An Objective Test for Assessment of Low Back Pain Using Neurospectroscopy

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Introduction

A person with persistent pain undergoes an exhaustive round of interviews and examinations by pain physicians, physiotherapists, psychiatrists and clinical psychologists in order to obtain a diagnosis. Long questionnaires frequently assist the multidisciplinary pain management team to determine the type and origin of the pain. Despite this extensive examination procedure, the diagnosis remains subjective [1]. MRI of the spine can identify structural damage or pathology, however, the poor correlation between the presence of pathology and pain [1,2] highlights the current subjective understanding of the nature of pain and the multifactorial interplay of pathology, nociceptive inputs, psychological processes and pain behaviour [3-5]. Low back pain is one of the most prevalent and disabling conditions in medical practice [6]. MR neurospectroscopy can monitor biochemical changes in specific regions of the brain that are associated with disease processes [7]. The SCS-based method of analysis is unique in that it provides accurate, reliable classification of the large amount of spectroscopic data while ensuring spectral identity is retained and a degree of confidence is given in the diagnosis. Clearly, if neurospectroscopy combined with SCS could identify pain with a high level of accuracy, it would provide the first objective method for monitoring pain. The aim of this study was to determine if neurospectroscopic data analysed using a statistical classification strategy could discriminate low back pain subjects from control subjects.

Materials and Methods

Subjects with low back pain were recruited through a Pain Management Centre. Thirty-two subjects with low back pain volunteered to take part in the study. Thirty-three age- and sex-matched volunteer control subjects without pain were also recruited. All pain subjects underwent a comprehensive multidisciplinary evaluation by a pain physician, physiotherapist and psychiatrist or clinical psychologist. Evaluation included history, examination, standardised instruments for assessment of pain, mood, disability, other measures of psychological function and appropriate MRI of the lumbosacral spine. The specific physical diagnosis based on presumed causative factors or pathology differed between subjects in the low back pain group. Subjects were placed in a MR scanner, (1.5 Tesla clinical MR scanner, (GE, USA) and the head fixed in position using a standard head coil. After conducting localising scans, MR spectra were obtained from the three locations of interest (left anterior cingulate cortex, left prefrontal cortex, left thalamus). Single-voxel spectroscopy (8 cm^3 volume) was then acquired using the STEAM pulse sequence with an echo time of 25 ms and repetition time of 1500 ms. 256 signal averages were acquired per data frame with an eight-phase cycling scheme (2048 data points per spectroscopy frame with a spectral bandwidth of 2500 Hz).

Results

SCS-based classifiers were developed using the 0-4-ppm spectral region for either the first derivatives or rank-ordered first derivatives of each MR spectrum [8]. Maximally discriminatory spectral subregions determined using genetic algorithm based optimal region selection were used to develop classifiers using Linear Discriminant Analysis with bootstrap crossvalidation, the outputs from which were combined using Wolpert's Stacked Generalizer to form one meta classifier each for the thalamus and prefrontal cortex. For the anterior cingulate cortex, meta classifier formation was not necessary as perfect classification was achieved by the rank-ordered first derivative spectra. SCS-based classifiers discriminated low back pain subjects from control subjects with accuracies of 100% (anterior cingulate cortex), 98% (thalamus) and 94% (prefrontal cortex). Discriminatory spectral regions contributing to the discrimination of pain versus no pain included those observed visually, ie GABA at 3.03, 1.91, 2.31 ppm; glycine at 3.57 ppm, glucose at 3.25-3.9 ppm; glutamate at 3.76, 2.08 and 2.34 ppm; and glutamine at 3.71, 2.15 and 2.46 ppm, respectively as well aspartate (2.82 ppm), lipid resonances (0.90, 1.3 ppm), myoinositol (3.28 and 3.64 ppm) and macromolecules at 0.5-0.9 ppm.

Discussion and Conclusions

The neurospectroscopy method provides a non-invasive, "diagnostic" test for the assessment of chronic pain where the pain levels vary over time. For those patients in moderate to severe pain during the 6 months prior to the MR exam, but not at the time of the exam, they still registered as positive for pain. It means that there is a "chemical memory" of pain in the brain, an important result from this study and of high clinical relevance. In conclusion, neurospectroscopy combined with the mathematical SCS method allows the detection of changes in cerebral metabolites associated with pain with very high accuracy. It also identifies those chemicals that are changing in the brain with the presence of pain. The ability to detect and monitor changes associated with specific pain conditions will lead to an understanding of underlying mechanisms, assist in the rational choice of new therapies and the tailoring of treatment on an individual basis.

References

(1) Deyo, R. A. *Arch Intern Med* 2002, *162*, 1444-1447.
(2) Jensen, M. C., et al *N. Engl. J. Med.* 1994, *331*, 69-73.
(3) Willis, W. D, et al. *Journal of Clinical Neurophysiology* 1997, *14*, 2-31.
(4) Gamsa, A. *Pain* 1994, *57*, 17-29.
(5) Turk, D. C. *Acta Anaesthesiol.Scand.* 1999, *43*, 885-888.
(6) Deyo, R. A.; Weinstein, J. N. *New Eng. J. Med.* 2001, *344*, 363-370.
(7) Ross, B.; Bluml, S. *The Anatomical Record* 2001, *265*, 54-84.
(8) Lean, C. L., et al In *Annual Reports NMR Spectroscopy*; Webb, G., Ed.; Academic Press, 2002; Vol. 48.