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Functional Somatic Symptoms in Children and Adolescents: The Stress-System Approach to Assessment and Treatment

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Online Supplement 4.2

The Biological Embedding of Experience: How Stress Weaves Its Way Into the Body

In this supplement to Chapter 4, in approximately the temporal order in which the terms came into use, we list some of the terms that are used to refer to the biological processes through which life experiences alter the function and structure in the stress system and in the body and brain more generally. When reading the science literature, the reader will find that different scientists use different terms to discuss how life experiences – and stress, in particular – weaves their way into the body.

Experience-dependent plasticity, also known as *developmental plasticity*, refers to functional and structural changes of neuronal circuits in response to experience, an idea first proposed by William James in the nineteenth century (James 1890; Fu and Zuo 2011) (see Fu & Zuo [2011] for pictures of plasticity changes). In Chapter 4 of *The Principles of Psychology* (Volume 1), James examined how structural changes in the brain correlated with the habitual behaviour of animals. Although the plasticity changes in the brain are typically emphasized, plasticity changes also occur in other tissues.

Stress reactivity refers to the magnitude of endocrine, autonomic, or neural response to a stressor. The term was used extensively in physiology

research from about the 1950s. Persistent changes in stress reactivity – that is, a change in function – of the HPA axis and autonomic nervous system of women with a history of severe early-life stress was first demonstrated two decades ago (Heim et al. 2000).

Priming, used from about the 1950s, refers to the idea that experience of a stimulus will make the processing of subsequent stimuli of that type more efficient. More recently, **stress-induced neuroinflammatory priming/immunological priming** – also known as **immunological memory** – has been used to refer to the idea that prior stress (and glucocorticoid exposure) potentiates the neuroinflammatory response to a subsequent immune challenge (Frank et al. 2016; Brenhouse and Schwarz 2016).

Up-regulation and down-regulation are, respectively, the processes of increasing or decreasing the response to a stimulus, usually by changing the number of available receptors. The term **down-regulation** appears in the immunology and endocrinology literature in the 1970s.

Allostasis, as discussed in Chapter 4 and Online Supplement 1.2, refers to the adaptive resetting of a set-point to a new baseline level (Sterling and Eyer 1988; McEwen 1998)

Developmental programming, also known as *in utero*, *fetal*, or *perinatal programming*, refers to the idea that exposure to stress during sensitive periods of development either in utero or during early postnatal development may lead to altered programming (reprogramming) of tissue structure and function, predisposing the child to subsequent health problems (Lucas 1991).

Metabolic imprinting, a synonym for *fetal programming*, is used to describe how nutritional experiences of early life – usually in utero – lead to altered programming (reprogramming) of tissue structure and function (Lopes et al. 2017).

Neuroprogression refers to the pathological reorganization of the central nervous system – including aberrant changes in neural activation and

connectivity, and neural loss secondary to oxidative stress – in PTSD and other mental health disorders (Berk 2009). Neuroprogression is a helpful way of understanding the multidimensional changes that underpin illness progression in psychiatric disorders.

Stress gets under the skin seems to have been first introduced in immunology research by Daniel Andrews and Mark Smyth to communicate the idea that immune cells were able to detect early signs of cellular dysregulation – caused by physical stress – even in the absence of non-self-signals (i.e., pathogens) or inflammation, and even before pathological changes, such as genesis of tumour cells, had begun (Andrews and Smyth 2008).

Biological embedding of early experiences, also known as *developmental programming*, refers to the process whereby stress, the social environment, or early experience *gets under the skin* (see above) (Hyman 2009; McEwen 2012; Nelson 2013). The idea of stress getting under the skin was then used by Stephen Hyman to refer to the biological processes by which environmental factors interact with the genome to influence brain development – thereby biologically embedding early experiences (Hyman 2009).

Epigenetic changes in gene expression or gene function is defined as ‘molecular factors and processes around DNA that are mitotically stable and regulate genome activity independent of DNA sequence’ (Skinner et al. 2010, p. 8). In other words, epigenetic processes are ones that affect DNA (gene expression or gene activity in protein transcription) by making changes to structures around the DNA: the DNA itself remains the same (see Jawaid et al. [2018] for a summary). The evolving meaning of the term *epigenetics* since it was coined by Conrad Waddington in the 1940s is described by Skinner and colleagues (2010).

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