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The frequency and reliability of cortical activity using a novel strategy to present pressure pain stimulus over the lumbar spine

Charles W. Gay[a,*], Mark O. Papuga[b], Mark D. Bishop[c], Paul Dougherty[e,f,g]

[a] Rehabilitation Science Program, University of Florida, Gainesville, FL, USA
[b] Department of Research, New York Chiropractic College, Seneca Falls, NY, USA
[c] Department of Physical Therapy, College of Public Health and Health Professions, University of Florida, Gainesville, FL, USA
[e] Department of Research, New York Chiropractic College, Seneca Falls, NY, USA
[f] Department of Orthopedics, School of Medicine, University of Rochester, Rochester, NY, USA
[g] Canadaigua VA Medical Center, Canadaigua, NY, USA

HIGHLIGHTS

- Novel MR compatible pressure algometry.
- High frequency of individuals showed cortical activity within the primary somatosensory cortex, insula and anterior cingulate cortex.
- Good to excellent run-to-run reliability for peak-voxel activity.
- Fair to excellent run-to-run reliability for cluster-size.
- Potential limitation is stimulus-presentation related artifacts.

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ABSTRACT

Background: The blocked stimulus presentation strategy, in fMRI study designs, is an important means to study brain function related to a particular stimulus. Specifically, applying pressure stimuli perceived as painful to different anatomical regions has been used to improve our understanding of central sensitization, which is an important clinical phenomenon in chronic pain.
New method: This paper introduces a novel MR-compatible device used to apply pressure pain stimuli to the lumbar spine of 13 subjects in the supine position. We present the frequency of individuals and within-subject reliability of cortical activity in the following brain regions: the primary somatosensory cortex, insula and anterior cingulate cortex bilaterally.
Results: Using the novel MR-compatible device, a high frequency of individuals showed cortical activity within the a priori brain regions. There was good to excellent run-to-run reliability for peak voxel, while cluster size was less reliable. We found a higher than expected association between stimulus presentation and movement artifacts.
Comparison with existing method(s): Unlike previous methods, the current strategy can apply pressure stimuli to subjects over the lumbar spine while they lay supine. Previous methods required subjects to lay prone.
Conclusions: This strategy could be used for evaluating pressure stimuli related central sensitization associated with back pain.

1. Manuscript

1.1. Introduction

Functional magnetic resonance imaging (fMRI) combined with psychophysical stimuli has been employed to study cortical sensitization in people with chronic low back pain (cLBP). To date, research groups have differed in their positioning of subjects in the scanner, and the location on the body where the psychophysical

* Corresponding author at: Rehabilitation Science Program, University of Florida, Box 100154, UFHSC, Gainesville, FL 32610-0154, USA. Tel.: +1 352 273 5220; fax: +1 352 273 6109.
E-mail addresses: chaz.gay@phhp.ufl.edu (C.W. Gay), opapuga@nycc.edu (M.O. Papuga), bish@phhp.ufl.edu (M.D. Bishop), Paul.Dougherty@va.gov (P. Dougherty).

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Table 1
Inclusion criteria separated by group.

Asymptomatic subjects	Symptomatic subjects
No LBP in the last 3 months	LBP > 3 months in duration from L1-SI joint
No pain elicited upon deep palpation or mechanical maneuvers of lumbar spine	Pain elicited upon deep palpation or mechanical maneuvers of the lumbar spine
mODI score of <10%	mODI score of ≥20%
Baseline NPRS <3	Baseline NPRS ≥3
No pain on pressure algometry ≤5 kg/cm^2	Pain on pressure algometry ≤5 kg/cm^2

LBP = low back pain; mODI = modified Oswestry Disability Index; NPRS = Numerical Pain Rating Scale.

stimuli is applied (Giesecke et al., 2004; Kobayashi et al., 2009). Giesecke et al. (2004) psychophysical approach was applying pressure stimuli to the nail bed of a finger while subjects lie supine in the scanner. While, Kobayashi et al. (2009) used pressure stimuli to the lumbar spine while subjects lie prone in the scanner. Considering that the majority of fMRI studies place the subject in the supine position, we decided to test the feasibility to extend the work of Kobayashi et al. (2009) by creating a method to apply pressure stimuli to the lumbar spine while the subject lies supine.

Here we describe a novel approach to presenting pressure stimuli to the lumbar spine. First, we describe the custom built MR-compatible algometer. Second, we assess the frequency of cortical activity within three a priori brain regions, bilaterally, at the individual level. In addition we describe the scan-to-scan reliability of two commonly reported matrixes of brain function, cluster-size and peak-voxel *T*-score, for each of the six brain regions. We assess the relationship between stimulus presentation and movement related outliers. And finally, we report on the relationship between stimulus presentation and movement artifacts.

2. Materials and methods

2.1. Study design

This paper describes a novel MR-compatible device that was used to apply pressure pain stimuli to the lumbar spine of subjects in the supine position. The frequency and reliability estimates of BOLD responses were secondary analyses of pooled data from a pilot-fMRI project. That project examined cortical responses to "moderate" pressure pain stimuli applied to the lumbar spine with the MR-compatible device.

2.2. Participants

Thirteen participants (six females; average age ± standard deviation 42.5 ± 10.5 years) were pooled for this study. All participants read and signed an informed consent approved by the University of Rochester institutional review board. All subjects were recruited via flyers posted on the campus of the University of Rochester. The pooled sample included participants with (N = 8) and without low back pain (N = 5). Participants were eligible if they were between the ages of 30 and 65, greater than 5 ft 2 in. tall and weighed less than 300 lbs. Specific inclusion criteria are listed in Table 1 for participants who had and did not have low back pain, respectively. Exclusion criteria included pregnancy, cauda equine syndrome, spinal neoplasia or metastatic disease, destructive joint pathology, progressive neurologic deficits (such as peripheral neuropathy, lumbosacral radiculopathy, myelopathy, or neurogenic claudication), previous lumbar, hip, or pelvis surgery, chronic migraine headache, fibromyalgia, irritable bowel syndrome, chronic pain from other sources (such as thalamic stroke), contraindications to MRI (such as metal implants or claustrophobia), or ongoing legal proceedings (such as workers' compensation).

2.3. Description of MR-compatible pressure algometer device

The MR-compatible device was created using a single stage electro-pneumatic pressure regulator connected to a pneumatic aluminum piston, see Fig. 1. The piston was 2.2 in. tall, with a 1/2 in. stroke length, and fitted with a 1 cm^2 rubber tip. This system had a maximum inlet pressure of 3000 PSI that was generated by a 125 ft^3 compressed nitrogen tank. The pressure throughout the system was dynamically controlled via custom written Labview software (version 10.0.1; National Instruments; Austin, TX) in conjunction with a National Instruments A/D board (National Instruments Corp. Austin, TX). The pneumatic aluminum piston was housed in a raised 4-in wooden-platform, with a cutaway section, which allowed the rubber tip to come in contact with the subject. Subjects were placed on the platform so that the L5 spinous process was in contact with the rubber tip.

2.4. Session procedures

Following a screening session, all subjects returned for a 2-h session at the Rochester Center for Brain Imaging. After subjects completed MR safety-screening and demographic questionnaires, they completed the following: a 15-min response training, fitting to the pressure algometer device (5-min), pressure pain threshold and tolerance testing (10-min), a multiple-random-staircase procedure to identify pain intensity levels of "no pain", "mild pain", "moderate pain" and "intense pain" (45-min), and then underwent a 30-min MRI session. Greater detail is provided below.

2.5. Response rating training

Subjects were instructed on how to provide ratings of pain intensity using a custom built finger spanning device (FSD). Subjects were told that the thumb and index finger touching each other corresponded to 'no pain' and that the maximum distance achievable between the two fingers corresponded to 'worst imaginable pain'. The FSD was calibrated to each subject. Because the FSD is an unaccustomed activity for most people, subjects practiced using the device with a simple visual attention task. This task consisted of two 5-min blocks, where subjects were asked to use the FSD to fill a bar graph to a value between 0 and 10. Subjects were presented a random value (between 1 and10) for 5 s followed by a zero for 5 s. Subsequently, subjects used the FSD to provide continuous pain ratings during MR scanning procedures.

2.6. Identification of pressure pain threshold and tolerance

Subjects were strategically place on the MR-compatible pressure algometer so that the rubber tip of the testing apparatus was in contact with the 5th lumbar spinous process. The amount of pressure that was (1) first perceived as painful (pressure pain threshold) and (2) no longer tolerable (pressure pain tolerance) was identified using an ascending method of limits. For pressure pain thresholds, subjects were instructed to press the first button when they "first feel pain" from the pressure. For pressure pain tolerance, subjects were instructed to press the second button "when the pain is too much". Pressure stimuli were applied to the lumbar spine for a 5-s duration and then increased in increments of 0.5 kg/cm^2 at a rate of 1.0 kg/cm^2/s until the subjects pressed the 2nd button (i.e. pain tolerance) or to a maximum of 18 kg/cm^2. If subjects did not press the 2nd button, 18 kg/cm^2 was recorded as pain tolerance and the trial discontinued.