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Tolerability of caloric vestibular stimulation in a persistent pain cohort

Dear Editor,

Persistent pain is a major healthcare problem worldwide, costing billions of dollars each year and being commonly refractory to existing treatments [for citations, see 1]. We read with interest the recent research article by Hagiwara et al. [2] in your journal, in which it was reported that active, but not sham, galvanic vestibular stimulation (GVS), significantly modulated experimental pain in 16 healthy volunteers. GVS stimulates the vestibular system via direct current applied to bilateral mastoids, inducing activation in various vestibular, cognitive, affective and pain-related brain regions. A simpler and better-known method for such stimulation is caloric vestibular stimulation (CVS), which has been used for decades to diagnose brain death and vestibular disorders. This technique involves irrigation of cold water into the external ear canal, eliciting subjective vertigo and observable nystagmus. Small case series report that CVS can reduce pain in post-stroke thalamic pain syndrome [see e.g. 3] as well as pain following spinal cord injury or amputation [reviewed in 4; see also 5]. Both CVS and GVS are now being examined in a variety of neurological and psychiatric therapeutic contexts, and in cognitive neuroscience studies [reviewed in 4, 6–8].

Hagiwara et al. [2] note that some post-stroke pain patients [3] found the administration of CVS to be intolerable, even if the technique induced pain relief. They reported that GVS, on the other hand, was well tolerated by their healthy subjects, thus proposing that if GVS also reduces pain in persistent (chronic) pain patients, it would be a tolerable therapeutic option when CVS is not tolerated. The issue of CVS tolerability is important to examine because the technique is exceedingly easy to administer, is inexpensive, requires no special equipment, and — if shown to be efficacious — could be readily implemented by medical practitioners and potentially self-administered by patients (albeit with prior training and due care). If CVS is inaccurately perceived to be poorly tolerated, this could prevent its appropriate examination as a potential simple and readily accessible therapeutic brain stimulation technique.

We conducted a convenience-based non-randomised effectiveness trial of CVS (using iced water), with a single-blinded control for short-term pain modulation effects (an ice-pack applied to the forehead), in 8 patients with phantom limb pain (PLP), 12 with spinal cord injury pain (SCIP), 14 with complex regional pain syndrome (CRPS; types I & II), and 4 with non-specific persistent pain (NPP) [1,9]. We report the modulation effects of CVS on persistent pain and allodynia in detail elsewhere [1, see also 9], but in summary, a single session of cold-water CVS significantly reduced pain relative to the ice-pack control within 30 minutes post-intervention. Although the magnitude of pain reductions in some groups was modest and there were many non-responders, the CRPS group appeared most responsive and also exhibited striking cases of allodynia modulation following CVS.

Here we report findings on tolerability of CVS administration in this persistent pain cohort. Participants provided written, informed consent, in accordance with a protocol approved by the Alfred Health Human Research Ethics Committee, Austin Health Human Research Ethics Committee, and Monash University Human Research Ethics Committee. All procedures [see 1] satisfied the standards of the Declaration of Helsinki (1975). All 38 patients rated their pain and, if applicable, allodynia, before and after CVS, and in addition 25 patients (11 CRPS, 9 SCIP, 3 PLP, 2 NPP) also formally rated their experience of CVS. The latter included whether CVS was uncomfortable or painful (including intensity scores), and whether they experienced nausea or headache (and associated intensity) or other symptoms. These 25 patients were additionally asked if they would repeat the procedure if it reduced their pain by 50% or more for 1 week or for 1 month. Vertigo and nystagmus occurred for all patients following CVS, as expected. Fig. 1 depicts the formal CVS tolerability data and Fig. 1 caption describes additional results. We found the vast majority of patients reported that despite finding the procedure uncomfortable or painful, or experiencing side-effects, they were willing to repeat the intervention if it helped their pain.

Our data show CVS to be a well-tolerated intervention in a persistent pain cohort. While GVS, if shown to be therapeutically efficacious, may be an option for patients who are not able to tolerate CVS (such as our patient with repeated emesis; see Fig. 1 caption), our data suggest such subjects are not observed frequently in persistent pain cohorts. A recent study [10] of CVS side-effects in the vestibular diagnostic setting reported that of 130 patients, 75 (58%) experienced undesirable symptoms including nausea (50%), vomiting (5%), and headaches (12%). However, distress and nausea ratings were generally low (<3/10), except in 19 (15%) patients who discontinued testing early. For that study though, it is important to note that vestibular dysfunction patients were examined, not persistent pain patients. Patients with persistent pain are usually familiar with, and therefore more willing to undergo, uncomfortable interventions especially to treat rather than just diagnose their condition. Moreover, CVS in diagnostic settings is part of an overall suite of investigations [10] that is more onerous than the single CVS sessions used in the present study.

Importantly, tolerability of CVS needs consideration in the context of other persistent pain treatments and the consequences of poorly treated persistent pain. For example, oral pharmacotherapy frequently causes side-effects of longer duration and of far more concern than transient nausea/headache, and can be associated with dependence, sedation and mortality risk, while ketamine infusions are frequently ceased due to intolerable adverse

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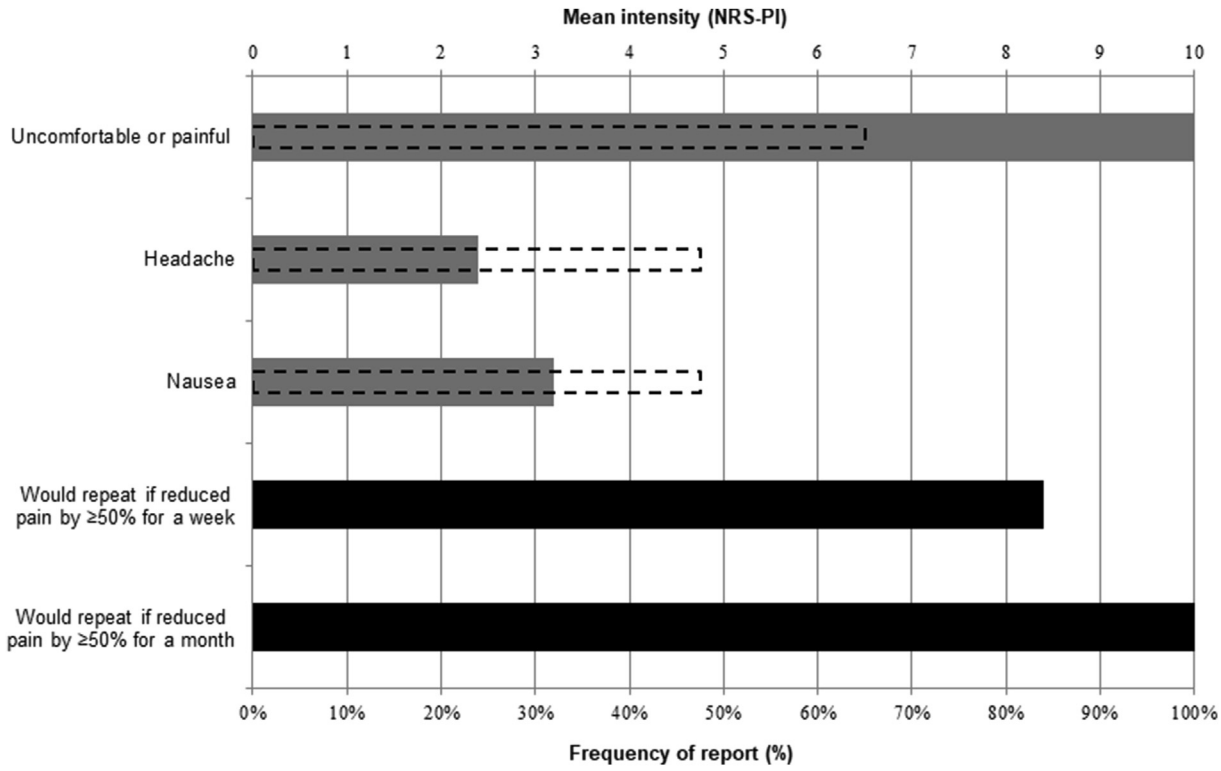

Fig. 1. Tolerability and side-effects of CVS and patient willingness to repeat the intervention if it reduced their pain by 50% or more for one week or for one month. Solid bars indicate percentage of patients (N = 25 with formal tolerability data available) while dotted lines indicate the reported mean intensity of CVS-induced discomfort/pain and side-effects. Duration of nausea was not captured but tended to be transient. The frequency of headache may be an underestimate as delayed headache was not captured (delayed nausea is considered unlikely). As shown, twenty-one (84%) stated they would repeat CVS if it reduced their pain by ≥ 50% for 1 week. In addition, 1 stated 'maybe', 1 stated 'yes, but only for my worst pain', and 2 stated 'no' but 'yes' for a pain reduction lasting 1 month. Twenty-five (100%) stated they would repeat CVS if it reduced their pain by ≥ 50% for 1 month. Tolerability for repeat CVS sessions showed some variability (sometimes worse, sometimes better), but generally no change in patient willingness to repeat the intervention if it helped their pain. However, 1 patient who had said 'no' to repeating CVS if it reduced their pain by 1 week, but 'yes' for 1 month, changed to 'no' for both 1 week and 1 month after a subsequent CVS. Other minor occasional symptoms were also reported including fatigue, hot flush, and feeling of a water-logged ear. Of the 13 patients for whom there were no formal CVS tolerability data, review of qualitative experimental session notes revealed the following informal comments: 7 were considered to have tolerated CVS well, 1 experienced repeated emesis that lasted several hours (no intramuscular or parenteral anti-emetic was administered, he reported no PLP relief from CVS, and he was not offered nor would have accepted a repeat CVS); 1 had strong nausea, 1 had mild nausea, 2 had no tolerability comments documented, and 1 tolerated a first CVS well but asked for a subsequent CVS to cease due to ear pain. There were no side-effects of the ice-pack procedure other than the intended cold-related discomfort.

psychological side-effects, and invasive persistent pain interventions may involve significant initial discomfort and longer-term morbidity risk [for citations, see 1]. In the context of available persistent pain management options, the side-effect profile of CVS reported here suggests it is likely to be considered an acceptable intervention, notwithstanding some patients for whom the technique will not be tolerated.

It remains to be determined with carefully conducted randomised controlled trials whether CVS is an efficacious therapeutic intervention for managing persistent pain. However, it is clear from the data we present here that tolerability of CVS in such cohorts should pose no barrier to investigating the technique or to its potential implementation.

Authorship statement

The authors confirm that they meet the requirements for authorship.

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