Title: Complementing conceptual models of persistent somatic symptoms with mathematical formalization

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Complementing conceptual models of persistent somatic symptoms with mathematical formalization

As reported in this journal (Smith et al., 2019; Lane et al., 2018; Henningsen et al., 2018), increasing attempts are being made to translate computational science into psychosomatic medicine. Here, we argue for the next step: a mathematical formalization and experimental testing of psychosomatic mechanisms exemplified by a recently published pilot study.

Computational modeling has been used for several decades to mathematically describe complex phenomena. This is witnessed in applications addressing various complex problems ranging from systems neuroscience (e.g. modeling of action potentials in neurons) to cognitive psychology (e.g. disentangling the interplay of reinforcement learning and working memory). The computational approach has been translated to complex clinical problems in neurology (e.g. neural control of eye movements) and psychiatry (for an overview see: Petzschner et al., 2017). The basic idea of computational models is that clinical disorders – or, in a broader view, bodily and psychological mechanisms – can be modeled by casting them in the form of mathematical equations.

Recently, Smith et al. (2019) proposed an embodied (neuro-)computational framework mapping biopsychosocial processes. The authors illustrate this conceptual model with regard to the role of social support in health and disease and suggest a broad applicability of this model for psychosomatic medicine. Similarly, in an earlier paper, Lane et al. (2018) described an elaborate mechanistic model how early adversities could be linked to a biased competition favoring physical over emotional pain. Both models are intuitively plausible to the clinician and highlight the active nature of perception. Being based on Bayesian models of perception and referring to corresponding neural networks, the models are computational in nature. The mentioned authors themselves emphasize the potential for quantitative modeling and the need for experimental designs that provide further empirical support.

The mathematical formulation of computational models forces researchers to be very explicit about their theories. As impressively demonstrated by Marewski and Mehlhorn (2011) who attempted to mathematically specify verbal process models of decision making, conceptual models are often underspecified relative to the process data against

which they can be tested. If the definitional clarity needed is found, these mathematical models then allow for computational predictions (e.g. regarding behavior, learning curves or the measurable experience of bodily sensations) that can be empirically tested. Models can then be refined on the basis of empirical data, leading to an interplay between data-driven and theory-driven approaches. Subsequently, such theory-driven models can be translated into clinically oriented experiments. These models can then be tailored to fit data from clinical subgroups resulting in an iterative process to an improved understanding of the object of research. The relevance of extending conceptual computational models with mathematical formulization and experiments has recently been emphasized by researchers of the EURONET-SOMA Group, in their joint effort to improve diagnosis, treatment and care for patients with persistent somatic symptoms (PSS). [I suggest to add a ref here of EURONET-SOMA, e.g. Weigel et al J Psychosom Res 2017]

With a presumed multi-factorial etiopathogenesis and, in particular, an underlying interaction of bodily and psychological mechanisms, PSS are a prime example of a complex problem accessible to a computational modeling approach. Building upon previous work applying a Bayesian approach to PSS (Van den Bergh et al., 2017; Edwards et al., 2012), the EURONET-SOMA Group proposed a theory to explain PSS as erroneous inferences within the „predictive coding” paradigm of brain functioning (Henningsen et al., 2018). This theory conceptualizes an erroneous interplay between expectations and sensory inputs in PSS.

A recent effort in psychosomatic medicine has complemented the aforementioned conceptual model with mathematical formalization (Lehnen et al., 2018). The effort captures the relationship between sensory input, expectation and outcome in patients suffering from one of the most frequent and clinically highly relevant PSS, namely functional dizziness. The approach is based on a mathematical head motor control model, which has been validated in healthy subjects and in patients with neurological disease (Lehnen et al., 2008; Sağlam et al., 2014). Head mechanical characteristics are modeled with a transfer function using three parameters (head moment of inertia, stiffness and viscosity). This allows for a simulation of head movement when these parameters are altered, e.g. by an experimental increase in the head moment of inertia, an experimental set-up challenging the interplay between sensory input and expectation. Like in patients with lesions to sensory input (e.g. vestibulopathy) and in patients with deficits forming

internal expectations (e.g. cerebellar disease), a specific discrepancy between predicted and measured head movement unravels a deficit in this interplay.

A recent pilot study applied this computational model and experimental set-up to patients with functional dizziness (Lehnen et al., 2019). Findings from this study suggest that patients indeed display head motor control deficits comparable to patients with structural lesions (vestibulopathy, cerebellar disease) pointing at sensory-motor dysfunction in PSS, i.e. a disrupted interplay of expectation and sensory input as conceptualized in the “predictive coding” paradigm of PSS. This gives an example of how conceptual computational models can be complemented with quantitative rigor and experimental testing. The computational conceptual models by Smith et al. (2019) and Lane et al. (2018) promise to stimulate similar computational-experimental endeavors, with the potential to greatly widen our understanding and treatment options of PSS and, even more general, our understanding of the interaction of biological, psychological, and social factors in health and disease.

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