Quantitative Susceptibility Mapping of the motor cortex in ALS and PLS patients: A Biomarker for Upper Motor Neuron Dysfunction

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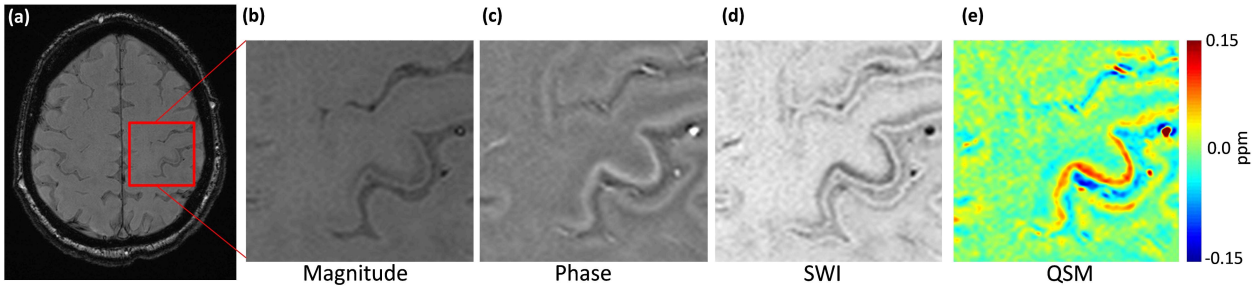
TARGET AUDIENCE: Researchers and clinicians interested in application of quantitative susceptibility mapping (QSM) in ALS and PLS.

PURPOSE: Motor Neuron Disease is a progressive neurodegenerative disease characterized by lower- (LMN) and upper motor neuron (UMN) dysfunction in ALS and mostly UMN dysfunction in PLS. The diagnosis is currently based on clinical assessment, electrodiagnostic studies and exclusion of other diseases. Electromyography effectively detects LMN degeneration but there is no definite technique for demonstrating UMN involvement and UMN findings on clinical examination may not occur until late in the disease course. A method that detects early UMN involvement and accurately monitors disease progression is highly desirable especially for future clinical trials and strategies for early intervention. We investigate the importance of quantitative susceptibility mapping (QSM) analysis of susceptibility weighted imaging (SWI) data in ALS and PLS patients. We compared the QSM values with presence of UMN signs in these patients.

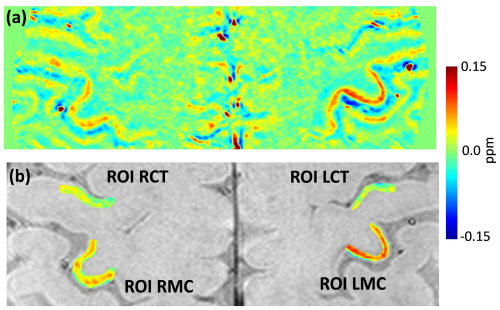
METHODS: Nine ALS and three PLS patients were included in the study. MRI scan was performed using a Siemens 3T scanner, and included a 3D gradient-echo (FLASH) sequence with velocity compensation for QSM (TR = 28ms, TE = 20ms, FOV = 230×172mm^2, matrix = 384×288, slice thickness = 1.5mm, nominal resolution = 0.6×0.6×1.5 mm^3, number of slices = 72-96) as well clinical T1- and T2-weighted scans. The QSM processing was performed with a software package developed in-house using Matlab (Matlab 2014a, The MathWorks). The phase images were unwrapped followed by high pass filtering to remove the background field to generate the filtered phase map. Susceptibility weighted images were generated by creating a phase mask from the filtered phase map and multiplying this mask four times with the magnitude images[1]. QSM images were calculated from the filtered phase maps and magnitude data using the iterative Susceptibility Weighted Imaging and Mapping (iSWIM) algorithm[2,3]. To evaluate the susceptibility changes, ROIs were drawn into the right (RMC) and the left motor cortex (LMC). For control, susceptibility values were calculated from ROIs in the anterior border of precentral gyrus on the right (RCT) and left (LCT). We correlated the susceptibility values between the primary motor cortex (in the hand knob area) and the anterior border of precentral gyrus with presence of UMN signs (spasticity and hyperreflexia) and also most affected side of symptoms.

Figure 1



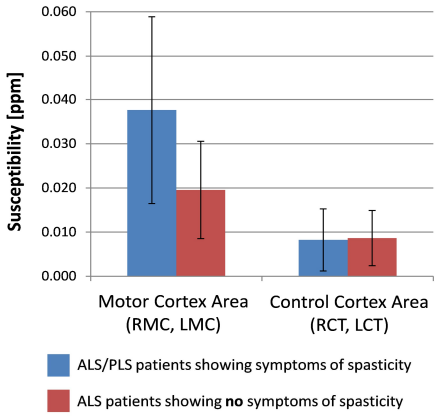
RESULTS: Fig. 1(a) shows an axial T1-weighted magnitude image in the upper motor cortex level of an ALS patient. The four images on the right present a zoomed detail of this region (red rectangle). In Fig. 1(b) the magnitude image is shown, (c) demonstrates the unwrapped and high-pass filtered phase image, (d) shows the SWI and (e) the QSM image. Increased hypointensity is noted in the SWI images in the grey matter of primary motor cortex (posterior border of precentral gyrus; Brodmann area 4) and not in the adjacent cortex including the anterior border of precentral gyrus. This can be quantified using QSM image. This is seen in a subgroup of ALS patients and all 3 PLS patients. Fig. 2(a) shows the QSM image of the right and left motor cortex of an ALS patient, (b) visualizes as a color-coded QSM overlay on the magnitude image where the four ROIs were drawn. Fig. 3 displays the susceptibility values from motor- and control cortex area of ALS/PLS patients having symptoms and no symptoms of spasticity. Patients with spasticity symptoms have significant higher susceptibility values in the motor cortex area than those who do not ($p<0.043$). In the patient group showing symptoms of spasticity the susceptibility in the control cortex area is significant lower than in the motor cortex area ($p<0.001$).

Figure 2



DISCUSSION: T2 hypointensity in the motor cortex in ALS has been described before[4-7] but the increased resolution of SWI makes it visible within the cortical layers of the motor cortex in a band like fashion within the grey matter. The QSM processing and analysis of the motor cortex and control area enables the quantification of signal changes, which can be seen morphologically in phase or susceptibility weighted images. In our short series there is a significant correlation between QSM values and presence of UMN signs (spasticity). However, as seen in our cohort, these changes are not seen in every ALS patient and might be related to the duration of disease and as well as subgroup of patients who had pronounced UMN symptoms. These types of heterogeneity of ALS patients are noted before and iron deposits on pathology are not found in all cases[8].

Figure 3



CONCLUSION: Our results suggest QSM could be a quantitative tool to detect changes in the upper motor neuron (UMN) as they are present in ALS and PLS. Larger prospective studies will be needed to find the incidence, sensitivity and specificity of this sign in ALS patients and to establish its prognostic value.

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