

# A Single-dose, Placebo-controlled, Cross-over Study To Evaluate Lps-induced Hyperalgesia In Healthy Volunteers

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## Background and aims

PainCart<sup>®</sup>, CHDR's comprehensive and validated nociceptive test battery, is used in early-phase clinical studies investigating the analgesic effect of novel compounds. This study investigated whether intravenous administration of lipopolysaccharide (LPS), when combined with evoked pain tests, is suitable as a pharmacological model to study treatments for inflammatory pain.

## Methods

This was a placebo-controlled, randomized, cross-over study in 24 healthy males. Twelve subjects were administered a bolus of 1ng/kg LPS intravenously, and twelve 2ng/kg LPS. Before days of placebo/LPS administration, subjects completed a full study day without any administration, but with identical pain threshold testing. PainCart<sup>®</sup> (Electrical burst and -stair, Heat, Pressure and Cold pressor test) and blood sampling were performed pre-dose and up to 10hr post-dose. Data were analysed with a repeated-measures ANOVA.

## Results

Mean age was 30.8 ±9.5 years. Overall, no significant effect on pain detection- or tolerance thresholds (PDT, PTT) or Area Under the Curve (AUC) was found in any of the PainCart<sup>®</sup> modalities. Results suggest that LPS solely has a subtle hyperalgesic effect around 2-4hrs post-LPS administration in selected PainCart<sup>®</sup> modalities (Figure 1), corresponding with the cytokine and stress hormone concentration peaks (e.g. TNF-α: Figure 2).

## Conclusions

This study found that the human endotoxemia model is not suitable for studying inflammatory hyperalgesia in healthy volunteers.

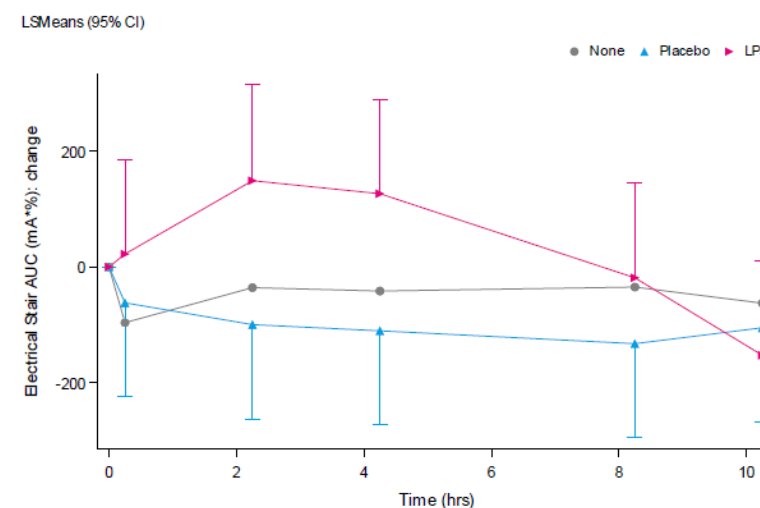


Figure 1: Electrical Stair test results: AUC after 2ng/kg LPS administration

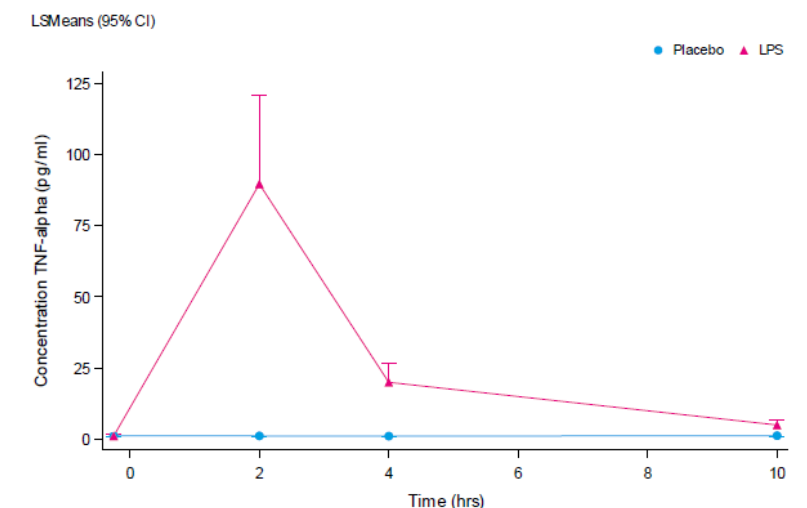


Figure 2: TNF-α concentration after 2ng/kg LPS administration

