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Open-label placebo hypoalgesia: what works for whom under which circumstances

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Open-label placebo (OLP) hypoalgesia is increasingly proposed as an ethical and clinical relevant way to optimize analgesic treatment effects for a variety of populations.[1–11] Although effects are usually somewhat smaller for OLP than for deceptive placebo procedures, meta-analyses have concluded that there is at least a small-to-medium effect on outcomes, such as pain or other self-reported complaints (eg, distress).[2,3,11] These meta-analyses also showed that OLP procedures might work better in clinical populations than in healthy subjects. However, the evidence for effects on physiological or behavioral outcomes and long-term clinical outcomes is more limited.[2,3,6,8,11] More importantly, evidence varies between studies, with a large heterogeneity between study designs, populations, and outcomes.[2–4,7,8,11] Most of the studies in this field compared an OLP condition with a non-OLP condition within a specific patient group. With this type of comparative treatment/no-treatment design, there is usually less attention for the mechanisms that might contribute to the effectiveness and feasibility of OLP hypoalgesia treatments. The few studies focusing on specific mechanisms of OLP suggest that similar psychosocial and neurobiological mechanisms might play a role in both OLP and non-OLP treatments.[1,2] Moreover, there is some evidence that the way of communication, specifically the level of suggestiveness and positive expectations, seems to have an enhancing effect on the outcomes of OLP.[2,3] The more convincing and extended the placebo mechanisms are explained, the stronger the effects seem to be on both expectancies and clinical outcomes.

In an empirical study by Tang et al.[9] published in this issue, it was investigated whether and to what extent providing healthy participants with choice over placebo administration facilitates OLP hypoalgesia. The authors compared an extended OLP procedure, consisting of 10-minute face-to-face discussion on the placebo effect and a short news report video, with choice about the treatment with a non-choice OLP condition and a no-treatment condition. Although a comparison with a non-OLP condition was missing in this study, the current findings suggests that the OLP effect may be enhanced by providing choice over treatment administration. In terms of mechanisms, expectancy for pain relief fully mediated the choice effect at enhancing OLP hypoalgesia, suggesting that choice about treatment options in the case of OLP directly affects treatment expectancies and in turn strengthens the effects on hypoalgesia. Interestingly, there was no effect of OLP without choice. The current study therefore suggests that choice over treatment initiation could be an essential way for offering OLP in an acceptable way in a clinical situation and for improving pain outcomes during OLP hypoalgesia.

Future studies should focus on mechanisms underlying OLP procedures in several ways. First, mechanisms have to be studied related to aspects of choices, such as choice for elements as part of the OLP treatments or choice for alternative non-OLP treatments. There is also a need for studies on elements related to the OLP procedures, such as experienced efficacy of OLP procedures or belief in empirical evidence of OLP. Finally, mechanisms related to treatment components, such as the trustworthiness of the treatment and prescriber, and ethical issues, such as the level of choice for alternative treatments, are crucial for applications in clinical populations.[2,3,5] An important additional step are the studies of OLP procedures with the possibility of choice in clinical populations, as suggested for hydrocortisone treatments to reduce dexamethasone-induced neurobehavioral side effects in children with acute lymphoblastic leukemia.[10] There is an urgent need for studies that compare different types of OLP conditions (eg, choice for OLP and the availability of other treatment options) in clinical populations, to disentangle the most optimal circumstances for OLP procedures. These studies might finally help to unravel the conditions of how to make OLP an ethical, cost-effective and empirically based treatment and to understand when and under which circumstances OLP might be effective for different populations.

Conflict of interest statement

The author has no conflicts of interest to declare.

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