camh
Centre for Addiction and Mental Health

February 18, 2014

Editorial Board, Neuroimage

Dear Sir or Madam:

Please find enclosed our manuscript entitled, *Bootstrapping Multi-atlas Segmentation Using Multiple Automatically Generated Templates for the Segmentation of the Whole Hippocampus and Subfields* by Jon Pipitone and colleagues.

In this manuscript we describe a novel automated MRI hippocampal segmentation algorithm optimised to perform well with only a small number of manually segmented training images. We believe this is an important contribution because the expertise and effort needed to perform manual segmentation can be prohibitive for many clinicians and researchers, and yet existing automated methods generally require between 30 to 80 training segmentations. This situation makes it infeasible to use these methods for segmentations based on histological-based digital segmentations (because of their rarity), high-resolution digital atlases (because of the time needed to segment these images), or when exploring new protocols or the effect of variations on a segmentation protocol.

It is for these reasons that we developed the automated segmentation algorithm, mischievously named MAGeT-Brain, which takes advantage of the neuroanatomical variability that exists in the target population being studied to bootstrap a large template library from a small set of manually segmented images. In this manuscript we rigorously validate this approach on multiple disease populations, and compare our segmentations with existing popular methods (e.g. FSL and FreeSurfer). We find that MAGeT-Brain produces very reliable and consistent segmentations of the whole hippocampus when compared with manual segmentations, and is competitive with exiting methods. Finally, we have made our algorithm available publically online for use by other groups, and are pursuing the contribution of our segmentations to the Alzheimer's Disease Neuroimaging Initiative image database.

We believe that the technique we have developed and our findings are a significant contribution to the neuroimaging community, specifically for those

researchers interested in large scale studies of the hippocampus in the context of normal brain function and different forms of brain dysfunction.

We hope you find the enclosed manuscript meets the high standards of NeuroImage.

Sincerely,

Jon Pipitone
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