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Effects of caffeinated chewing gum on muscle pain during submaximal isometric exercise in individuals with fibromyalgia

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HIGHLIGHTS

- We tested if caffeinated chewing gum reduces muscle pain during exercise in individuals with fibromyalgia.
- Clinical pain severity was associated with muscle pain intensity during exercise.
- Clinical pain severity was associated with the magnitude of caffeine effects.
- More symptomatic individuals may benefit more from caffeinated chewing gum.

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ABSTRACT

Physical activity is important to manage symptom of fibromyalgia (FM); however, individuals with FM typically experience augmented muscle pain during exercise. This study examined the effects of caffeinated chewing gum on exercise-induced muscle pain in individuals with FM. This study was conducted with a double-blind, placebo-controlled, cross-over design. Twenty-three patients with FM completed a caffeine condition where they consumed a caffeinated chewing gum that contains 100 mg of caffeine, and a placebo condition where they consumed a non-caffeinated chewing gum. They completed isometric handgrip exercise at 25% of their maximal strength for 3 min, and muscle pain rating (MPR) was recorded every 30 s during exercise. Clinical pain severity was assessed in each condition using a pain questionnaire. The order of the two conditions was randomly determined. MPR increased during exercise, but caffeinated chewing gum did not attenuate the increase in MPR compared to placebo gum. Clinical pain severity was generally associated with the average MPR and the caffeine effects on MPR, calculated as difference in the average MPR between the two conditions. The results suggest that more symptomatic individuals with FM may experience greater exercise-induced muscle pain, but benefit more from caffeinated chewing gum to reduce exercise-induced muscle pain.

1. Introduction

Fibromyalgia (FM) is a chronic pain condition characterized by widespread musculoskeletal pain and several comorbid symptoms (e.g., fatigue, depression, sleep disturbance). The underlying mechanisms to explain this clinical disorder are still unclear; however, an impairment of pain mechanisms within the central nervous system has been suggested as a potential mechanism of FM symptoms [1, 2]. Currently, several therapeutic approaches are available to treat FM symptoms, and accumulation of evidence generally indicates that regular exercise (e.g., aerobic exercise, resistance exercise, yoga, tai-chi) will lead to the reductions in severity of clinical symptoms and improvement in physical functions [3–8]. However, research shows that individuals with FM are generally less physically active [9, 10], and high attrition rate from exercise programs is well-documented in this clinical population [5]. Therefore, there is a great need for more research to develop strategies that will lead to the promotion of physical activity among this clinical population.

Evidence demonstrates that individuals with FM are more sensitive to a variety of experimental pain stimuli, including pressure, heat, cold, and electrical stimuli, compared to healthy controls [1]. Research indicates that muscular contraction during exercise also produces naturally-occurring pain in the exercising muscles in healthy adults [11, 12], and a recent study shows that individuals with FM report a greater intensity of muscle pain during exercise compared to healthy controls [13]. Therefore, it is possible that the augmented muscle pain may serve as a negative behavioral determinant of physical activity among individuals with FM [13], suggesting a need to develop strategies

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to reduce an intensity of muscle pain during exercise to promote regular exercise among this clinical population.

Caffeine is an active food ingredient that has been consumed by approximately 80% of world's population, and it is known that caffeine serves as an adenosine receptor antagonist that leads to inhibitory effects on the central nervous system [14]. To be consistent with the inhibitory effects, there is some evidence in the literature that a moderate to large dose of pre-exercise caffeine ingestion (5–10 mg kg^{-1} body weight) typically reduces an intensity of muscle pain in the legs during moderate intensity cycling in healthy adults [15–17]. Furthermore, more recent research in this area tests the effects of a smaller dose of caffeine, delivered in commercially available products, on exercise-induced muscle pain. Some investigators examined the hypoalgesic effects of energy drink that contains 179 mg of caffeine on leg muscle pain during moderate intensity cycling in healthy adults, and found that muscle pain intensity in the legs was reduced during exercise [18]. Furthermore, other investigators reported reductions in muscle pain intensity in the forearm during a grip task that was held until exhaustion in a caffeine condition where healthy adults ingested 100 mg of caffeine from a caffeinated chewing gum [19]. Together, these recent studies suggest that commercially available caffeinated products, which may serve as a more convenient means to consume a fixed dose of caffeine, can also successfully reduce muscle pain during exercise. On the other hand, several studies show that caffeine does not reduce muscle pain during exercise; however, it appears that these studies are typically conducted with more trained, active individuals [20–23]. Together, there is evidence in the literature suggesting the hypoalgesic effects of caffeine on exercise-induced muscle pain; however, it is currently unclear whether caffeine ingestion reduces muscle pain during exercise in individuals with FM.

Together, these observations from previous research suggest the beneficial effects of pre-exercise caffeine ingestion on muscle pain during exercise among healthy adults. However, there is currently no empirical data in the literature regarding the effects of caffeine ingestion on muscle pain during exercise among individuals with FM. This investigation is potentially important because previous research suggests that muscle pain intensity serves as a negative determinant of their physical activity levels [13]. If the hypoalgesic effects of caffeine were identified, the findings could suggest that pre-exercise caffeine intake may be used to promote physical activity via reduced muscle pain during exercise. Therefore, the present study aimed at testing the effects of a small dose of caffeine, delivered in a commercially available product, on muscle pain during exercise in individuals with FM.

2. Materials and methods

2.1. Participants

Individuals with FM were recruited to participate in this study using campus-wide email advertisement, and existing database of FM patients from our previous study. The inclusion criteria for this study were 1) age of 18 years old or older, and 2) clinical diagnosis with FM by their physicians based on the 1990 American College of Rheumatology diagnostic criteria consisting of a history of widespread pain for at least 3 months and pain in at least 11 of 18 tender point sites on digital palpation [24]. However, the individuals with FM were excluded from the study if they 1) indicated any medical contraindications for exercise or caffeine ingestion, 2) were currently pregnant or breastfeeding, or 3) were planning to be pregnant or breastfeed in the near future. The present study aimed at examining the effects of caffeine on muscle pain responses to exercise to promote regular physical activity among individuals with FM. Therefore, to maximize external validity of the potential findings from this study, the individuals were allowed to use their FM medications during their participation in this study. However, they were asked not to change their medications during the study period. The study was fully approved by an institutional review board, and all participants signed a consent form before participating in the study.

2.2. Assessment of perceptual responses to exercise

2.2.1. Muscle pain rating

Muscle pain was the primary outcome measure in this study, and the intensity of muscle pain in the working muscles during exercise was assessed using the Muscle Pain Rating (MPR) scale [11]. The MPR scale is constructed in a vertical alignment with 12 numbers (0, ½, 1–10) ranging from 0 to 10, and among the 12 numbers, nine numbers are paired with pain descriptors (e.g., 0 = no pain, 10 = extremely painful). To avoid possible ceiling effects of pain assessment, the MPR scale allows the participants to respond with greater numbers than 10 if the participants experience a greater intensity of muscle pain than extremely intense pain. The participants were asked to rate the intensity of muscle pain in the exercising forearm honestly and accurately, and verbally provide a number on the MPR scale to investigator that best corresponded to the intensity of localized muscle pain they were experiencing.

2.2.2. Rating of perceived exertion

Level of exertion during exercise was assessed using the Ratings of Perceived Exertion (RPE) scale, and RPE generally represents how hard exercise feels to exercisers at a moment of assessment [25]. Perceived exertion is a psychological construct that has been frequently used as a subjective measure of exercise intensity in numerous exercise science studies [26]. The RPE scale is constructed in a vertical alignment with 15 numbers ranging from 6 to 20, and among the 15 numbers, nine numbers are paired with the verbal descriptors (e.g., 6 = no exertion, 20 = maximal exertion). The participants were asked to rate the level of exertion honestly and accurately, and verbally provide a number on the RPE scale to investigator that best corresponded to the level of exertion they were experiencing.

2.2.3. Exercise stimulus to induce muscle pain and exertion

Submaximal isometric handgrip exercise consisting of squeezing a handgrip at 25% MVC for 3 min was used as an exercise stimulus to induce muscle pain and exertion in the present study. Previous research shows that this submaximal isometric handgrip exercise produces strong muscle pain (MPR = 4–5) and physical demand that is perceived to be hard (RPE = 15) in healthy adults [12]. Also, clinical data have shown that individuals with FM experience very strong to extremely intense pain (MPR = 7–10) during this submaximal isometric handgrip exercise [13]. Together, these data demonstrate that this exercise protocol can induce a sufficient intensity of muscle pain and level of exertion to observe the potential effects of caffeine on the perceptual variables, and validate the exercise protocol to test the aim of this study.

2.3. Procedures

This study was conducted with a double-blind, placebo-controlled, cross-over design. The participants completed three experimental sessions on separate days consisting of a familiarization session, which was conducted first of all for every participant, a caffeine session, and a placebo session. The order of the caffeine and placebo sessions was determined at random. To ensure the double-blind design, only one investigator (MU) was aware of the nature of the caffeine and placebo sessions, and provided other investigators either a piece of caffeinated chewing gum or non-caffeinated chewing gum without informing the investigators or the participants of the nature of the sessions. These blinded investigators then conducted all sessions with the blinded participants. One investigator (KM) was designated to perform all preliminary data analyses.

The participants first reported to our laboratory to complete the familiarization session. During the familiarization session, the participants were asked to sign a consent form, and then to fill out several self-report