Documentation of Acute Neck Pain in a Patient Using Functional MR Imaging
D Marks, P Valsasina, M Rocca, M Filippi

Citation

Abstract
Neuroimaging was applied to provide visual documentation of the presence of pain in a patient complaining of long-term neck pain. Activation in the pain-related brain matrix was increased after induced pain, compared with a resting baseline condition, and decreased after the pain had subsided somewhat.

INTRODUCTION
Pain is a very subjective sensation, and documenting the presence and magnitude of pain depends on the statements and descriptions of the patients themselves. Standard but imprecise pain rating tools include happy to sad faces, with a limited numeric score of 0 to 5 (Wong 2001).

The anterior cingulate cortex (AnCg), the medial prefrontal cortex (MPFC), the medial temporal lobe (MTL), and the postcentral gyrus (the primary somatosensory cortex - S1) are the principle areas of the brain which process pain (Ochsner et al., 2006; Ploghaus et al., 2001).

The activation of specific brain areas is associated with haemodynamic changes (Ogawa 1990), which can be identified using functional MR imaging (fMRI) with Blood Oxygen Level Dependent (BOLD) signals. Researchers have demonstrated that using fMRI, the sensation of pain can be imaged (Davis 1995; Borsook 2006).

Studies to date have evaluated the concept and performance characteristics of MR imaging of pain, but in general have not been applied to individual cases (there are a few reports in patients with headache), and case-specific use is the subject of this article. We applied the technique of fMRI to a patient with chronic and disabling neck pain, in order to demonstrate in an objective manner independent of the patient’s statements that pain was in fact present. We employed a method of analysis imposed by the structure of the experiment, including planned head movement between sequential scans.

METHODS
Patient M.I. is a 50 years old male who suffers from chronic and acute episodes of neck pain. Four years previously had suffered neck and shoulder injury when the car he was driving was struck by another automobile. He suffers from chronic pain in his left neck and left shoulder, with numbness, which can be induced by specific neck movement, and is relieved by analgesics, physical therapy and treatment by a chiropractor.

Pain intensity was scored using the Wong-Baker FACES Pain Rating Scale.

IMAGING OF PAIN
Functional MR imaging was used to provide visual documentation of the presence of pain. The patient lay within a GE Cigna 3-T Signa 11X Excite MRI scanner. fMRI was performed as described by Marks et al (2007), with pain stimuli of a constant intensity to capture steady state functional data.

A short localizer MRI scan was performed to verify that the field of view was within the skull, and to assure the absence of “ghost” images. A high-resolution full volume structural / functional MR scan was then obtained, using fast SPGR imaging (146, 1.0-mm thick axial slices, no spaces, TR = 8, TE = 3.2, FOV = 24 cm, 256 £ 256 matrix). These T1-weighted images provided detailed anatomical information for registration and 3-D normalization to a standard brain atlas.

Changes in the BOLD MRI signal were measured using a
gradient-echo echoplanar sequence. fMRI was acquired at three different time points: 1) without pain; 2) with severe pain; and 3) with diminished pain. Each of the three fMRI sessions lasted 110 seconds each. EPI parameters were: TE 35, TR 2000, 55 measurements, 18 slices per location, interleaved, flip angle 90, delay after acquisition-minimum, slice thickness 6 skip 1, matrix = 128x128, field of view = 28.

A baseline structural anatomic scan and a baseline fMRI #1 were performed in the pain-free state. The patient then sat up, and pain was induced after fMRI #1 but before fMRI #2 by the patient moving his neck in a way known to him to induce pain. After performing this maneuver, the patient reported that he experienced significant (5/5) pain in his neck, although he did not feel anxiety, fear or depression. A second anatomic (for alignment) MRI and fMRI #2 were then performed (high pain state). After this second imaging session, the patient exited the MRI, took oral analgesics, and waited about 10 minutes for his pain to significantly (2/5) subside. He then underwent the final anatomic MRI and fMRI #3 in the lessened pain state.

DATA ANALYSIS

All image post-processing was performed on an independent computer workstation running Linux (RedHat Enterprise, version 3.2). fMRI data were analysed using statistical parametric mapping software (SPM2) developed by Friston et al. (1995). Prior to statistical analysis, all images from each fMRI session were realigned to the first one to correct for subject motion, spatially normalized into the standard space of SPM, and smoothed with a 6-mm 3D-Gaussian filter.

To perform statistical analysis on fMRI data, we employed a technique similar to that used in a case report on aura spreading in a patient with migraine (Welch 1998), which investigated trends in image intensity with progressive fMRI scans. In the case of our patient, we investigated trends in image intensity every 10 scans (taking 6 scans per session). SPM and single-subject models were used to perform the following statistical analyses:

Trend analysis: the selected scans from each session were entered in a statistical model where the intensity of pain was used as covariate. The scores used for grading pain were 0, 2 and 1 for the fMRI sessions with no pain, maximum pain and less pain, respectively. The aim of this statistical model was to detect which voxels correlated significantly with the intensity of pain.

Analysis of variance (ANOVA): the selected scans from each session were entered in a one-way ANOVA model to detect significant heterogeneity in the image intensity among the three different fMRI sessions. A post-hoc T-test was then used to compare signal intensity between the maximum pain condition and the other two conditions (i.e., no pain and less pain).

RESULTS

Following are the results of the two models (Trend Analysis and ANOVA, p <0.05 corrected for multiple comparisons). The patient scored pain at baseline as 0/5.

The trend analysis showed, during the max pain (5/5) condition, an increased activation of the left primary sensorimotor cortex, the left superior, middle, and inferior frontal gyrus, the bilateral intraparietal sulcus, the bilateral precuneus, the bilateral cingulum, the bilateral insula, the left thalamus, the left superior and middle temporal gyrus (Table 1, Figure 1).

The ANOVA analysis showed, during the pain condition, an increased activation of the left primary sensorimotor cortex, the left superior, middle, and inferior frontal gyri, the left intraparietal sulcus, the left precuneus, the bilateral cingulum, the left insula, and the visual cortex, bilaterally (Table 1, Figure 2). Comparison was made between fMRI #3 (pain 2/5) and fMRI # 2 (pain 5/5) and all the described activations were significantly reduced, correlating with the partial resolution of pain.

Table 1. Activation noted during fMRI.

<table>
<thead>
<tr>
<th>Location</th>
<th>Trend analysis</th>
<th>ANOVA</th>
<th>Baliki 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>left SI</td>
<td>Yes</td>
<td>Yes</td>
<td>SI 11</td>
</tr>
<tr>
<td>bilateral intraparietal sulcus</td>
<td>Yes</td>
<td>Left</td>
<td></td>
</tr>
<tr>
<td>bilateral precuneus</td>
<td>Yes</td>
<td>Left</td>
<td></td>
</tr>
<tr>
<td>bilateral cingulum</td>
<td>Yes</td>
<td>Left</td>
<td></td>
</tr>
<tr>
<td>bilateral insula</td>
<td>Yes</td>
<td>Left</td>
<td></td>
</tr>
<tr>
<td>bilateral superior and middle temporal gyris</td>
<td>Yes</td>
<td>No</td>
<td>Thalamus</td>
</tr>
<tr>
<td>Bilateral visual cortex</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

Legend Table 1. Activated areas during pain stimulation, yellow areas are common for both methods of analysis. Comparison to the study of Baliki is given.
Figure 1. Results of the trend analysis showing voxels significantly correlated with the intensity of pain across the three fMRI sessions. During the pain condition, an increased activation of the left primary sensorimotor cortex S1, the left superior, middle, and inferior frontal gyri, the bilateral intraparietal sulcus, the bilateral precuneus, the bilateral cingulum, the bilateral insula, the left thalamus, the left superior and middle temporal gyrus was detected.

Figure 1a. Lobes of the Cerebrum, provided for orientation. 
http://upload.wikimedia.org/wikipedia/commons/2/2b/Illu_cerebrum_lobes.jpg

Figure 1b. Postcentral gyrus, shown for comparison. 
Brodmann area 3 is in red, area 1 in green, and area 2 in yellow. 
http://upload.wikimedia.org/wikipedia/en/ac/Ba1_2_3.png

Figure 2. ANOVA

Figure 2. Result of the ANOVA analysis showing voxels significantly more activated during the maximum pain condition, compared with the other two conditions (i.e., no pain and less pain). During the pain condition, an increased activation of the left primary sensorimotor cortex, the left superior, middle, and inferior frontal gyrus, the left intraparietal sulcus, the left precuneus, the bilateral cingulum, the left insula, and the visual cortex, bilaterally, was detected.

DISCUSSION

A number of researchers have previously used fMRI to image active brain activity corresponding to painful stimuli (Davis 1995; Delapaz 1995; Lorenz 2005; Gelner 1994; Schulz-Stübner 2004). We used these techniques to provide a visual validation of the presence of pain within a clinical setting. When patient M.I. experienced maximum pain, by moving his neck in a manner known by him for several years to consistently result in very significant pain, activation of the brain relative to the baseline state was observed via fMRI (#2) in areas characteristic for processing of pain, confirming that the activation seen corresponded to and was causally related to the induction of the sensation of pain.

When pain had subsided somewhat for M.I., with analgesics and after the passage of 10 minutes, the magnitude of activation seen (fMRI #3) was significantly less (2/5) than at the point of maximum (5/5) pain (fMRI #2). This correlated with the reported (by the patient) partial resolution of the sensation of pain, and was taken as additional evidence that the brain activation observed was causally related to the presence of pain.
The transmission of sensory nociceptive information is influenced by multiple factors to form the resulting pain experience (Melzack and Casey, 1968). For example, mood (Rainville et al., 2005; Villemure et al., 2003; Zelman et al., 1991), attention (Miron et al., 1989), and cognitive factors, such as beliefs held with respect to the pain (DeGood and Tait, 2001), all impact on how an individual experiences a painful stimulus. The changes on MRI for patient M.I. were not related to coincidental or concurrent phenomena such as anxiety, fear, depression or other explanations, which patient M.I. stated not to have experienced during the imaging session.

Acute studies in chronic pain patients show less consistent activation in response to physical pain stimuli particularly in the prefrontal cortex (PFC) and anterior cingulate cortex (AnCg). The primary somatosensory cortex S1 (lateral postcentral gyrus, Brodmann areas 3, 1 and 2) as is illustrated in Figures 1a and 1b, was not activated as often (in contrast to healthy subjects). Apkarian (2005) reviewed 68 studies of acute induced physical pain in normal subjects and 30 studies of pain associated with clinical pain conditions. With the exception of the PFC and thalamus, there was a significant decrease in activation in individuals with chronic pain in AnCg, S1 and SII and insula. Increased PFC activation in the chronic pain patients is thought to be related to the stronger cognitive, emotional and introspective components and is compatible with the observation that chronic pain patients have decreased sensory processing accompanied by enhanced emotional/cognitive processing (Apkarian et al., 2005).

Both the ANOVA and the Trend Analyses showed agreement for activation in most areas (Table 1), in the presence of pain. On the other hand, Trend analysis but not ANOVA picked up activation for the left thalamus, left superior and middle temporal gyrus, ANOVA but not Trend analysis found activation in the bilateral visual cortex. It has been shown in healthy volunteers that limbic areas such as the AnCg, the medial PFC and the MTL are associated with pain-related fear or anxiety during pain processing (Ochsner et al., 2006; Ploghaus et al., 2001). Mee et al (2006) evaluated acute pain in chronic pain patients. They found less consistent activation in response to physical pain stimuli particularly in the PFC and AnCg. S1 is not activated as often (in contrast to healthy subjects).

Clinical depression is known to enhance the response to chronic pain (Bair et al., 2003; Gaskin et al, 1992; Mangelli et al., 2002). Negative mood is also related to the magnitude of overall pain experience (Currie and Wang, 2005; Salovey and Birnbaum, 1989). Chronic pain has been associated with development of cognitive impairment, although Patient M.I. did not complain of cognitive impairment, and tested normal on Mini Mental Status exam (data not shown).

Sundstrom et al (2006) studied regional blood flow in 45 patients with chronic neck pain, which is the condition our patient M.I. suffers from. Patients with and without chronic whiplash syndrome were included. Decrease in rCBF in the right temporal region close to hippocampus, and increased rCBF in left insula were seen. Differences were noted, which suggested different pain mechanisms between patients with chronic neck pain of traumatic and non-traumatic cause.

Baliki (2005) used fMRI to examine brain activation when joints were palpated, in a single patient study (as was ours). Mechanical stimulation of the painful joints of this patient with psoriatic arthritis activated the thalamus, insular, S1 and SII and the mid-AnCg. Use of a COX-2 inhibitor decreased reported pain intensity and brain activity 1 hour of administration. The anterior insula and SII correlated with pain intensity

CONCLUSIONS

Neuroimaging can play a useful confirmatory role in documenting the presence or absence of the sensation of pain in patients complaining of a pain syndrome.

ACKNOWLEDGEMENTS

We thank St.Vincent’s Medical Center in Birmingham, Alabama USA for the generous donation of imaging time, and for Cooper Green Mercy Hospital also in Birmingham for use of their clinical facilities.

Figures 1a and 1b were used with permission to copy and distribute under the terms of the GNU Free Documentation License, Free Software Foundation.

References


Author Information

DH Marks
Cooper Green Mercy Hospital, Department of Medicine, 1515 Sixth Avenue South, Birmingham, Alabama 35233 U.S.A.

P Valsasina
Neuroimaging Research Unit, Institute of Experimental Neurology, Scientific Institute and University Ospedale San Raffaele, Via Olgettina 60, 20132 Milan, Italy.

MA Rocca
Neuroimaging Research Unit, Institute of Experimental Neurology, Scientific Institute and University Ospedale San Raffaele, Via Olgettina 60, 20132 Milan, Italy.

M Filippi
Neuroimaging Research Unit, Institute of Experimental Neurology, Scientific Institute and University Ospedale San Raffaele, Via Olgettina 60, 20132 Milan, Italy.