META-ANALYSIS OF PLACEBO RESPONSES IN CENTRAL NEUROPATHIC PAIN: IMPACT OF SUBJECT, STUDY, AND PAIN CHARACTERISTICS

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INTRODUCTION / AIM

The placebo response is a complex construct related to psychobiological effects, as well as natural history and regression to the mean. Moreover, patient and study design characteristics have also been proposed as significantly affecting placebo responses. The aim of the current investigation was to identify factors that contribute to variable placebo responses in clinical trials involving individuals with central neuropathic pain.

METHODS

We performed a systematic review and meta-analysis of placebo-controlled trials examining pharmacological and non-invasive brain stimulation interventions for central neuropathic pain. Study design, subject characteristics, and pain ratings for the placebo group were extracted from each trial. Pooling of results and identification of moderating factors were carried out using random effects meta-analysis and meta-regression techniques.

RESULTS

A total of 39 published trials met the inclusion criteria (spinal cord injury [SCI], n=26; stroke, n=6; multiple sclerosis [MS], n=7). No significant publication bias was detected. Overall, there was a significant effect for placebo to reduce central pain (-0.64, CI: -0.83 to -0.45). Smaller placebo responses were associated with crossover-design studies, longer pain duration, and greater between-subject baseline pain variability. There were no significant effects for neurological condition (stroke vs. MS vs. SCI) or the type of intervention (e.g., pharmacological vs. non-invasive brain stimulation). In a planned sub-analysis, the severity of damage in the spinal cord also had no significant effect on the placebo response.

DISCUSSION / CONCLUSIONS

Further study is warranted to identify factors that may explain the impact of pain duration on the placebo response at the individual subject level.

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