient vegetables, fruit, and yogurt—to make sure that he had energy for the program and that he was looking after his microbiome, the bacterial community in his gut, which plays a key role in body regulation (see Chapter 10). Third, David needed to restart the antidepressant (an SSRI) that had helped him previously, because the team would be unable to work with him if his mood remained low. In addition, since antidepressants improve the brain's plasticity, they would help his body reset pain set-points and so on (see references in Online Supplement 1.3). Fourth, he needed to go outside the house every day. At first he could mobilize to the front gate, but he had to increase the distance by a minimum of two metres a day. He also needed to re-engage with his physiotherapist. These pre-program interventions would prepare him for the rigours of the Mind-Body Program. David implemented all the above interventions over a six-week period. Subsequently, after his two-week inpatient admission, he was walking with a normal gait, and his pain had decreased significantly. He maintained his improvements over the summer holidays, after which he returned to school full time and initiated ongoing therapy.

Text Box 5.1: How to shift the circadian clock back to a normal, healthy rhythm

The human sleep cycle, which follows the 24-hour circadian clock, can shift itself only about two hours a day (equivalent to two time zones). When trying to move away from a very disrupted sleep cycle—for example, a reverse sleep cycle of sleeping during the day—some children prefer

to reset their clocks gradually by going to bed two hours later each day until the targeted sleep time is reached. Going to bed earlier (e.g., by two hours each day) generally does not work. Alternatively, it is much faster and also potentially easier for the child to accumulate sleep debt by staying up all day, all night, and all of the following day, and to then go to bed at the targeted time.

The situation of 14-year-old Kim, whose academic achievement consistently fell short of her parents' expectations, was more complicated.

First, the team engaged Kim and her parents in an education session about how the body responds when it is pushed too hard, and when it does not get enough sleep. Feedback from the separate cognitive assessment was crucial in highlighting that parental expectations that Kim become a lawyer or a doctor were inappropriately high. To address these issues, a referral was made to see the school counsellor, which would help Kim begin to think about other potential career options. The sleep intervention was implemented only after these issues had been aired and Kim's parents had given their explicit consent that she did not need to study into the wee hours of the morning. At that point, the team told Kim and her parents that the first step in treating the fainting events and NES was to regulate Kim's sleep, and that good sleep would, in turn, help Kim's body to regulate itself. A sleep intervention—a more appropriate bedtime, a going-to-bed relaxation exercise, the addition of regular exercise to Kim's daily routine, and the temporary use of some melatonin (for a three-month period)—was implemented. Kim's sleep settled quickly, and her headaches, fatigue, and abdominal pain settled of their own accord. Kim then began to work on strategies to manage her fainting episodes and NES (see Chapter 14). Because the frequency of these events had also decreased with the sleep intervention, this work took place at a slower, more relaxed pace; the pressure and uncertainty were gone since both Kim and her family could see that she was getting better.

The situation of Abigail was even more complicated—and unfortunate.

In addition to having a long history of functional somatic symptoms, 17-year-old Abigail had strong beliefs that medication was bad for the

body, and she disliked psychologists and psychiatrists intensely. These attitudes made it difficult for her to engage with the mind-body team. It was not possible, for example, to determine whether melatonin or treatment of Abigail's untreated depression could help her improve the quality of her sleep. Even if Abigail had agreed to trial melatonin or other medications, her strong belief system that these substances would somehow disagree with her would have potentially overridden any therapeutic effect, known as the *nocebo response* (see Chapter 12). It was also not possible to explore mood issues in other ways, to address Abigail's relentless catastrophizing that intruded into her sleep on a nightly basis, or to teach Abigail strategies for down-regulating her arousal. Nor was it possible to engage her in the physiotherapy component of the Mind-Body Program. Abigail felt ashamed and angry that she had developed functional neurological symptoms, and she rejected any interventions that the team had to offer. She transitioned into the adult medical system, where she continued to seek alternate explanations for her health problems. She was eventually lost to follow-up.

As previously noted, in some children the sleep intervention is especially complicated because it is intertwined with the treatment of anxiety, depression, or pain, and also with the need to discontinue unhelpful medications—such as opiates and benzodiazepines—that the child has been prescribed in an effort to manage pain, distress, sleeplessness, and arousal. In this context, when it is necessary to use off-label medications to stabilize the sleep of a child admitted to the first author's Mind-Body Program, the medications are used on an interim, short-term basis, as one small part of an intensive multidisciplinary program—with its concurrent physical, psychological, occupational, and school interventions. And as Winfried Rief and colleagues note in a recent article, enriched 'social and physical environmental stimulation' of the type we provide in the inpatient setting plays an important role in generating positive effects for medications used in psychiatric practice (Rief et al. 2016, p. 51). Once sleep has been stabilized for a period of time—usually a three- to six-month period—any medications that were used to stabilize sleep are withdrawn. The exception is when medications are used also to treat comorbid depression or anxiety.

Fig. 5.3 Line drawing of Jai. This line drawing shows Jai dangling over the edge of his wheelchair at the beginning of his admission into the Mind-Body Program (© Kasia Kozłowska 2019)

Jai was a 14-year-old boy presenting with a six-week history of painful fixed dystonia in the neck—which twisted his head to the left—a four-week bilateral leg weakness and difficulties with coordination of his legs, and a two-year history of irritable bowel syndrome. On assessment for the inpatient Mind-Body Program, Jai presented in a wheelchair, his neck supported by a Miami J collar. He was in constant pain and a chronic state of hyper-arousal (manifest by an elevated respiratory rate of roughly 25 breaths per minute). Jai's chronic pain was punctuated by painful neck spasms—brought on by any attempt to change his position—during which he would turn white, shake, and clench his teeth. His body was generally twisted, and he dangled out over the edge of the wheelchair in a C-shape (see Fig. 5.3). He was unable to stand or mobilize independently, and his mother and nursing staff helped him with all activities of daily living. At night, Jai was unable to initiate sleep. He would eventually fall asleep between midnight and 2 a.m., only to wake in pain 3–4 hours later, at which point he begged the nurses to transfer him back to his wheelchair because he was unable to manage the pain in

his twisted position in the bed. On presentation he was medicated with high doses of diazepam for the dystonia and oxycodone hydrochloride (an opioid medication) for pain. A month into the admission he disclosed severe and long-standing anxiety and depression.

Jai's sleep intervention began with simple sleep hygiene measures, moved to a combination of sleep hygiene measures and simple medications with a reasonable evidence base, and subsequently moved to a complex intervention using off-label medications. This last, complex intervention, monitored by a child psychiatrist (KK) and a pharmacist specializing in psychopharmacology, was necessary in order to simultaneously manage arousal and sleep, pain and opiate/benzodiazepine withdrawal, and mental health issues. The intervention is described in further detail below. (For the rationale behind our choice of medications and references, see Online Supplement 5.1.)

- *Establishing a regular bedtime/waking schedule.* In addition to setting a reasonable schedule, we banned electronics in the late evening (which would otherwise contribute to keeping Jai awake into the early hours of the morning).
- *Opening of curtains and switching on room lights in the morning to ensure exposure to the bright Australian sunlight.*
- *Melatonin* (3 mg, then 6 mg, then 9 mg) to help Jai with sleep initiation. This helped a little.
- *Decreasing arousal (in this case, by adding nighttime clonidine).* Together with the melatonin, the clonidine enabled Jai to fall asleep at night at his 11 p.m. bedtime, but it failed to keep him asleep. Jai continued to wake with pain and to remain awake in the early hours of the morning.
- *Using quetiapine to improve sleep quality and length* (25 mg titrated to 75 mg). Jai's sleep normalized; he did not awake from pain in the middle of the night; and he stopped experiencing each night as a form of torture (twisted, in pain, and, in terms of mobility, helpless). The improved sleep also increased his capacity to participate in the program.
- *Discontinuing benzodiazepines.* The diazepam was ceased on admission into the program because of its addictive properties.
- *Discontinuing opiates.* Although opiates alleviate pain in the short term, using them to alleviate chronic pain ends up potentiating the pain (for references see Online Supplement 5.1). In this context, the

opiates were slowly withdrawn over a period of months (for details see Khachane et al. [2019]).

- *Trialling botulinum toxin type A (Botox)*. The botulinum toxin decreased both the frequency of Jai's debilitating neck spasms and the pain associated with them.
- *Quetiapine* was changed to mirtazapine (7.5 mg titrated to 22.5 mg) when Jai disclosed long-standing severe anxiety and depression. Despite significant sleep disruption during the changeover, Jai's sleep eventually settled at the higher dose. After roughly six weeks on mirtazapine, Jai's mood began to improve, and his pain settled even further.
- *Self-hypnosis* was added to the sleep routine once the team discovered that Jai was highly hypnotizable (see Chapter 15). Jai used self-hypnosis to help him position his body for sleep and to help him fall back to sleep if he awoke.

The entire sleep intervention, as described above, took three months. It was six months into his Mind-Body Program before Jai could sit and sleep in a normal position, and seven months into the program before he started to stand independently and mobilize on crutches, and was discharged. One month after discharge—after more than eight months of illness—he began to walk independently. For a detailed description of Jai's case and all components of the intervention with Jai, see Khachane and colleagues (2019).

Sleep Interventions as the Groundwork for Effective Treatment

In the Mind-Body Program, we celebrate good sleep and highlight it as the child's first therapeutic achievement on the path toward health and well-being. We also ask the child to protect her sleep at all costs—no late nights or sleeping in until things have settled. Unless the child comes from a culture where naps are part of the sleep routine, we avoid naps during the day and replace them with rest times, during which the child implements self-regulation strategies.

The vignettes in this chapter highlight the many different interventions that clinicians can use to help stabilize the child's sleep: education about sleep, circadian alignment, the management of electronic devices, sun exposure on waking, the addition of regular exercise to the daytime routine, relaxation, hypnosis (or other regulation techniques) at bedtime, and prescribing melatonin and other medications.

The use of medication requires that a child psychiatrist or paediatrician be a core member of the multidisciplinary team and that the risks of using medication (because of the potential side effects) and of not using medication (because of the potential for chronic illness and disability) be carefully assessed. While the concerns about inappropriate and long-term use of unnecessary or ineffective medications are important to keep in mind, we know from our clinical experience that—unless and until the child obtains good, restful, restorative sleep—other interventions are much less likely to succeed, and improvement is likely to be minimal or far too long in coming. Failing to treat functional symptoms—including disrupted sleep—efficaciously has its own risks. From a neurobiology perspective one can expect that the neurophysiological dysregulation, brain connectivity changes, and brain plasticity changes that occur in functional somatic disorders may become irreversible—and the presentation chronic—if the patient's neurobiological system is not stabilized in a timely fashion. In this context, we have included multiple vignettes, ranging from clinical scenarios in which the sleep component can be easily managed to ones in which the sleep component is especially difficult or even impossible to treat. Our hope is that this range of cases will help the reader to understand the diversity of presentations for functional somatic symptoms and also to understand the resulting need for flexibly adjusting to the challenges presented by each particular patient.

* * *

In this chapter, we have seen that the circadian clock and the stress system are closely interconnected, that activation of the stress system can adversely affect the circadian clock, and that disruption of the circadian clock can activate or dysregulate the stress system. These interconnections can create a vicious cycle that contributes to the child's lack of well-being—*dis-ease*—and to the emergence of functional somatic symptoms.

Early goals in any treatment are to shift the child toward better sleep, a healthier circadian rhythm, and coordination of circadian rhythms between body systems. Not only will the child's sense of well-being—of physical and psychological ease—improve, but achieving these preliminary goals will result in a better-regulated stress system and will facilitate the treatment of functional somatic symptoms. In Chapter 6 we discuss the autonomic system and its role in generating functional somatic symptoms.

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