

Whole-brain voxel-based Susceptibility-Weighted Imaging (SWI) analysis: normal cortical and subcortical values, and preliminary results in post-traumatic epilepsy

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Introduction: Susceptibility-weighted imaging is a recently developed magnetic resonance imaging (MRI) technique based on a 3D gradient echo (GRE) sequence that provides a unique contrast by combining magnitude and phase information. The resulting sequence has high sensitivity for the in-vivo detection of materials with high magnetic susceptibility, namely paramagnetic materials such as iron deposits and deoxygenated hemoglobin [1]. Clinical applications include detection of microhemorrhages and shearing injuries in trauma. This technique has recently been applied to pathologies ranging from multiple sclerosis to brain tumors [2]. Nevertheless, there is limited knowledge of how the normal range of SWI values compares with traditional T2*-weighted 2D GRE images. We present a novel methodology based on Statistical Parametric Mapping (SPM) [3] for the voxel-by-voxel analysis of SWI images. Preliminary results found in post-traumatic epilepsy (PTE) patients are also presented.

Methods: The study comprised eighteen healthy volunteers (9 females) with mean±standard deviation (SD) age of 31.6±10.4 years and range of 20-59 years. A preliminary group comparison study enrolled two male patients with history of post-traumatic epilepsy: patient A, 47 years old with MRI-evident lesions; patient B, 55 years old with no evidence of lesions using traditional MRI techniques. All volunteers and patients signed an informed consent and the hospital's ethics committee approved the study. Data was acquired in a 1.5T scanner (Magnetom Avanto, Siemens, Erlangen) using the SWI 3D sequence with the following parameters: TR=49 ms; TE=40 ms; flip angle=15°; receiver bandwidth=80 Hz/Px; 1 slab with 88 slices with slice thickness=1.5 mm; FOV=256x256 mm²; matrix=256x256 and 1x1x1.5 mm³ voxel size. Magnitude and Phase components were obtained. SWI magnitude data was imported to SPM8 and normalized to ICBM template space using the EPI template image, and preserving concentrations. Subsequently, a Cerebral Spinal-Fluid (CSF) mask was applied to all images and mean values for every subject were calculated using an in-house built Matlab script. Individual data volumes were then normalized to CSF values in order to minimize subject variability and scanner differences. Finally, anatomical masks derived from WFU Pickatlas [4] were applied to each individual for the determination of normal SWI magnitude values. Tissue data were correlated by Spearman's rank to age and were compared by Mann-Whitney's test according to gender. Patient data were compared to normal population using SPM8 t-test analysis (p <0.001 uncorrected) using age and sex as co-variables, and were further compared using normal 99% confidence ellipses of anatomical VOI values.

Results: The Table shows the SWI magnitude mean±SD values as a percentage change from CSF values. Here negative values mean increased tissue magnetic susceptibility such as an increased iron tissue concentration in substantia nigra [5]. Significant (p<0.05) negative correlations with age are observed for gray and white matter (WM), occipitoparietal WM, corpus callosum, parahippocampus, pallidum, putamen, thalamus and red nucleus (correlation coefficients range: -0.581 to -0.384), suggesting an increase in magnetic susceptibility with age, attributable to an increase in iron content of some tissues [6, 7]. Significant (p<0.05) differences were found regarding gender with increased magnetic susceptibility of the frontal lobe and occipitoparietal WM, pallidum and cerebellum in men and in the corpus callosum in women. The Figure shows SPM t-test maps superimposed on FLAIR sequence for patient A. Top and bottom image sets respectively show increased and decreased magnetic susceptibility regions, spanning predominantly the frontal right hemisphere, which are related to the known traumatic injury locations. Decreased magnetic susceptibility may be related to edematous pathophysiological process, as they seem to agree with hyperintense signals in the FLAIR sequence in the frontal region. The plot shows normal 99% confidence ellipse for the amygdala and hippocampus and values for patients A and B. Regarding subcortical and mesencephalic structures patient A shows susceptibility differences in the amygdala, hippocampus, parahippocampus, hypothalamus, and substantia nigra. Patient B shows an increase in susceptibility in the pallidum and putamen corresponding to lesions not depicted in the conventional MR examination. In addition, changes were observed in the red nucleus, substantia nigra, hypothalamus, and also in the hippocampus and parahippocampus, which may explain the epileptic symptoms in this patient.

Tissue	% change normCSF
Gray-matter	-1.0±3.3
White-matter	3.2±2.4
Frontal WM	-0.9±3.9
Occipitoparietal WM	3.5±2.2
Cerebellum	-14.2±6.7
Brainstem	-1.9±5.0
Red nucleus	-1.8±3.9
Substantia Nigra	-1.1±5.4
Amygdala	12.8±3.6
Hippocampus	12.6±2.7
Parahippocampus	6.9±5.0
Caudate	7.7±2.6
Putamen	5.7±4.8
Pallidum	-10.8±3.9
Thalamus	10.1±2.2
Hypothalamus	17.6±6.5
Corpus Callosum	2.8±3.2

regarding gender with increased magnetic susceptibility of the frontal lobe and occipitoparietal WM, pallidum and cerebellum in men and in the corpus callosum in women. The Figure shows SPM t-test maps superimposed on FLAIR sequence for patient A. Top and bottom image sets respectively show increased and decreased magnetic susceptibility regions, spanning predominantly the frontal right hemisphere, which are related to the known traumatic injury locations. Decreased magnetic susceptibility may be related to edematous pathophysiological process, as they seem to agree with hyperintense signals in the FLAIR sequence in the frontal region. The plot shows normal 99% confidence ellipse for the amygdala and hippocampus and values for patients A and B. Regarding subcortical and mesencephalic structures patient A shows susceptibility differences in the amygdala, hippocampus, parahippocampus, hypothalamus, and substantia nigra. Patient B shows an increase in susceptibility in the pallidum and putamen corresponding to lesions not depicted in the conventional MR examination. In addition, changes were observed in the red nucleus, substantia nigra, hypothalamus, and also in the hippocampus and parahippocampus, which may explain the epileptic symptoms in this patient.

Discussion: A voxel-based SPM approach was presented for the analysis of SWI images and normal magnitude values were determined. The combined use of SPM t-test maps and 99% confidence ellipses derived from anatomical masks shows potential for assessment of magnetic susceptibility changes in brain tissues in a more sensitive and user-independent manner. The method also seems to highlight lesions not observed in conventional MRI.

References: [1] EM Haacke et al. AJNR 2009. 30: 19-30. [2] S Mittal et al. AJNR 2009. 30: 232-252. [3] A Mechelli et al. Curr Med Imag Reviews 2005. 1: 105-113. [4] JA Maldjian et al. NeuroImage 2003. 19:1233-1239. [5] LO Thomas et al. AJNR 1993. 14: 1043-1048. [6] Haacke EM et al. JMRI 2007, 26:256-264. [7] SL Harder et al. AJNR 2008. 29:176-183.

