



Sickness behavior mediates the effects of inflammation on self-rated health

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Conclusions

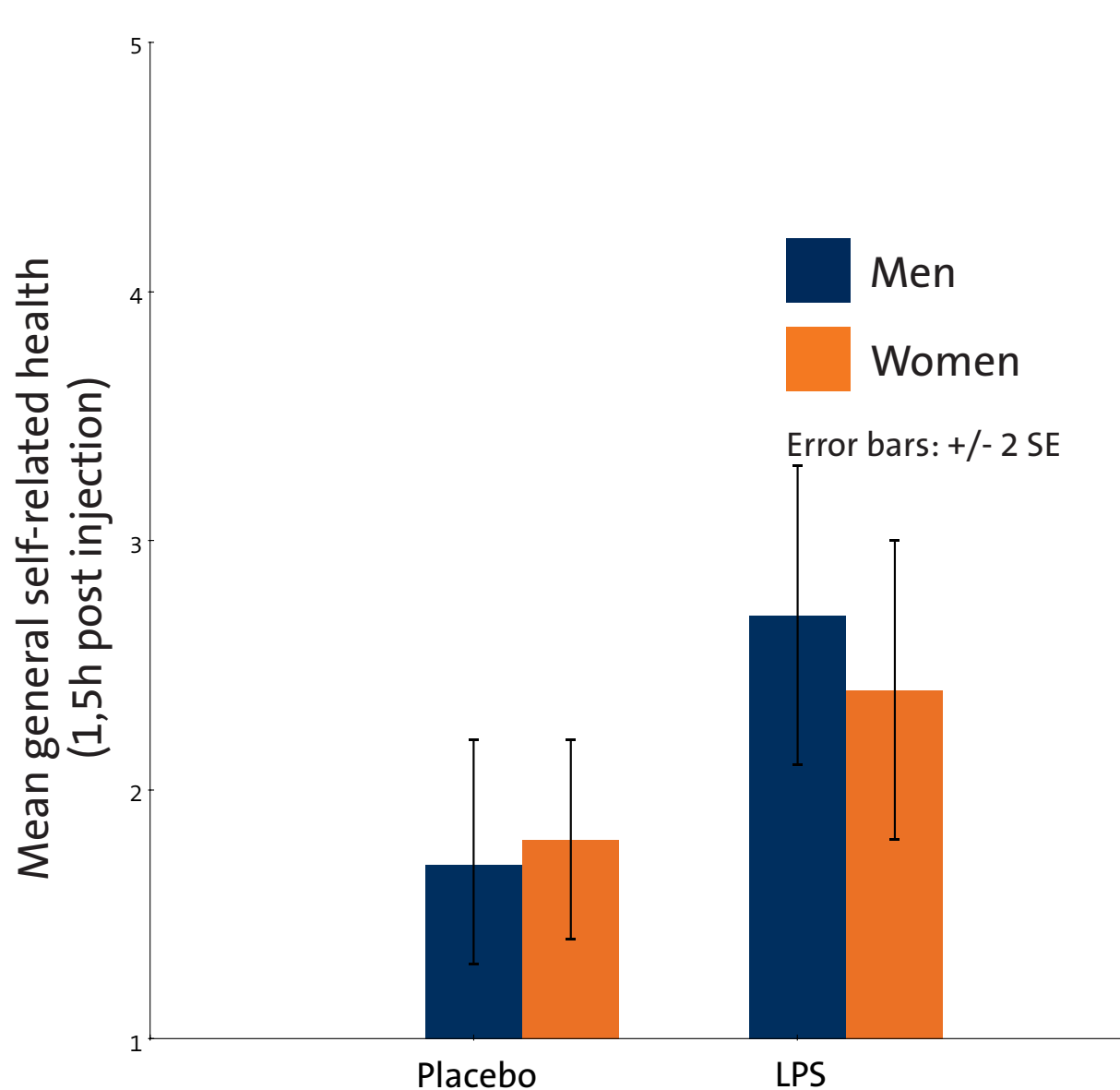
Self-rated health (SRH), both general and framed to refer to the current moment, can be actively manipulated by immune activation. This highlights the importance of inflammatory activity in subjective health ratings. We could show that subjectively perceived sickness behavior is the main mediator of the changes in SRH, not the level of inflammatory activity itself.

Background and Aim

Self-rated health (SRH) is a powerful and reliable predictor of future ill-health, although many of its determinants (such as pain, mood and fatigue) are known to fluctuate over time. Furthermore, SRH has repeatedly been associated with inflammatory levels in cross-sectional studies. The aim of the study was to determine how inflammation relates to SRH in an experimental setting, and how perceived sickness behavior contributes to subjective health ratings.

Hypotheses

- SRH should be affected even during a transient immune activation as provoked by lipopolysaccharide (LPS).
- Current SRH, rated with a shorter time reference, would be more readily affected by LPS provocation than general SRH, which rates the overall health over a longer period of time.
- Inflammation affects SRH through the sickness behavior it induces, as a subjective experience of inflammation.



Differences in general self-rated health in the LPS group versus placebo

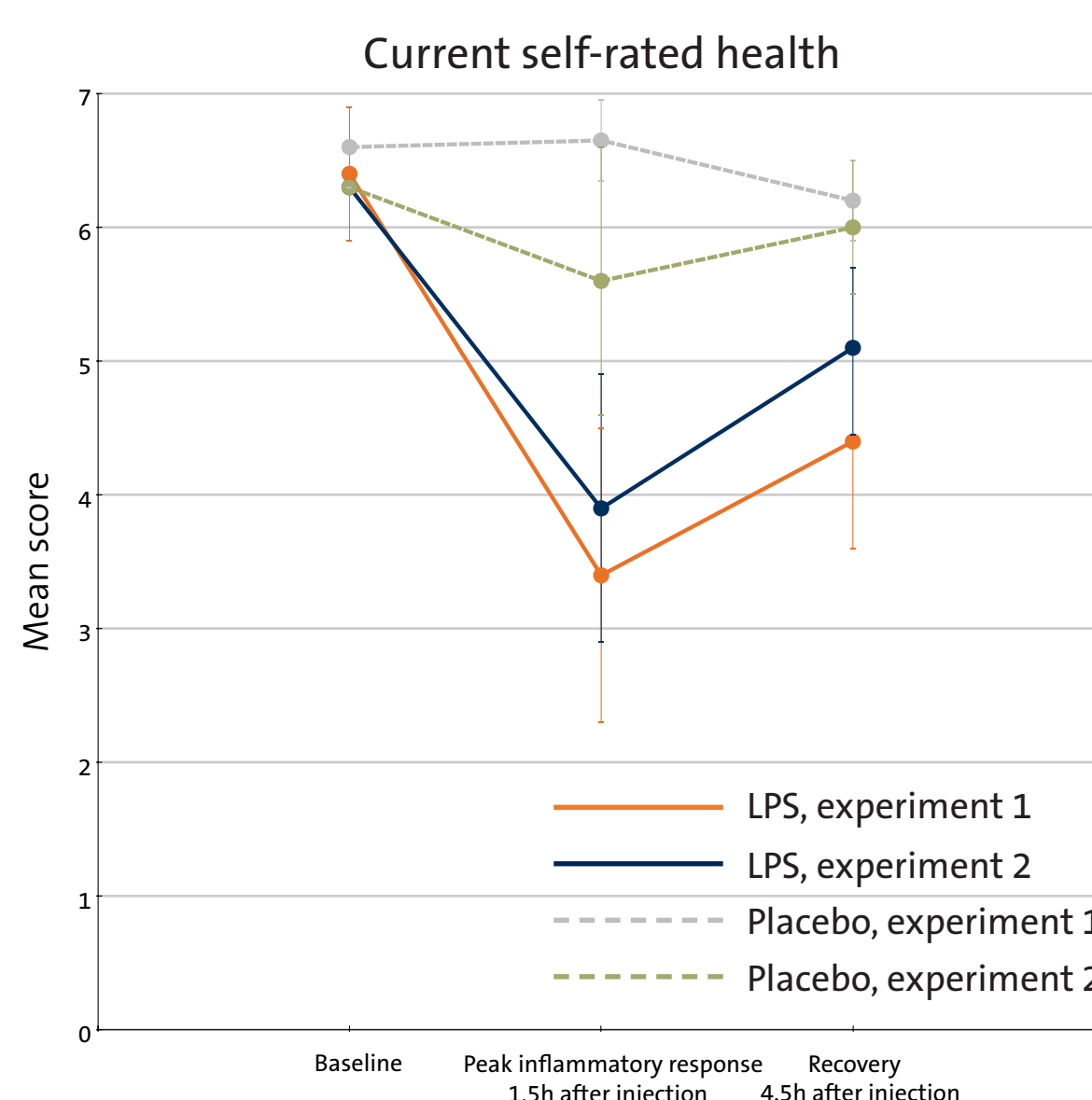
General SRH worsened after LPS injections. There was no difference between men and women. Measured 1.5h post injection with lipopolysaccharide (0.6ng/kg body weight, Experiment 2) or placebo (saline). Means and standard error are depicted for the scale: 1=very good, 2=good, 3=neither good nor poor, 4=poor, 5=very poor

Method

The experiments were double-blind and randomized, varying in dose, design and timing of tests.

In the first experiment, eight healthy participants (7 men) were injected intravenously (i.v.) twice 28 days apart, once with 0.8 ng/kg body weight LPS and once with saline in a within-subjects design (Experiment 1). One year later, 52 healthy participants were injected i.v. with either 0.6 ng/kg LPS (n=31, 18 women) or saline (n=21, 11 women) in a cross-over design (Experiment 2).

Sickness behavior and plasma levels of pro-inflammatory cytokines were assessed before and after injection, at 1.5 h and at 4 or 4.5 h (for each experiment respectively) after injection. Sickness behavior was assessed using a newly developed questionnaire, SicknessQ. Cytokines were analyzed using multiplex Luminex immunoassay. To be able to distinguish between general SRH (“How is your general health?”) and current SRH (“health right now”), both ratings were assessed. Current SRH was assessed in both studies before injection, at peak inflammatory response (1.5 h after injection) and at the end of the studies (4.5/5 h after injection in the respective experiment). General SRH was measured at baseline, at 1.5 h and 4.5 h after injection in Experiment 1. However, general SRH was only assessed once in Experiment 2 (at 1.5h), to keep the ratings unbiased from previous ratings due to the general nature of this health statement.

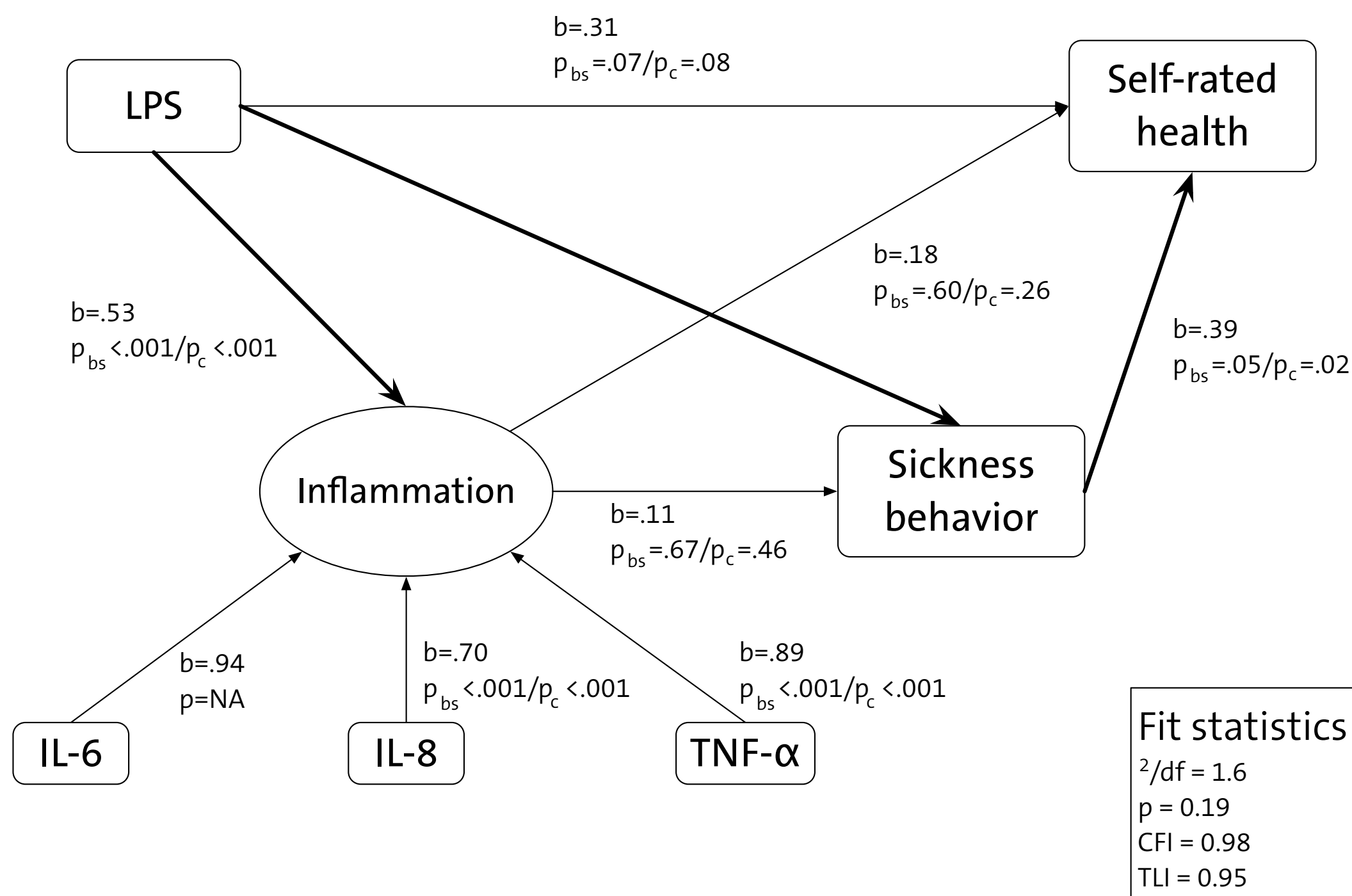


Changes in current self-rated health over time

Current SRH worsened after LPS injections. The ratings had not reached the baseline value at the end of the experiment. Measured pre and post injection with lipopolysaccharide (LPS, 0.8ng/kg body weight in Experiment 1, 0.6ng/kg body weight in Experiment 2) or placebo (saline). Means and standard error are depicted for the scale: 1=very poor, 2=poor, 3=somewhat poor, 4=neither good nor poor, 5=rather good, 6=good, 7=excellent.

Path analysis for general self-rated health

The model describes the relationship between acute immune provocation, inflammation, perceived sickness behavior and self-rated general health status, at 1.5 h after injection with LPS/placebo. Significant direct pathways are depicted with bold arrows. LPS injection increased inflammation and sickness behavior directly ($b=.53$, $p_c/p_{bs} < .001$), but with only a trend towards a direct path to general SRH ($b=.31$, $p_c=0.07/p_{bs}=0.08$). The only significant path from LPS stimulation to decreased general SRH, was by an indirect path via sickness behavior ($b=.20$, $p_c=.03/p_{bs}=.05$). p_{bs} =bootstrapped p-value; p_c =conventional p-value.



Results

- SRH (current and general) deteriorated 1.5 h after LPS injection ($p < .001$) compared to placebo.
- Current SRH was more strongly affected by experimental immune provocation than general SRH.
- The worsening of SRH during experimental immune provocation was statistically mediated by sickness behavior ($p=.02$ for general SRH, $p<.001$ for current SRH), but not by inflammatory levels alone.

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My current projects concern emotional regulation and brain activity during experimental inflammation, pain sensitivity and neuroinflammation in allergic patients as a model for chronic inflammation, and the effects of inflammation on CBT treatment for chronic pain patients.

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