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Editorial

Imaging the Amyotrophic Lateral Sclerosis Brain: The Motor Band Sign

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Clinicians and researchers who study and treat patients with amyotrophic lateral sclerosis (ALS) are often frustrated by the limited evidence for ALS on brain MRI examination, even in patients with extensive upper motor neuron involvement. A common view is that MRI assessment of ALS patients is generally unrewarding except to exclude other diagnoses. However, MRI-detectable ALS findings may depend on the extent of clinical involvement, the field strength, sequences and make or model of the MRI machine used, and the experience of the MRI radiologists. MRI findings that are somewhat specific for ALS include MRI evidence of cortical atrophy and T2/FLAIR hyperintensities in the corticospinal tracts.[1] However, the utility of these findings has been questioned.[2]

In this issue of the journal, Chung and colleagues address the prevalence of an MRI finding in patients with ALS and primary lateral sclerosis (PLS), termed the "motor band sign" (MBS).[3] The MBS is a unique MRI feature visualized using a post-hoc analysis of images acquired using a gradient-echo MRI sequence termed susceptibility-weighted MRI (SWI), which accentuates the identification of material which is more magnetizable than the surrounding brain tissue, such as occurs with the presence of multivalent cations (e.g. iron). The use of SWI in patients with ALS or PLS sometimes produces a curvilinear "band" of a decreased signal which is observed in the precentral gyrus in the cortical grey matter. In some cases, this finding is prominent in the region of precentral gyrus associated with the "hand area" (termed "hand knob"), as the region appears like a knob or an omega sign. In previous work, the MBS MRI signal has been found to correlate with upper motor neuron involvement clinically and *ex vivo* MRI and pathological examination demonstrated increased iron accumulation in the cortical grey matter of precentral gyrus in middle and deep layers of cortex, sparing superficial layers.[4] The iron was present extracellularly as well as in small cells thought to be microglia. The basis for the observation of iron in the cerebral cortex is unknown but a microglial iron deposition has sometimes been observed in other neurodegenerative disorders, and the pattern of deposition may account for the apparent banding pattern.

In the present study, Chung et al have attempted to determine the prevalence of MBS using SWI in ALS and PLS in a retrospective study of a small sample of 13 ALS and 5 PLS patients at their centre over several years, as well as 10 age- and gender-matched controls without known disease.[3] This work follows previous observations of MBS from the same group, also reported in this journal.[5] Patients had extensive routine MRIs using a number of sequences, and data were subsequently analyzed for SWI imaging. Independent clinical analysis was performed using a "global upper motor neuron score" based on spasticity and hyperreflexia in the contralateral limbs. The authors showed an MBS in approximately 70% of ALS patients and 80% of PLS patients, with no MBS being observed in controls. These data are certainly of interest given the high rate of observation of MBS in the ALS and PLS groups in this study.[3] The limitations or this study are evident, a very small sample population, the retrospective nature of the study, the absence of investigator blinding, the data being derived from a single centre and the complicated workflow where bias may have been introduced to influence patient selection for SWI. Observation of the MBS is not limited to SWI. MBS can be observed in ALS and PLS using other MRI sequences such as T2, FLAIR and diffusion-weighted MRI (DWI). However, the observation of MBS is much higher with SWI than using these other sequences.[6]

These observations regarding the high prevalence of the magnetic susceptibility of precentral cerebral cortex and MBS in ALS and PLS are also supported by other investigations. A recent Italian study has shown increased magnetic susceptibility in precentral gyrus in ALS patients with upper motor neuron involvement compared to controls.[7] This Italian group has also attempted to use the extent of hypointensity of the motor cortex as a tool to distinguish clinical ALS phenotypes (e.g. upper motor neuron predominant ALS, lower motor neuron predominant ALS, ALS mimics). A study of 64 patients, 48 of whom had ALS and 16 patients who were ALS mimics demonstrated that motor cortex hypointensity was significantly higher in ALS patients with upper motor neuron involvement compared to ALS mimics or controls.[8] A German study from one centre which only studied nine ALS patients using SWI as part of a larger imaging study found that seven of these ALS patients exhibited a MBS (~80%).[6] A second Italian group has observed hypointensity in motor cortex by SWI in 76% (62/82) of ALS patients, but also in 13/33 controls as part of a larger MRI imaging assessment.[9]

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These observations of Chung and colleagues raise the tantalizing possibility that brain MRI with SWI may play a useful role in the diagnosis of ALS and PLS, a role that potentially will also be valuable in therapeutic trials to assess upper motor neuron involvement. To establish the value of the MBS sign as a diagnostic biomarker will likely require a prospective study with larger sample sizes from multiple centres. This larger sample would also include patients who are being investigated for suspected ALS, including patients who may not be meeting the criteria for definite ALS, ALS mimics and other disease and healthy controls. Longitudinal studies like the Canadian ALS Neuroimaging Consortium (CALSNIC) could provide data to help determine if MBS and SWI are sensitive to monitoring progressive cerebral degeneration.

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