Hippocampus subfield segmentation reliability is improved by non-linear realignments between scan-repetitions at 7T and 3T.

Thomas B Shaw[1], Steffen Bollmann[1], Nicole T Atcheson[1], Lachlan T Strike[2], Christine Guo[3], Katie L McMahon[4], Jurgen Fripp[5], Margaret J Wright[2], Olivier Salvado[5,6], and Markus Barth[2]
[1]*The Centre for Advanced Imaging, The University of Queensland, Brisbane, Australia,* [2]*The University of Queensland, Brisbane, Australia,* [3]*QIMR Berghofer Medical Research Intstitute, Brisbane, Australia,* [4]*Queensland University of Technology, Brisbane, Australia,* [5]*CSIRO Health and Biosecurity, Brisbane, Australia,* [6]*CSIRO Data61, Sydney, Australia*

Synopsis

MR image quality is affected greatly by participant movement. Anatomical image quality can be improved by acquiring consecutive anatomical scans and combining them to boost SNR and sharpness. We aimed to find the optimal combination method of three repetitions of high-resolution turbo spin-echo (TSE) scans, commonly used for hippocampus subfield segmentation. We used non-linear realignment between the TSE repetitions in a range of participants at 3T and 7T and found that image segmentation reliability and sharpness were higher for the non-linear realignment technique, as compared to linearly realigned, and averaged methods. Hippocampus image segmentation greatly benefits from this technique.

Introduction

Increasing spatial resolution for MRI improves segmentation of various tissue types or anatomical structures[1]. Large movement artefacts increase partial volume effects and decrease interpretability of anatomical scans for clinicians and automatic/manual segmentation protocols. Therefore, there is a need to acquire multiple repetitions of a single sequence to improve signal-to-noise ratio (SNR), which leads to longer scan times. This includes dedicated Turbo-Spin Echo (TSE) scans for hippocampus segmentation. With longer acquisition times comes a higher propensity for participant movement, which can deteriorate image quality leading to increased costs and unusable data, and patients with neurodegenerative disorders, elderly, young, and highly anxious participants are particularly likely to move in the scanner.[3]
Image segmentation is especially affected by MRI movement artefacts. Therefore, in order to ameliorate movement artefacts, improve image segmentation reliability, and increase sharpness and SNR, we implemented a non-linear realignment technique to improve hippocampus subfield segmentation at 7T and 3T in healthy controls, Motor Neuron Disease (MND) patients, and adolescent participants. Inherently, segmentation algorithms rely on high sharpness and SNR for registration. Therefore, we chose to assess segmentation reliability based on registration success and sharpness.

Methods

In order to test the robustness of the technique on a range of participants, we acquired a 2D TSE sequence thrice per participant at both 7T ($0.4 \times 0.4 \times 0.8 mm^3$) and 3T ($0.5 \times 0.5 \times 1.0 mm^3$) acquired orthogonal to the hippocampus proper in four samples of participants: at 7T, 11 patients diagnosed with MND (Age, M=59.36, SD=7.65), 11 age-matched control participants (HCs, M=60.23, SD=7.65), and 29 young healthy participants (YHPs, M=26.31, SD=0.66) and at 3T, 24 adolescent participants (details) An anatomical whole-brain T1w MP2RAGE[4,5] (.9mm iso) was also acquired (7T: TR/TE/TIs=4300ms/2.5ms/840,2370ms; 3T (TR / TE / TIs = 4000ms / 2.9ms / 700ms / 2220 ms).
Pre-processing of images included isotropic resampling to $0.3 mm^3$ ($0.5 mm^3$ for 3T), bias field correction and intensity normalisation[6]. To examine registration precision and segmentation reliability, we compared three separate methods (1) *Non-Linear*, (2) *Linear*, and (3) *Average*. The *Non-Linear* method involved creating a minimum deformation average template using ANTs SyN registration[7,8] (Fig 1.) The three repetitions were iteratively deformed to a synthetic template as to not bias any repetition in the realignment process. For the *Linear* method, we first used FSL[9] to concatenate images in time, then estimating the registrations between the repetitions with MCFLIRT[10], then averaging the 4-dimensional images. The *Average* method involved taking the scanner-outputted arithmetic mean.
Intuitively, image registration is benefited by images with higher sharpness, better SNR, and more refined details. Therefore, registration consistency will be increased between participants if the realignment method is more successful. To test the three methods, we co-registered each participant from each group to group-specific templates using ANTs, for each method (*Non-Linear*, *Linear*, *Average*, see Figure 1). This yielded 12 templates (e.g., MND-*Linear*, Healthy controls-*Non-Linear*, adolescents-*Average* etc.). Then, each of these templates were labelled using Automatic Segmentation of Hippocampus Subfields (ASHS)[3]. Participants' scans were also labelled using ASHS in a common space (Figure 2). The resulting templates and individual scans were compared using Dice overlaps[11] between the group template and the individual for each method (*Non-Linear, Linear, Average*). In this way, we could determine the resulting segmentation reliability of each method. The sharpness of each image was also compared for each of the three methods by calculating the median of the derivative of a Gaussian applied to the TSE at 1mm FWHM as described in Fonov & Collins (2018)[12].

Results

Fig. 3 shows the results of each realignment method on two subjects, one with excessive movement (as rated by three raters) and one with limited movement. When collapsing across all participant groups, Dice overlaps for the *Non-Linear* method were significantly higher than for *Linear* and *Average* Fig 3; N=51; ** = *p*s < 0.001, Wilcoxon rank sum tests).
When comparing sharpness between the three methods (Figure 5), we found differences between all three groups ($p < 0.001$), with *Non-Linear* showing higher sharpness than *Linear* and *Average* (** = *p*s < 0.05). No difference was found between *Linear* and *Average*. ($p = .982$, Wilcoxon rank sum test). 3T results found the same pattern of results for sharpness.

Discussion and conclusion

We examined the effect of realignment strategies for multiple repetitions of high-resolution images of the hippocampus at both 3T and 7T and found a *Non-Linear* realignment strategy produces more reliable and sharper segmentations than a *Linear* or *Average* method. *Non-Linear* realignment therefore improves the robustness of brain image segmentation and mitigates the effects of motion artefacts in high-resolution anatomical MRI.
Hippocampus subfield segmentation can benefit from non-linear registrations when participant motion between scans is an issue. It is proposed that due to the high computational cost, non-linear realignment be used judiciously in participants with high inter-scan motion, as determined by metrics such as sharpness or qualitative assessment.

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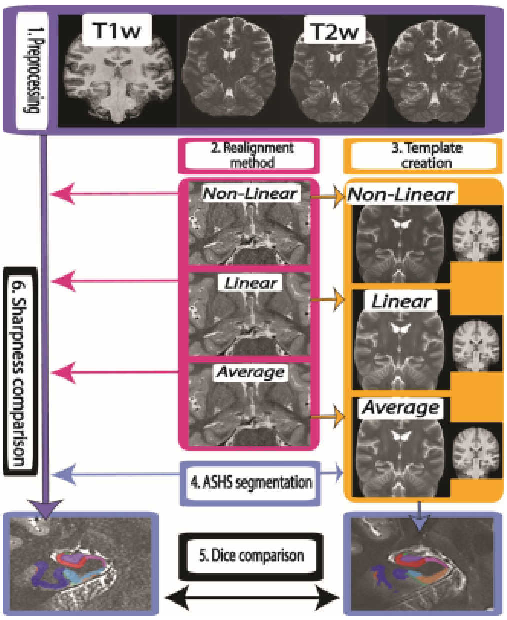
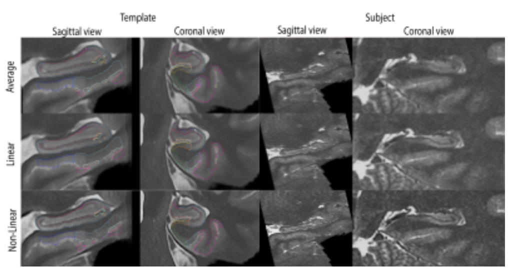
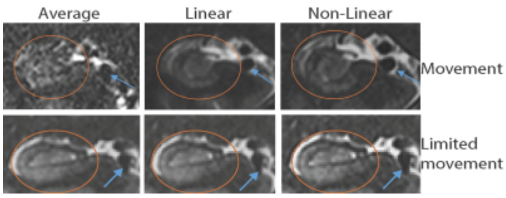
Figures



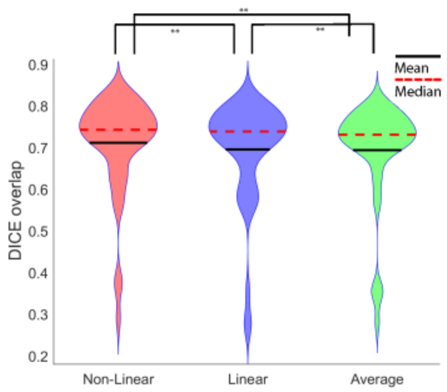
Processing pipeline. Input images (purple) are processed before the realignment methods are performed (in pink, *Non-Linear*, *Linear*, *Average*). Next, templates are constructed for each of the methods (yellow). The individuals and templates are segmented in a common space (blue) before Dice comparisons (black). Sharpness for individual images is also measured for each method (6). All views show hippocampi for a coronal single-subject view. This processing pipeline was performed for each method (Non-Linear, Linear, and Average) and each group (YHPs, MND, HCs, 3T adolescents).



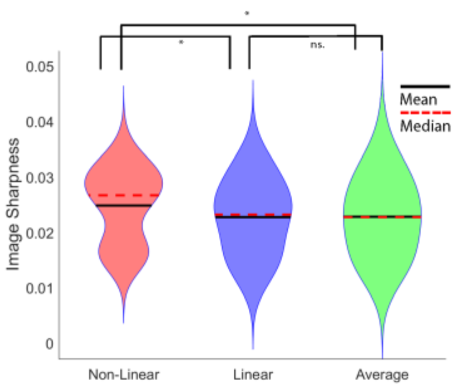
Sagittal and coronal views of the alignment in the hippocampus after the three realignment procedures (*Non-Linear*, *Linear*, *Average*) for the method-templates (left, labelled) and a representative YHP subject that benefited from the non-linear realignment technique (right). Views capture the left hippocampus, and both hippocampi in a coronal single-subject view. Edges of the ASHS template segmentations have been superimposed as coloured lines.



Left to right: *Average*, *Linear*, and *Non-Linear* realignment examples from a participant with more movement (top) and less movement (bottom) with ellipses over the right hippocampus (coronal plane); blue arrows denote a common vessel.



Violin plot for the three realignment methods (*Non-Linear, Linear, Average*) of Dice overlap scores between individual subject TSEs and its respective method-template, collapsed over all groups. ** = *p*s < 0.001, Wilcoxon rank sum tests).



Violin plot for the three realignment methods of sharpness scores of individual subject TSEs, collapsed over groups. * = *p*s < 0.05, Wilcoxon rank sum test.