Serial Magnetic Resonance Spectroscopy of the Human Brain – Atlas-based Automated Volume Registration with High Precision and Reproducibility.

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Purpose: A challenge for serial MRS studies is volume placement reproducibility (1-7). Typically, this has relied on visual registration which is prone to significant operator bias. Therefore the consistency of ROI placement can be relatively poor, intra-centre and worse inter-centre. Our new atlas-based automated protocol allows the exact ROI placement from one scan session to the next. Moreover it can be utilized for multi-centre studies to ensure identical ROI placement.

Methods: The Talairach Atlas (8), integrated into a software interface (9-11), was used to guide volume placement, eg, the putamen, and register the spatial co-ordinates of this structure to normalized, averaged MR images MNI305 (12,13). We have linked these software to our new volume placement protocol to allow us to precisely register the MRS volume translation and rotation matrices defining their atlas-based spatial location, for both the initial scan, and then from one

scan session to another (Figure 1). By precise registration of the high-resolution anatomical MR images acquired during 2 scan sessions. calculating and the displacements in translation and rotation, we then imported and automatically adjusted the MRS translation and rotation matrices such that the MRS volume is located in exactly the same place for the second scan. From the baseline session, an anatomical image and MRS ROI parameters were obtained. During the next session, the anatomical image is registered to the baseline image using SPM8 (14). This step takes less than one minute. The resulting affine transformation was then applied to the baseline MRS ROI to obtain the new positional parameters for the next scan session. The new method was tested using two manual visual ROI placement strategies in the supplementary motor area for control



and Parkinson's disease (PD) patients. Strategy 1 where the ROI were centered on the midline and the position in the sagittal plane was based on the AC-PC line. This protocol was used for both the baseline and follow-up scans. Strategy 2 used both landmarks and printouts of the baseline ROI placement to guide the new MRS ROI placement.

Results: Using the new strategy, there was no ROI mismatch between scans. Using strategy 1, the average percent overlap between the predicted and actual follow-up ROI placement is $56 \pm 27\%$ for ten PD patients. Using strategy 2, the average percent overlap between the predicted and actual follow-up ROI placement is $79 \pm 15\%$ for ten PD patients.

Discussion: Since the complement of metabolites in an MR spectrum depends on both the composition (GM+WM), and anatomical position, accurate ROI placement is crucial. The data presented here illustrate how much error can occur depending on the visual technique chosen, and how this is mitigated using the new technique.

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