Does Massage Therapy affect Brain Metabolites?

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Citation

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Abstract

This performed study was to examine changes in brain metabolites following Light Touch (simulated massage) and Swedish massage (deep tissue massage) detected by MR Spectroscopy. The results showed no significant alteration in brain metabolites before and after Light Touch or Swedish massage.

INTRODUCTION

Despite the widespread acceptance of massage by the populace as an alternative treatment for a wide variety of ailments, the physiological mechanisms of massage therapy are not well understood. Massage therapy has been shown to have direct benefits, including improved circulation; cumulative rise in oxytocin; decrease in basal hypothalamic-pituitary axis activity; enhanced feelings of relaxation and increased feelings of well-being; and reduction in measures of anxiety, depression and pain. ([1]). Reports have cited the effectiveness of massage therapy in treating symptoms associated with at least 20 pathological conditions, as well as decreasing the pain and anxiety associated with pregnancy and childbirth ([2]).

Magnetic Resonance Spectroscopy (MRS) is a simple and non-invasive method to quantify brain metabolites. It has been used to study brain tumors ([3]); ischemic disease; inflammatory and demylenating diseases; and psychiatric illnesss ([4,5,6]). In our study we used MRS to directly measure the concentration of brain metabolites in the four regions of the brain that are part of the limbic-cortical-striatal-pallidal-thalamic tract (LCSPT) as this pathway is known for its importance in the regulation of mood and emotion, suspected of abnormal functioning in depression, and for which MRS studies have demonstrated differences between mood disordered patients and healthy subjects ([7,8,9,10,11,12,13,14,15,16,17,18,19,20,21]). We then examined any significant changes in these metabolites after the massage therapy sessions.

MATERIALS AND METHODS

Five healthy subjects (ages 21-28) were enrolled. The massage protocol was a randomized complete cross-over design where each subject received either five weeks of Swedish massage (deep tissue) followed by five weeks of Light Touch (simulated massage) or five weeks of Light Touch followed by five weeks of Swedish massage. Subjects were scanned prior to their entering either the light touch or the Swedish massage arms. They also received a scan within a week of completing their light touch and Swedish massage arms. In summation, each subject was scanned three times, at the baseline, after five weeks and after ten weeks. All MR scans were performed on a Siemens Sonata 1.5T scanner. The scans consisted of 3-plane T1 inversion recovery turbo spin echo (for voxel localization), an axial FLAIR (to screen for brain pathology), followed by four single voxel spectroscopies, localized on Thalamus, Lenticular Nucleus (Lent.Nuc.), Pre-Frontal Cortex (PFcortex) and Anterior Cingulate (Ant.Cing.). The SVS parameters were: TR = 3s, TE = 30ms, averages (NEX) = 128, number of points = 1024, voxel dimensions = 20×20×20 mm^3. A water reference scan was collected for each location (NEX=4) for quantification. After the subject was taken out of the scanner, a phantom scan was performed to check for day-to-day fluctuation. All spectra were analyzed with LC Model ([22]) running on an off-line Linux workstation.

RESULTS

All subjects successfully completed the study. A typical spectra is shown in figure 1. Spectra from all the voxels in every subject were of high quality. The LC Model fit to the spectra was good and the following metabolites could be quantified in all the regions: N-acetyl aspartate (NAA); creatine (Cr); choline (Cho); inositol (Ins); glutamate (Glu); glutamine + glutamate (Glx). The day-to-day fluctuations

(from the phantom scans) were negligible (CVs< 5% for all peaks). Table 1 shows the mean metabolite concentrations at all the four voxel locations at base line (BL), and after each massage arm (LT = light touch and SM = deep tissue Swedish massage). Only the major metabolites with precise fit and low CV are shown. The high p-values indicate that metabolite concentrations at baseline and after each arm of massage do not present any statistically significant differences. The result did not change when ratios with respect to creatine were used.

Figure 1

Figure 1: A) The Anterior Cingulate voxel positioning in a 21 y/o volunteer. B) The corresponding spectra with fitting from LCModel software.

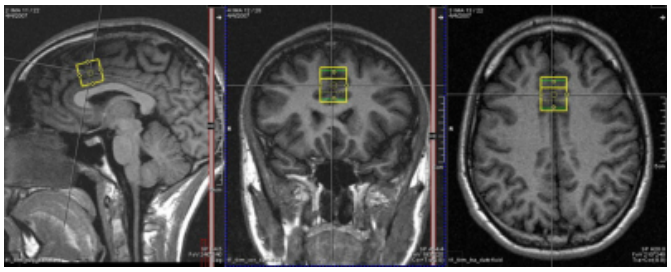

Figure 2

A) The Anterior Cingulate voxel positioning in a 21 y/o volunteer. B) The corresponding spectra with fitting from LCModel software.

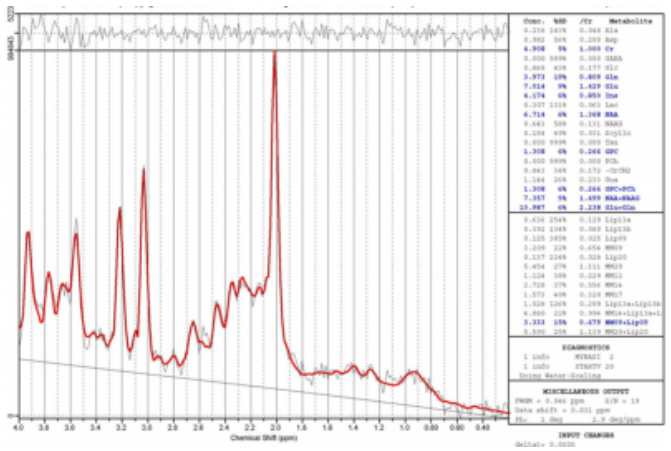

Figure 3

Table 1: Average metabolite concentrations from 5-subjects in mMol, from 4 voxel locations. The f and p values are from one way repeated measures analysis of variance (ANOVAR) statistics.

Location	Metabolite	BL	LT	SM	f	p
Lent.Nuc.	Cr	6.19	6.24	6.00	1.07	0.387
Lent.Nuc.	Ins	3.25	3.68	3.00	4.97	0.053
Lent.Nuc.	Cho	1.50	1.49	1.43	0.55	0.596
Lent.Nuc.	NAA	7.52	7.71	7.47	0.57	0.587
Lent.Nuc.	Glx	12.20	11.63	11.96	0.52	0.621
Thalamus	Cr	5.62	5.65	5.38	1.61	0.259
Thalamus	Ins	3.49	3.63	3.61	0.34	0.720
Thalamus	Cho	1.66	1.62	1.59	0.40	0.683
Thalamus	NAA	8.86	9.21	8.70	1.44	0.293
Thalamus	Glx	10.13	10.14	9.44	1.71	0.241
PFcortex	Cr	5.17	5.44	5.27	0.98	0.417
PFcortex	Ins	3.84	4.03	4.15	0.58	0.583
PFcortex	Cho	1.43	1.48	1.34	0.95	0.426
PFcortex	NAA	8.19	8.22	8.19	0.01	0.993
PFcortex	Glx	10.56	10.56	10.77	0.03	0.968
Ant.Cing.	Cr	5.57	5.52	5.33	1.90	0.211
Ant.Cing.	Ins	4.63	4.12	4.22	2.13	0.181
Ant.Cing.	Cho	1.44	1.36	1.30	3.14	0.099
Ant.Cing.	NAA	7.73	7.57	7.29	1.99	0.198
Ant.Cing.	Glx	11.72	10.89	10.86	1.02	0.403

DISCUSSION

Massage and massage therapy is a popular multi-billion dollar industry. It is estimated that over 11% of the U.S. population has had a massage, and the annual massage expenditure falls between $4-6 billion per year (Eisenberg [2,23]). Nearly three-quarters of individuals who see a massage therapist do so because of a specific health complaint they previously discussed with a physician ([24]). Approximately 32% of individuals seen by general practitioners have reported going to a massage therapist. Massage therapy is one of the Complementary and Alternative (CAM) therapies with the highest physician referral rate ([25,26]). Massage is purported to have a myriad of different benefits, including improved circulation, enhanced feelings of relaxation, increased feelings of well-being, reduction in measures of anxiety, depression, and pain ([1]). Massage therapy has been reported to be effective in treating symptoms associated with at least 20 pathological conditions, as well as decreasing the pain and anxiety associated with pregnancy and childbirth ([2,27]). Despite massage therapy's widespread public acceptance and frequent use, very little is known about its mechanism of action. This was the impetus for the White

House Commission on Complementary and Alternative Medicine (2002) to call for more research investigating massage therapy.

The fundamental principle underlying all magnetic resonance techniques is that certain atomic nuclei, including several found in compounds relevant to human biology and pharmacology [e.g., hydrogen (^{1}H), lithium (^{7}Li), carbon (^{13}C), fluorine (^{19}F), sodium (^{23}Na), and phosphorus (^{31}P)], when placed in a magnetic field will absorb and emit radiofrequency energy, with the precise frequency of their "resonance" dependent on the nucleus itself and the strength of the local magnetic field. Similar atomic nuclei in different molecules or even in different locations within the same molecule will absorb and re-emit energy at slightly different frequencies because of small differences in their local electrical milieu. These small differences in resonance frequency can be transformed into MR spectra, which are displayed in graphic form as plots of energy emission intensity as a function of frequency. MR spectra are used in turn to identify and quantify compounds in vitro and in vivo. ^{1}H-MRS allows the measurement of several major brain chemicals and metabolites based on the variation in resonance frequency of hydrogen nuclei in these different chemicals. Some ^{1}H-MRS visible metabolites include N-acetyl containing compounds (NA) such as n-acetyl aspartate (NAA); glutamate; gamma amino butyric acid (GABA); total creatine; choline-containing compounds; myo-inositol (MI); glutamine and lactate ($_{5,28,29}$). Some of these metabolites are involved in basic aspects of brain structure and function, but are not necessarily associated with a particular neurotransmitter system or circuit. NAA is a putative neuronal marker, which is reduced in conditions of neuronal damage or loss ($_{30}$). MI is an organic osmolyte and possibly a glial marker ($_{5}$). Creatine, which reflects the sum of creatine and phosphocreatine, reflects high-energy phosphate metabolism. Glutamate levels in rats increase modestly during development reaching adult levels around the time of weaning. GABA, which is derived from glutamate, is one of the predominant inhibitory neurotransmitters in the CNS.

In our pilot study we could not detect any effect on MRS by massage. There are three possible explanations for this finding. First, it is possible that massage produces changes in metabolites, but these metabolites are not the ones we chose to measure, and are not the ones that are accurately measured with standard sequences available on 1.5 T scanners. For example, complex spectral peaks (such as GABA and Asp) are difficult to resolve with accuracy with the methods used in the current study. Second, it is possible that we chose the wrong areas of the brain to examine. The regions chosen for study were picked on accepted understanding of brain function and regional control of mood and emotion. It is entirely possible that other areas of the brain are more affected by massage, for example amygdale or hippocampus ($_{31,32,33}$). Third, it is possible that massage produced changes in the regions of the brain and the metabolites we selected to measure, but the changes were below detectability, i.e., ~ twice the reproducibility, in this small group of subjects. Thus, we estimate that our power to detect statistically significant would fall below 0.8 for metabolite changes of less than 9% for our most reproducible determinations of regional metabolites, but for a few less precisely determined regional metabolites would have to have been less than 25%. There are limitations to MR Spectroscopy. Most importantly, it can only measure the concentrations with 5% error (CV<5%), and this accuracy drops for metabolites with lower concentrations. Consequently, if massage therapy induced chemical changes of less than 5%, it would be undetectable with our present methods.

CONCLUSION

Regional metabolite concentrations for NAA, Cr, Cho, Ins, Glu and Glx obtained by MRS scans were consistent and reproducible. No statistically significant differences in brain metabolites could be detected between the pre- and post-treatment spectra. The overall conclusion then is that Swedish massage does not seem to alter brain metabolite concentrations; either no change occurred at all within the concentrations, or any changes that did occur were so minute they could not be detected by current scanning technology. Even though the study does not support claims that massage therapy affects brain metabolites, the study was only focused on locations within the brain indicated for their known importance in the regulation of mood and emotion. It remains possible that certain sections of the brain not examined could exhibit altered brain metabolite concentrations after massage therapy.

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