

The Power of Expectation: Placebo and Nocebo Effects on inflammation-induced Sickness Symptoms

Justine Schmidt, Institute of Medical Psychology and Behavioral Immunobiology, University Hospital Essen, Germany

Systemic inflammation typically triggers a characteristic pattern of unspecific bodily and psychological symptoms – collectively known as “sickness behavior” – including fatigue, pain, depressed mood, and anxiety. These symptoms reflect arise from immune-to-brain communication and are clinically relevant across a wide range of conditions, from chronic inflammatory and psychiatric disorders to side effects of immunotherapy and vaccination. While their biological underpinnings are increasingly well understood, psychological factors that might influence the experience of sickness symptoms, particularly treatment expectations, remain underexplored.

This talk addresses how positive (placebo) and negative (nocebo) expectations may shape inflammation-induced sickness symptoms, particularly drawing on evidence from human experimental endotoxemia. Within this translational experimental model, injecting low-dose lipopolysaccharide (LPS) induces a safe and transient systemic inflammatory response in healthy volunteers, providing a unique and controlled framework for investigating how psychological and pharmacological factors modulate inflammation-induced sickness symptoms.

Employing this experimental model, we recently demonstrated that treatment expectations, shaped through physician-patient communication, can modulate bodily and affective symptoms of sickness – even in the absence of an active anti-inflammatory medication – and can further enhance the efficacy of pharmacological treatment. Importantly, these modulatory effects on self-reported sickness symptoms occurred independently of measurable changes in peripheral inflammatory markers, suggesting that mechanisms distinct from direct immune modulation may mediate expectation effects, which warrants further illumination.

The talk will place findings from experimental endotoxemia within the broader context of placebo and nocebo research and discuss their clinical and translational implications. In particular, it will consider the potential of expectation-based interventions to complement pharmacological treatments and improve symptom management across conditions characterized by systemic inflammation and inflammation-induced sickness symptoms.