SPMMouse: A new toolbox for SPM in the animal brain

S. J. Sawiak[1], N. I. Wood[2], G. B. Williams[1], A. J. Morton[2], and T. A. Carpenter[1]

[1]Wolfson Brain Imaging Centre, University of Cambridge, Cambridge, United Kingdom, [2]Department of Pharmacology, University of Cambridge, United Kingdom

Introduction

Voxel-based morphometry is widely used in the human brain for analysing morphology in the normal and pathological brain and is most commonly performed with the SPM (Statistical Parametric Mapping) software [1]. Although some groups have used the software in preclinical studies, this is most commonly by using fake headers with geometric parameters similar to human brains and a coherent, easy to use approach has not been widely available.

Here we present a new open-source toolbox allowing SPM to work readily with the mouse and marmoset brains with an easy to use interface for extending the toolbox to other brains. The toolbox may also be of use to researchers of the human brain investigating extreme populations such as early paediatrics and severe brain injured groups. We demonstrate the application of this toolbox here to show voxel-based morphometry in the R6/2 Huntington's mouse brain [2].

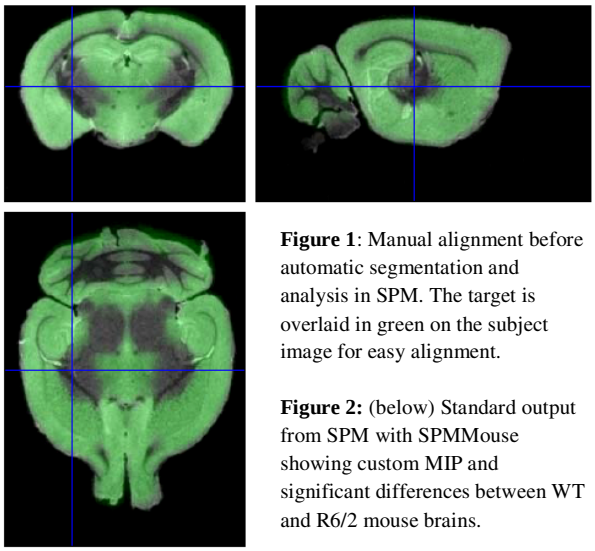
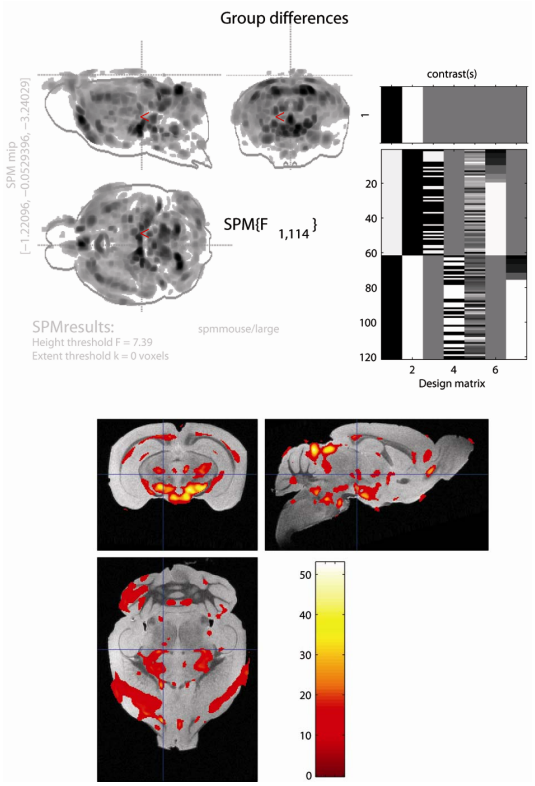


Figure 1: Manual alignment before automatic segmentation and analysis in SPM. The target is overlaid in green on the subject image for easy alignment.

Figure 2: (below) Standard output from SPM with SPMMouse showing custom MIP and significant differences between WT and R6/2 mouse brains.



Methods

The toolbox extends SPM's functionality with affine registration priors for the mouse and marmoset brains in addition to an easy to use interface allowing other brains to be added. The same interface allows new templates for maximum intensity maps (MIPs, or 'glass brains') to be created showing the final results. The prior knowledge algorithm for affine registration used in SPM requires reasonably close starting estimates and to facilitate this we have added an overlay target the Display Image function of SPM to make initial alignment straightforward. Additionally, a new mode allowing live display of registration progress allows visualisation of intermediate steps to spot any problems. Default parameters can be generated by simply loading a single image of the relevant brain and the toolbox will produce sensible values for all SPM programs from the measurements in the image header.

To demonstrate the toolbox, we used a previously described mouse brain atlas [3] to register 121 images from a population of R6/2 mice (a transgenic model of Huntington's disease) with wildtype (WT) littermate controls. Following approximate manual registration using the SPM interface, the affine priors supplied were used to register the images to the tissue probability maps (TPMs). Images were then segmented into tissue classes and the powerful general linear model (GLM) interface used to specify genotype along with sex, overall brain volume and age covariates with interactions modelled between main effects.

Results

Figure 1 shows a mouse brain being manually registered prior to segmentation and figure 2 shows the final output produced by the SPM software. The process is identical to that of human data processing which is heavily documented elsewhere, all of the changes necessary for dealing with differently sized brains are handled by the software. The *F*-test performed on the data to compare differences in grey matter concentrations between groups show extensive differences in line with those in the literature, in particular the basal ganglia and cortical involvement in pathology is clear.

Conclusion

SPMMouse has been demonstrated in the mouse brain as a straightforward addon to the SPM software for use in non-human brains. This software will be publicly-available and we hope will be of use to the scientific community using MRI for morphological phenotyping in a range of different animal models of disease and experimental conditions. The software is freely available online, contact the author for details.

References

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