



Painful effects of auditory startle, forehead cooling and psychological stress in patients with fibromyalgia or rheumatoid arthritis

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ABSTRACT

Objective: The aim of this study was to determine whether the clinical pain associated with rheumatoid arthritis or fibromyalgia would increase during standard laboratory tasks and, if so, whether these increases were linked with individual differences in psychological distress.

Methods: Twenty-three patients with fibromyalgia and 16 patients with rheumatoid arthritis rated changes in clinical pain after an acoustic startle stimulus, during painful forehead cooling, and during stressful mental arithmetic. In addition, pain tolerance was assessed during a submaximal effort tourniquet test, and patients provided ratings of distress on a standard Depression, Anxiety and Stress Inventory.

Results: Pain at rest was associated with depression scores in patients with rheumatoid arthritis, and was associated with stress scores in the fibromyalgia group. However, pain tolerance was unrelated to individual differences in psychological distress in either group. In patients with fibromyalgia, clinical pain increased after the acoustic startle stimulus and painful forehead cooling, and increased during stressful mental arithmetic. Arthritic pain also increased during forehead cooling and mental arithmetic in association with indices of psychological distress.

Conclusions: These findings suggest that processes linked with individual differences in distress aggravate pain in rheumatoid arthritis, whereas some other mechanism (e.g., failure of stress-related pain modulation processes or an aberrant interaction between nociceptive afferent and sympathetic efferent fibers) triggers stress-induced pain in fibromyalgia.

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Introduction

Fibromyalgia is characterized by chronic widespread pain, hyperalgesia and multiple somatic symptoms. The pathophysiology of fibromyalgia remains uncertain, but heightened excitability in central nociceptive circuits and impaired anti-nociceptive responses appear to be involved [1–6]. The pain of fibromyalgia increases during laboratory stress [7,8] and is exacerbated by negative mood [9], implying a link between disrupted pain modulation and stress-induced increases in pain.

Although subtle inflammatory changes may compromise central pain modulation in fibromyalgia [10], there is little evidence of systemic inflammation in peripheral tissues. In contrast, major inflammatory disturbances in the synovial joints lead to progressive destruction of cartilage and bone in rheumatoid arthritis [11]. Unlike fibromyalgia, effects of heterotopic noxious conditioning stimulation on sensitivity to pressure-pain are similar in arthritic patients and controls [12]. Furthermore, evidence of a link between psychological stress and

arthritic pain is mixed. On one hand, elevations in daily stress were found to be associated with increases in arthritic pain [13]; in addition, joint and bodily pain were greater at baseline and increased more during stressful laboratory tasks (giving a five-minute speech followed by discussing a recent conflict with someone close to them) in rheumatoid arthritis patients with a history of recurrent depressive episodes than in others with one or no depressive episodes [14]. On the other hand, joint pain did not change during these procedures in patients who considered that they had some control over external events and *decreased* in patients with a low sense of control [15]. Although the mechanism of this analgesic response is uncertain, it is interesting to draw parallels with normal opioid-mediated increases in pain tolerance when stress is perceived to be uncontrollable [16]. Thus, stressful laboratory tasks might augment pain only in association with depression in arthritic patients.

To investigate this in the present study, the nociceptive effects of various forms of laboratory stress and pain (stressful mental arithmetic, pain induced by cooling the forehead, and an acoustic startle stimulus) were compared between patients with fibromyalgia and rheumatoid arthritis, and were examined in relation to individual differences in depression, anxiety and stress. Experimental pain decreases in healthy participants during each of these procedures [17],

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presumably due to pain modulation mechanisms such as stress-induced analgesia, diffuse noxious inhibitory controls and distraction. To compare effects of distress on pain in fibromyalgia and rheumatoid arthritis, the mental arithmetic test had a forced failure rate of 75%. A similar task was found to evoke a strong negative affect, together with endogenous opioid release and reductions in pain in the most discouraged participants [18]. In addition to inducing distress, noxious forehead cooling might alter clinical pain by effects on autonomic arousal and/or sensitized nociceptive pathways [17,19]. The acoustic startle stimulus was included because it evokes an abrupt but momentary increase in psychological and physiological arousal associated with fear, the primary trigger of stress-induced analgesia [20,21]. As anti-nociceptive mechanisms appear to be compromised in patients with fibromyalgia [1–3], and pain increases in these patients during laboratory stress and negative mood [7–9], it was hypothesized that pain would increase in the group as a whole during each of the procedures employed in the present study. However, as anti-nociceptive mechanisms appear to be largely intact in patients with rheumatoid arthritis [12], it was expected that pain would decrease except in depressed participants [14].

Method

Participants

The procedures were carried out on 21 women and two men aged between 19 and 66 years (mean \pm standard error 43.6 ± 2.9 years) with fibromyalgia, and on 10 women and 6 men aged between 28 and 65 years (mean age 42.7 ± 3.0 years) with rheumatoid arthritis. In each case, the diagnosis was made by a rheumatologist or a general medical practitioner, based on a medical history and physical examination supplemented where necessary by blood tests and joint imaging to confirm the diagnosis. All patients with fibromyalgia met the criteria of the American College of Rheumatology [22], and patients with rheumatoid arthritis met the 1987 revised classification criteria for this condition [23]. Fibromyalgia had persisted for 6.5 ± 1.3 years and arthritis had persisted for 9.0 ± 2.0 years. Patients were asked to refrain from taking non-prescribed medication on the day of testing but were advised to take prescribed medication. In particular, 15 fibromyalgia patients and 14 patients with rheumatoid arthritis took non-steroidal anti-inflammatory drugs and/or steroids (six arthritic patients) to control their pain. Additional medications included anti-rheumatic drugs such as methotrexate and/or hydroxychloroquine (eight arthritic patients and one with fibromyalgia) and antidepressants (two arthritic patients and eight with fibromyalgia). Nevertheless, pain persisted to some extent in each case during the procedures described below.

Participants were recruited from a rheumatology clinic and through advertisements in community newspapers, the Arthritis Foundation of Western Australia and Murdoch University. Each participant provided informed consent for the procedures, which were in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee.

Procedures

The procedures were presented in the same order for each participant with a two-minute rest between each task. To minimize carry-over effects, the least demanding tasks were presented first. Participants initially filled out the short form of the Depression, Anxiety and Stress Scale [24], a 21-item self-report questionnaire that assesses the frequency of depression, anxiety and stress symptoms in the past week. The scale has acceptable internal consistency and test-retest reliability, and is well-validated against external criteria [24]. Full scale scores were later referenced against scores in a normal adult population [25].

Ten seconds before a startle stimulus (1000 Hz tone, 0.5 second duration, 100 dBA presented through headphones), participants recorded the intensity of their painful condition on a visual analogue scale where 0 corresponded to “no pain” and 10 to “pain as strong as it can get”. Immediately after the startle stimulus they rated pain again, and continued to rate pain at 10-second intervals for 60 s.

After resting for 2 min, a cylindrical metal bar (10 cm long, 1.3 cm diameter, with a temperature of 2 °C) was placed lengthwise across the participant's forehead and was rolled back and forth for 30 s. Participants rated the intensity of fibromyalgia or arthritic pain at 10-second intervals on the visual analogue scale, starting just before the bar was applied and continuing for 60 s after it was removed.

Two minutes later, participants were asked to rate pain intensity and then began to solve computer-generated additions and subtractions presented on a computer screen [18]. Participants were given up to 5 s to answer easy problems (e.g., $6 + 8 - 2$) and up to 11 s to answer hard problems (e.g., $116 + 138 - 12$) before the next one was presented. The difficulty of problems was automatically adjusted to ensure a 75% failure rate. After each problem, feedback such as ‘CORRECT’ (green), ‘INCORRECT’ (red) or ‘TOO SLOW’ (purple) appeared on the computer screen, and either a pleasant 3-note jingle (correct response) or an aversive loud beep (too slow or incorrect response) sounded for 1 s. The program paused at 5-minute intervals throughout the 20-minute task for participants to rate the intensity of their painful condition on a visual analogue scale.

Finally, in a submaximal effort tourniquet test, a blood pressure cuff was attached to the upper part of the non-dominant arm. The arm was then raised for 60 s to drain venous blood and the cuff was inflated to 200 mm Hg. After the arm was returned to the horizontal level, participants flexed and extended the wrist every few seconds until they decided to stop (defined as pain tolerance).

Statistical approach

Initially, differences between groups in indices of psychological distress (depression, anxiety and stress) were investigated with Student's *t*-test. Next, the association between these indices and pain at rest, pain tolerance and the maximum increase in pain during each task was investigated within each group with Pearson's correlation coefficient. Differences in these correlations between groups were explored with Fisher's *r*-to-*z* transformation.

Changes in pain at rest were investigated in a group (rheumatoid arthritis versus fibromyalgia) by time repeated measures analyses of variance with planned contrasts between one task and the next. Effects on pain ratings of the startle stimulus, forehead cooling and stressful mental arithmetic were investigated in separate group (rheumatoid arthritis versus fibromyalgia) by time (the series of ratings) repeated measures analyses of variance with planned contrasts between pain ratings before the task and at each time point thereafter. As pain intensity ratings before each of the tasks were greater in participants with fibromyalgia than in those with rheumatoid arthritis, differences between groups were also investigated in analyses of covariance with pain intensity before the task as the covariate. Pain reactivity in patients with rheumatoid arthritis was associated with indices of psychological distress during some of the laboratory tasks; therefore, changes in pain within each group at each point during each task were investigated in analyses of covariance with the psychological indices of distress as covariates. The aim of these analyses was to determine whether psychological distress accounted for increases in pain. Where appropriate, the Greenhouse–Geisser epsilon was used to correct for violations of the sphericity assumption in these analyses. Finally, differences in pain tolerance between the two groups were investigated with Student's *t*-test.

Data are reported as the mean \pm standard error, and the criterion of statistical significance was $p < .05$.

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