Nutrition 31 (2015) 315–323

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

Differential effects of repetitive oral administration of monosodium glutamate on interstitial glutamate concentration and muscle pain sensitivity

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ARTICLE INFO

Article history:
Received 16 April 2014
Accepted 24 July 2014

Keywords:
Microdialysis
Mechanical muscle sensitivity
Monosodium glutamate
Myofascial temporomandibular disorders
Diet
Pain

ABSTRACT

Objective: The aim of this study was to determine the relationship of high daily monosodium glutamate (MSG) consumption with glutamate concentrations in jaw muscle, saliva, and serum, and muscle pain sensitivity in healthy participants.
Methods: A randomized, double-blinded, placebo-controlled study was conducted to investigate the effect of repetitive consumption of high-dose MSG on glutamate concentration in the masseter muscles measured by microdialysis and muscle pain sensitivity. In five contiguous experimental daily sessions, 32 healthy participants drank MSG (150 mg/kg) or NaCl (24 mg/kg) diluted with a 400 mL soda. The concentrations of glutamate before and after the ingestion were assessed in dialysate and plasma samples on the first and last days. Saliva glutamate concentration was assessed every day. Pressure pain threshold, pressure pain tolerance, autonomic parameters (heart rate, systolic and diastolic blood pressures) and reported side effects also were assessed.
Results: No significant change was noted in the baseline concentration of glutamate in the masseter muscle, blood, or saliva, but the peak concentration in the masseter muscle increased significantly between day 1 and 5. A statistically significant increase in systolic and diastolic blood pressures after MSG administration was observed, as well as a significantly higher frequency of reports of nausea and headache in the MSG group. No robust effect of MSG on muscle sensitivity was found.
Conclusion: Interstitial glutamate concentration in the masseter muscle is not highly disturbed by excessive repetitive intake of MSG in healthy man.

This study was financially supported by the Danish Dental Association and Danish Medical Research Council. AS participated in collecting data and drafted the manuscript. LBH participated in the design of the study, planned the data collection, and performed the statistical analysis. EC participated in collecting data, performed the statistical analysis, and drafted the manuscript. GB, NS, and BG carried out the analysis of biosamples (dialysate, blood, and saliva) and drafted the manuscript. ME participated in the study design and coordination and helped to draft the manuscript. BC conceived of the study, participated in its design, and drafted the manuscript. PS conceived of the study, supervised this study, participated in its design and coordination, and helped to draft the manuscript.

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http://dx.doi.org/10.1016/j.nut.2014.07.011

Introduction

Temporomandibular disorders (TMDs) are chronic musculoskeletal pain conditions in the craniofacial region. TMD affects ~10 % of the population, with a higher prevalence in women than in men [1]. There are several known risk factors for myofascial TMD pain, such as age, sex, and psychological factors [2–4]. However, its pathophysiology is still poorly understood. There is some scientific evidence that lifestyle-related factors such as diet could play a role in health and disease, including musculoskeletal pain. For example, ingestion of certain food items is considered a migraine trigger [5,6], and there are some studies indicating an association between vitamin D deficiency and muscle weakness and muscle pain [7].

Monosodium glutamate (MSG) is a food additive that enhances flavor. Acute ingestion of MSG has been associated with adverse symptoms that include general weakness, muscle tightness or tenderness, flushing or sweating, headache, paresthesias, arrhythmias, and tachycardia in healthy individuals [8–11]. Evidence also exists that glutamate levels are significantly elevated in patients with migraine and tension-type headache compared with healthy controls [12–16]. Furthermore, growing scientific evidence has associated elevated muscle glutamate concentrations with certain chronic musculoskeletal pain conditions including myofascial TMDs [5,17–22]. These observations support the belief that local tissue concentrations of glutamate may influence muscle pain sensitivity [23]. Once MSG is ingested, skeletal muscles, including the masseter muscle, store most of the glutamate intramuscularly with a seven-to eightfold increase of concentration, although the elevation of the glutamate concentration is short lasting [9].

Previous research indicates that doses of up to 1 g/kg of MSG do not significantly cross the blood–brain barrier [24,25], which suggests that the effects of systemically administered MSG consumption could be mediated by peripheral rather than central nociceptive mechanisms. It is therefore conceivable that a high dietary MSG intake may elevate glutamate concentrations in skeletal muscles, which could be one lifestyle-related factor contributing to pain sensitivity in chronic musculoskeletal pain conditions including TMD and tension-type headache. However, it is not known whether increased dietary consumption of glutamate causes accumulation of glutamate in the masseter muscle to alter pain sensitivity.

The aim of this study was to determine the relationship of high daily MSG consumption with glutamate concentrations in jaw muscle, saliva, and serum, and muscle pain sensitivity in healthy participants. We hypothesized that daily administration of oral MSG for 5 d consecutively would elevate muscle, serum, and saliva glutamate concentrations and would be associated with increased reports of adverse effects (AEs; muscle tenderness, headaches) and measurable decreases in jaw muscle pressure pain threshold.

Materials and methods

Participants

Thirty-two healthy adults (>18 y; 16 women and 16 men, mean age ± SD = 23.6 ± 3.3 y, mean body weight ± SD = 70.2 ± 15.1 kg) were included in this randomized, double-blinded, placebo-controlled study. Participants were recruited by an ad posted at the Aarhus University and through a Web page. Exclusion criteria were craniofacial pain, serious psychological or physical illness, previous report of adverse reactions to MSG, and asthma. Informed consent was obtained from all participants. The study was performed in accordance with the Declaration of Helsinki, and the study protocol was approved by the local ethics committee (approval No. 1-10-72-197-12).

Study design

Figure 1 shows the experimental protocol of this study. Each participant was randomly allocated to either the MSG group (n = 22) or the placebo group

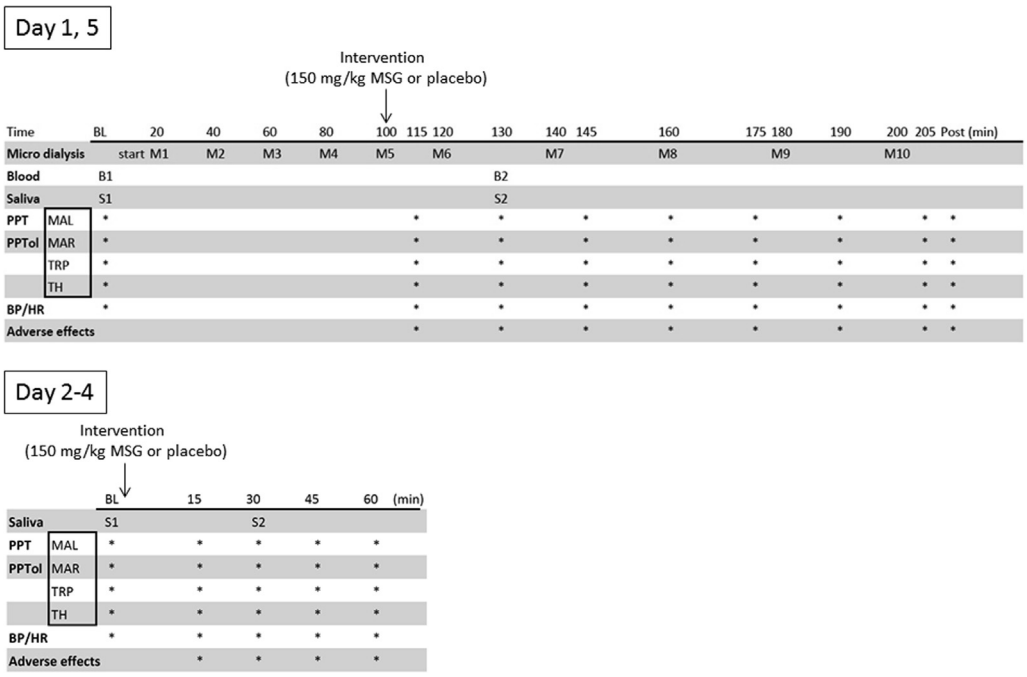

Fig. 1. Experimental protocol of this study. On day 1 and 5, dialysate samples (M1–M10) were collected every 20 min throughout the experiment. Blood samples (B1, B2) and saliva samples (S1, S2) were collected at baseline and 30 min post-ingestion. Day 2 to 4, only saliva samples were collected at baseline and 30 min after ingestion. Pressure pain threshold (PPT) and pressure pain tolerance (PPTol) were measured in the masseter left (MAL), masseter right (MAR), trapezius (TRP), and thenar (TH) at baseline and every 15 min post-ingestion, as well as blood pressure (BP) and heart rate (HR). Participants were asked to report adverse effects every 15 min after ingestion.