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Mentored Research: Randomised Study

Effects of mirthful laughter on pain tolerance: A randomized controlled investigation

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A B S T R A C T

Introduction: Chronic pain is a debilitating condition that affects many people. Currently, there is no single treatment known to cure or assure relief from chronic pain. Accordingly, the management of patients' discomfort is an integral part of treating chronic pain. Such treatment, however, is not effective for many patients. We investigated whether mirthful laughter provided by comic relief can influence pain tolerance and muscle soreness in young healthy participants.
Methods: Forty participants underwent a randomized controlled cross-over designed experiment. Each participant was exposed to a comedy video eliciting mirthful laughter and an uninteresting documentary. Delayed onset muscle soreness was induced in one leg at a time by eccentric exercise. Pain tolerance was tested using blunt force application and assessed subjectively using a visual analog scale.
Results: Watching the comedy video elicited a significantly greater irregular breathing pattern compared with watching the documentary video ($p < 0.001$). After watching the comedy, the participants' positive affect was increased ($\Delta 2 \pm 1$) while it was largely decreased (Δ-11 ± 2) after watching the documentary video ($p < 0.001$). Pain tolerance was decreased by 17 ± 5 N after viewing the documentary video ($p < 0.001$), but did not change significantly after watching the comedy.
Conclusions: Thirty minutes of watching a comedy eliciting laughter favorably influenced pain tolerance in healthy humans.
Clinical trial no.: #NCT02896075.

1. Introduction

Chronic pain is a debilitating condition that affects more people than any other (Institute of Medicine Committee on Advancing Pain Research and Education, 2011). Currently, there is no single treatment known to cure or relieve chronic pain. About half of all patients with chronic pain indicate little or no control over their pain (Michaelson, 2006). Accordingly, the management of discomfort is an integral part of treating chronic pain. Novel ways to effectively treat this condition are urgently needed as the population of older adults, who often suffer from osteoarthritis and low back pain, is increasing steadily (Ortman et al., 2014).

Laughter has often been considered 'the best medicine,' as it is known to provide a multitude of health benefits, including improvements in stress relief, endothelial function, immunity, resilience, and mood (Foley et al., 2002; Kuiper and Martin, 1998; Lefcourt et al., 1990; Neuhoff and Schaefer, 2002; Neureldein and Eid, 2018; Sugawara et al., 2010; Walter et al., 2007). In spite of the well-publicized notion that laughter helps those suffering from chronic pain, previous research on laughter affecting pain tolerance remains equivocal. Studies on post-surgical and nursing home patients have shown reductions in perceived pain after watching humorous videos compared with controls (Adams and McGuire, 1986; Rotton and Shats, 1996). A recent study attributed such effects to endogeneous opioid release (Manninen et al., 2017). However, findings from laboratory-based studies are not in agreement (Dunbar et al., 2012; Weisenberg et al., 1998).

The discrepancy may be due, at least in part, to methodological and experimental design issues that confound the interpretation. For example, there is not a standardized procedure to test pain tolerance. Some observational studies assessed the amount of pain medication (Rotton and Shats, 1996) while laboratory studies induced pain through various physical and physiological stimuli, including blood pressure cuff application and cold pressor test (Dunbar et al., 2012; Hudak et al., 1991; Nevo et al., 1993;

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Weisenberg et al., 1998; Weisenberg et al., 1995). Many of these studies did not provide proper control conditions, nor did they control for important variables such as sense of humor. More importantly, many studies did not confirm or quantify the amount of laughter elicited in the participants (Nevo et al., 1993; Weisenberg et al., 1995, 1998).

The primary aim of the present study was to investigate the effects of mirthful laughter on pain tolerance using a randomized controlled cross-over approach. In order to simulate chronic pain in healthy adults, eccentric resistance exercise was used to induce delayed-onset muscle soreness (DOMS) that develops a few days after the strenuous exercise (Byrnes and Clarkson, 1986). It was hypothesized that mirthful laughter would positively influence pain tolerance as well as muscle soreness. Prior to addressing the main research question, we first performed a preliminary study to identify a suitable method of evaluating pain tolerance that does not largely interfere with the sympathetic and cardiovascular system as these circulatory systems are known to interfere with the pain perceptions and responses (Randich and Maixner, 1984).

2. Methods

2.1. Participants

Forty adults (15 men and 25 women) 20–40 years of age were recruited from the University student body and the city surrounding the university using flyers. Participants were included if they were apparently healthy, normotensive, and free of musculoskeletal disease. Participants were excluded if they had known cardiovascular or musculoskeletal disease or if their pain tolerance was not reachable in a blunt force test on the quadriceps (maximal pressing force allowed by the IRB was 245 N). Participants were instructed to keep their normal daily routine including caffeine consumption throughout the study period to prevent the effects of lifestyle factors on pain tolerance measurements. The university's Institutional Review Board approved the study, and written informed consent was obtained from all participants. The present study was registered at the National Institutes of Health (ClinicalTrials.gov #NCT02896075).

2.2. Preliminary study to evaluate various pain tolerance tests

Hemodynamic factors are known to influence pain perceptions and pain responses (Bruehl and Chung, 2004) as the brain regions regulating the cardiovascular system are known to overlap substantially with those that contribute to anti-nociception (Randich and Maixner, 1984). In order to select the optimum pain tolerance protocol that would not evoke substantial hemodynamic responses, changes in blood pressure and heart rate in response to 3 commonly-used pain tolerance tests (blood pressure cuff occlusion, blunt force application on muscles, and cold pressor test) were compared. Participants were instructed to lie supine with a beat-by-beat blood pressure monitor (Portapres, Finapres Medical Systems, Enschede, Netherlands) that was placed on the middle phalanx of the middle finger on the left hand. The Portapres was connected to the WinDaq data acquisition software (DATAQ Instruments, Akron, OH) to record heart rate and blood pressure for later analysis.

A load cell (Transducer Techniques, Temecula, CA) attached to a pan head screw and metal handle was used to determine the load placed on the quadriceps of each participant. The force transducer applied blunt force and measured it through an amplifier (TMO-2, Transducer Techniques, Temecula, CA) connected to our data acquisition software (WinDaq). Blunt force was steadily increased until the participant indicated that the pain was not tolerable, at which point the test was terminated. The blunt force was applied half-way between the anterior superior iliac spine and the top of the patella. The specific spot was marked in order to avoid testing directly on the same exact spot that could inflict residual tenderness. The rate of increases in applied force was controlled through feedback on the WinDaq data acquisition system.

For the blood pressure cuff pain test, a standard blood pressure cuff was placed on the right upper arm. The cuff was gradually inflated at 15 mmHg per second until the participant indicated that they were at the limit of their pain tolerance (Rapid Cuff Inflation System, Hokanson Vascular, Bellevue, WA). Per the IRB guideline, the maximum blood pressure was set at 300 mmHg. The cold pressor test was performed with the participants submerging their hand up to their wrist in ice water of about 4 °C. Participants were told to remove hand when they reached their pain tolerance.

In an attempt to minimize the inter-investigator variability, one investigator (SL) performed all the experiments for all the participants.

2.3. Main experimental protocol

The main study was conducted using a randomized controlled cross-over approach. Participants reported to the laboratory a total of seven times. Participants underwent a preliminary testing session followed by three visits each for the two video watching interventions. The interventions were separated by a minimum of 1 week as a washout. Each intervention included one day of inducing muscle soreness in one leg through eccentric muscle contractions (see below); a second day of testing muscle soreness and pain tolerance and watching a 30-min video (either a comedy or documentary); and a third day of testing muscle soreness and pain tolerance again to see if the effects of the video viewing persisted the next day (i.e., 24 h after the video viewing).

The second intervention was identical to the first intervention except that muscle soreness was induced on the contralateral leg and the video was switched to either comedy or documentary. The order of the videos and legs was randomized by a research assistant flipping a coin, and participants watched a randomly assigned video. If the video was a comedy, the participants picked stand-up comedians of their choice in order to meet with their individual preference of comedy/humor. The video was watched for 30 min with two other people in the room to make it a social setting to induce a greater degree of laughter. When the video was a documentary, an uninteresting, serious documentary was chosen by the investigators.

2.4. Eccentric exercise

Participants began with a 5-min warm-up at 50 W on a cycle ergometer (Monarch Exercise, Vansbro, Sweden). Participants were then secured to the isokinetic dynamometer chair in a seated position with chest and waist straps (Biodex System 2, Shirley, NY). The movement began at a speed of 45°/second at a knee angle of 90°. The participants were instructed to resist maximally until full flexion was reached and completed 12 sets of 10 repetitions of eccentric maximal voluntary actions. Participants aimed for 70% or better of the previously-tested one repetition maximum for the eccentric phase. Exercise sets were separated by 1 min of rest. This protocol has been utilized successfully in previous studies to elicit delayed onset muscle soreness (Armstrong et al., 1991; Prou et al., 1999; Vassilis et al., 2008).

2.5. Body composition

The seven-site skin fold assessment was utilized to estimate body fat percentage using Lange skinfold calipers (Cambridge Scientific, Cambridge, MA). The body fat level was collected primarily as a descriptive variable but could potentially contribute to pain tolerance due to the association between body fat and inflammatory mediators (Gustafson, 2010) that could sensitize nociceptors to pain (Marchand, 2008).

2.6. Muscle strength

A reduction in muscle strength is an objective indication of muscle soreness (Byrnes and Clarkson, 1986). Knee extensors of both legs were tested for maximum strength using the isokinetic dynamometer (Biodex System 2, Shirley, NY). Both the concentric and eccentric phases of the strength test were set at a speed of 60°/second. Subsequently, isometric (static) muscle strength tests were performed. The lever was locked at 60° and then at 90°, and the participant was instructed to try to extend the leg and hold it for 5 s.

2.7. Pain

The visual analog scale pain score (VAS) is an established instrument for the assessment of subjective pain (Jensen et al., 1986) that has been found to be reliable (Price et al., 1983). It is a scale from 0 to 10 showing faces and descriptions of what participants may feel (Jensen et al., 1986). Participants picked the number (i.e., pain score) that corresponded best to how their sore leg felt. Participants also had their pain tolerance measured using the force test as an objective measurement.

2.8. Mood and psychological state

The Coping Humor Scale (CHS) and the Situational Humor Response Questionnaire (SHRQ) were administered to all the subjects (Martin, 1996). The Positive and Negative Affect Schedule (PANAS) was administered before and after watching the video to evaluate changes in mood state. High negative affect is characterized by subjective distress and unpleasurable engagement, and low negative affect by the absence of these feelings. Positive affect represents the extent to which an individual experiences pleasurable engagement with the environment (Watson et al., 1988).

2.9. Laughter

In order to quantify the amount of laughter, a Pneumotrace II respiration transducer (UFI, Morro Bay, CA) was worn above the umbilical region while watching the videos. The respiration transducer was attached to the WinDaq data acquisition system (DATAQ Instruments, Akron, OH) to record the data. The irregular respiratory pattern was taken as indications of laughter as previously described (Bloch, Lemeignan, & Aguilera-T, 1991; Svebak, 1975).

2.10. Statistical analyses

Descriptive characteristics were expressed as means ± SEM. Paired t-tests were conducted between the various outcomes of the comedy and documentary treatments with the probability level set at $p < 0.05$. To compare physiological changes caused by each pain tolerance test, linear mixed models were used. A random intercept was included for each participant since the experiment used repeated measures. ANOVA tables for each fitted model were constructed. In the case of significance, multiple comparisons were performed using the Bonferroni method. To control for important covariates and to investigate significant predictors of pain tolerance, linear mixed model analyses that include fixed and random effects were used. The linear mixed model included fixed and random effects, to predict the pain tolerance. The fixed component described the sample's relationship between the covariates, predictors, and pain tolerance while the random component described the variation within each participant. The inclusion of a random intercept for each participant in the mixed model was justified because of the large variance in pain tolerance. Predictor variables included leg, time, and treatment, while covariates included sex, SHRQ, CHS, PANAS scores, and body fat percentage. A simple ordinary least squares regression was used to investigate if a relationship exists between the time spent laughing and the change in pain tolerance. To determine the total variability in pain tolerance, the intraclass correlation coefficient (ICC) was calculated. Power calculations were performed using nQuery Adviser computer software (Statistical Solutions, Boston, MA). Sample size calculations were based on the number of subjects needed to detect significant changes in pain/soreness.

3. Results

A total of 51 participants were recruited beginning September 2016 through May 2017. 11 participants were excluded for having musculoskeletal injury or having a pain tolerance above the maximum cutoff. As a result, 40 participants were randomly assigned to the interventions and studied. No participants were lost during the interventions. The trial was terminated in June 2017 after an adequate sample size was reached and data were collected. Selected descriptive characteristics are shown in Table 1.

Participants were apparently healthy and had above average scores on the sense of humor assessment. As shown in Fig. 1, the percentage of participants that failed to reach their maximum pain tolerance was highest for the blood pressure cuff test, but was low for the blunt force test and cold pressor test. Hemodynamic changes were greatest during the cold pressor test and lower in the blood pressure cuff occlusion and blunt force tests. Based on these results, we selected to use the blunt force test as the pain tolerance test of choice for the main study protocol.

Eccentric resistance exercise was successfully used to induce delayed onset muscle soreness. Participants rated soreness in their leg as a 6.6 ± 0.2 using the VAS pain score. In all strength measures (concentric, eccentric, and isometric tests), the maximum torque was decreased ~10% at 48 h after the eccentric exercise compared with baseline values (data not shown).

Watching the comedy video elicited a greater irregular breathing pattern compared with watching the documentary video ($p < 0.001$, ES = 0.96). The amount of laughter amounted to ~10 min out of 30 min of the video watching. Positive affect increased (Δ2 ± 1) after watching the comedy but decreased (Δ-11 ± 2) after watching the documentary ($p < 0.001$, ES = 0.81). There were no significant changes or differences in the negative affect.

Pain tolerance in the sore leg decreased 17 ± 5 N after viewing the documentary ($p < 0.001$, ES = 0.50), but did not change

Table 1
Selected subject characteristics.

Variable	Mean (SD)
Males/Females (n)	15/25
Age (yr)	23 (4)
Body fat (%)	20 (8)
Heart Rate (bpm)	67 (12)
Systolic BP (mmHg)	116 (10)
Diastolic BP (mmHg)	57 (7)
Situational Humor Response Questionnaire Score	60 (7)
Coping Humor Scale Score	22 (3)
Baseline Pain Tolerance (N)	97 (49)

BP = blood pressure.

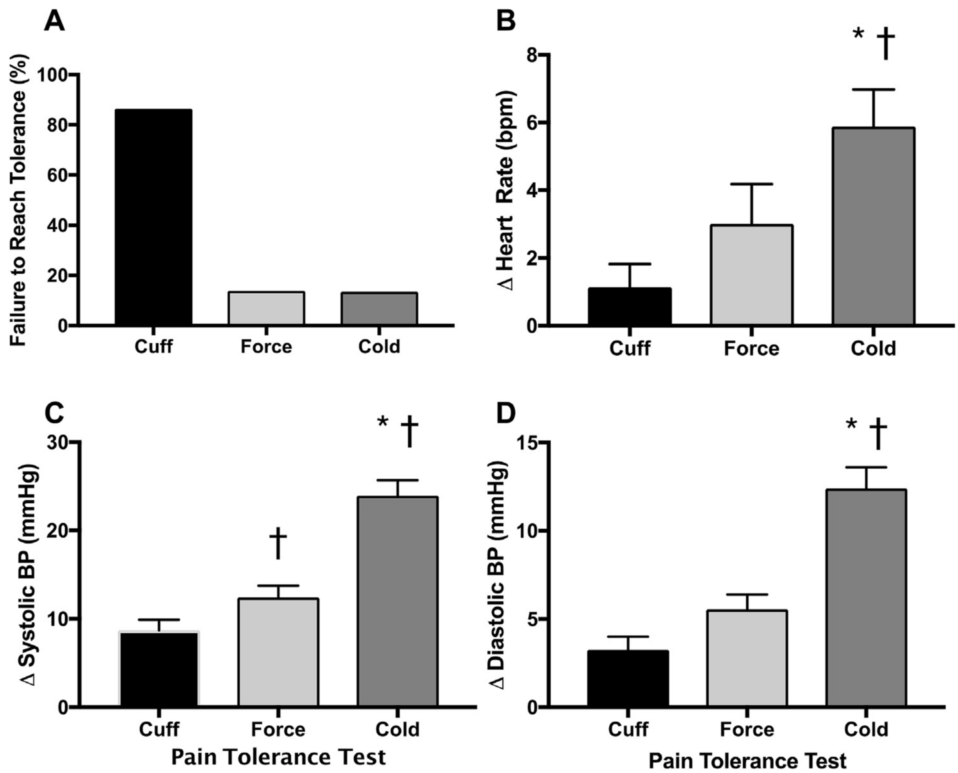

Fig. 1. Comparison of three different methods of testing pain tolerance; the blood pressure cuff test ("Cuff"), the application of blunt force on quadriceps ("Force"), and the cold pressor test ("Cold"). The percentage of participants that failed to reach their pain tolerance for each test is shown in A. Changes in heart rate and systolic and diastolic blood pressure (BP) are shown in B, C, and D. *p < 0.05 vs. Force test. †p < 0.05 vs. Cuff test.

significantly after watching the comedy (Fig. 2). Similar trends were seen in the control (non-sore) leg ($p < 0.001$, ES = 0.43) (21 ± 5 N vs. 2 ± 3 N). There were no significant changes in the VAS score from viewing either video. There were no significant differences in pain tolerance between the comedy and documentary at 24 h after viewing the videos. The calculation of ICC produced the model of 0.677 indicating that about 68% of the variability in pain tolerance was attributable to inter-individual differences. Since laughter was confirmed in the comedy trial through a greater irregular respiratory pattern compared with the documentary, we evaluated the dose-response relationship of the amount of laughter and pain tolerance. There was no relationship between the quantity of laughing and the change in pain tolerance after watching the comedy.

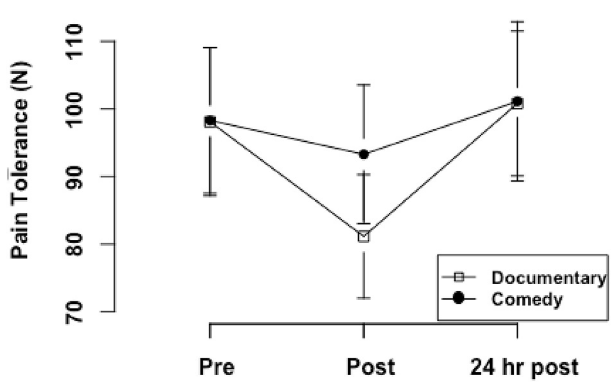

Fig. 2. Changes in pain tolerance with the comedy and documentary watching. Interaction is significant in the linear mixed model.

4. Discussion

In the present investigation, we first evaluated various methods of evaluating pain tolerance to see if these tests would elicit marked cardiovascular responses. The blood pressure cuff test caused the least cardiovascular responses, but a very small percentage of participants reached their maximum pain tolerance. The blunt force test was as effective as the cold pressor test in bringing participants to their pain tolerance without causing vast cardiovascular responses. Accordingly, the blunt force test was selected as the pain tolerance test of choice on the basis of the preliminary study. In the main experimental protocol using the randomized controlled crossover design, pain tolerance decreased significantly after viewing the documentary but was well preserved after mirthful laughter induced by watching the comedy. The present study demonstrated that mirthful laughter prevented a decrease in pain tolerance in healthy humans.

Previous laughter and pain investigations have produced discrepant findings. One reason for the equivocality may be that different methods of testing pain tolerance were used with the majority of these studies utilizing the cold pressor test. Peripheral and central nervous systems involved in cardiovascular regulation are connected to nervous systems that are involved in pain perceptions and responses (Randich and Maixner, 1984). For instance, anti-nociception is induced by elevations in arterial blood pressure (Colville and Chaplin, 1964; Kostowski and Jerlicz, 1978; Little and Rees, 1978). Therefore, using methods of pain tolerance that evoke substantial increases in heart rate and blood pressure potentially confounds the pain tolerance due to the simultaneous anti-nociception that could occur during the testing. In the present investigation, we provided evidence that there was a method of testing pain tolerance that minimizes such cardiovascular responses. The blunt force test on the quadriceps caused smaller changes in hemodynamic measures than the cold pressor test while still bringing the same percentage of participants to the limit of their pain tolerance. This investigation was the first to use blunt force as a method of testing pain tolerance in evaluating laughter and pain. In spite of the advantages of this technique, we also acknowledge that there may be shortcomings. For example, it is possible that the force may have caused localized injury to the point of contact causing an inflammatory response and potentially sensitizing pain receptors further (Marchand, 2008). Even though the point of force application on the quadriceps was slightly moved to an adjacent location for the second test, this could be a potential reason for which pain tolerance decreased significantly after viewing the documentary.

Overall, participants' pain tolerance decreased considerably after viewing the documentary. However, pain tolerance was preserved after viewing the comedy. The current findings contradict a previous study reporting that watching a humorous film did not reduce pain compared with a documentary film (Nevo et al., 1993). One notable difference is that we documented that laughter was indeed elicited in the participants using a stretch-sensitive strain gauge. Our findings are in agreement with a previous study, showing that social laughter elevated the pain threshold after a comedy compared with watching a neutral video (Dunbar et al., 2012). Interestingly, these investigators included a third group that watched a positive affect video and reported that the pain threshold in the social laughter group increased more than in the positive affect video group. Taken together, these results suggest that mirthful laughter provides benefits for pain tolerance above and beyond simple positive affect.

One alternative interpretation of the present findings is that watching the uninteresting documentary negatively impacted pain tolerance, while watching uplifting videos exerted no effects. In this context, the gate control theory is particularly relevant to the present study as it explains that pain is not a simple, direct outcome of the activation of pain receptor neurons, but instead, pain perception is influenced by the interaction between different neurons (Campbell et al., 2013). Neural structures in the spinal cord and brainstem modulate the experience of pain by functioning like a gate. The gate opens to increase the transmission from nerve fibers. When the gate is open, signals arriving in the spinal cord stimulate sensory neurons, which are then relayed upward to the brain and trigger pain. When the gate is closed, signals are blocked from reaching the brain and no pain is felt. Distraction, relaxation, and positive emotions can cause the gate to close, thereby decreasing pain (Campbell et al., 2013). After viewing the comedy, participants' positive affect increased significantly. Distraction was a likely factor as participants' attention was guided away from the prior pain tolerance test due to the comedy eliciting laughter. In the documentary intervention, the participants' positive affect was significantly decreased. This may have influenced the gate mechanism to remain open causing more pain impulses to be transmitted in the participants after viewing the documentary than the comedy.

5. Limitations

By design, the present study was conducted on young and healthy subjects. We reasoned that healthy participants may provide a "cleaner" platform because nociception in patients with chronic disease is influenced heavily by psychological state, concomitant medications, co-morbidities, and disease treatment (Sato et al., 2013). In an attempt to connect the young healthy population to the chronic pain population, we used eccentric resistance exercise to elicit delayed onset muscle soreness (DOMS). Although the leg was successfully made sore and painful, a comedy and the resultant laughter did not influence basal muscle soreness scale. It is likely that pain tolerance and muscle soreness may be modulated by very different mechanisms.

In an attempt to induce greater laughter responses, the comedy video was watched with two other people in the room to make it a social setting. When the video was a documentary, an uninteresting serious documentary was watched alone. Even though two people who watched the comedy video together with the participant had no interactions or conversations with the participants, it is possible that the "togetherness" may have contributed to the increase in positive affect.

6. Conclusions

Our present results indicate that 30 min of watching a comedy, which elicits mirthful laughter, can influence pain tolerance significantly compared with watching an uninteresting documentary. Further research is necessary to investigate endogenous pain modulation with laughter to identify potential mechanisms of providing pain relief. Additionally, future studies in a sample of individuals with chronic pain are warranted. It is possible that 30 min of a comedy stimulus provoking laughter can provide much needed pain relief that can potentially restore the quality of life of individuals suffering from chronic pain. The concept of laughter therapy goes back to the ancient Greeks, yet the research evidence to support its efficacy and benefits is currently lacking. More research is needed for this universally available therapeutic approach to be considered for addition to mainstream medical practice.

7. Clinical revelance

- Currently there is no single treatment able to provide relief from chronic pain. Laughter may be an impactful therapy for managing pain.
- Pain tolerance decreased significantly after viewing a 30-min documentary, but was well preserved after mirthful laughter induced by comedy watching.
- Mirthful laughter prevented a decrease in pain tolerance in healthy humans.
- Thirty minutes of a comedy stimulus provoking laughter can provide much needed pain relief that can potentially restore the quality of life of individuals suffering from chronic pain.

Conflicts of interest

None of the authors have any conflict of interest to disclose.

Conflicts of interest and sources of funding

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