# Open-Source Hypothalamic-ForniX (OSHy-X) Atlases and Segmentation Tool for 3T and 7T

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Summary

Segmentation and volumetric analysis of the hypothalamus and fornix plays a critical role in improving the understanding of degenerative processes that might impact the function of these structures. We present Open-Source Hypothalamic-ForniX (OSHy-X) atlases and tool for multi-atlas fusion segmentation for 3T and 7T. The atlases are based on 20 manual segmentations, which we demonstrate have high interrater agreement. The versatility of the OSHy-X tool allows segmentation and volumetric analysis of the hypothalamus and fornix from MRI scans. We also demonstrate that OSHy-X segmentation outperforms FreeSurfer segmentation of the hypothalamus (Billot et al., 2020) and fornix (Fischl et al., 2002). We have previously demonstrated the use of OSHy-X on a cohort of 329 non-neurodegenerative control participants and 42 patients with ALS to investigate reduced hypothalamic volume and its association with appetite, hypermetabolism and weight loss (Chang et al., 2022).

Statement of need

Segmentation of small structures of the brain including the hypothalamus and fornix is important for primary research of health and disease. One such disease that has implications for the volume of the hypothalamus is Amyotrophic Lateral Sclerosis (ALS). ALS is a fatal neurodegenerative disease that involves the degeneration and death of motor neurons in the brain and spinal cord. Neuronal death and gross volume loss has also been reported in the hypothalamus in ALS (Gorges et al., 2017) (Gabery et al., 2021) (Christidi et al., 2019). To measure such changes, methods for *in vivo* MRI segmentation of the hypothalamus and fornix include deep learning (Billot et al., 2020), seed growing techniques (Wolff et al., 2018), and manual segmentation (Gorges et al., 2017). There is a need to develop and distribute open-source atlases of these structures for more accurate and standardised segmentation. Here, we present the Open-Source Hypothalamic-ForniX (OSHy-X) atlases and tool for multi-atlas fusion segmentation for 3T and 7T. OSHy-X is an atlas repository and containerised `Python` script that automatically segments the hypothalamus and fornix at 3T and 7T in both T1w and T2w scans.

Methodology

Atlas

Twenty atlases were derived from manual segmentation of the hypothalamus and fornix, conducted by two tracers familiar with the hypothalamus and fornix (Chang & Shaw, 2021). Ten non-neurodegenerative disease participants and ten patients with ALS were selected at random from within the larger datasets of the EATT4MND and 7TEA studies for the tracing. Details of the acquisition parameters are outlined in our atlas repository (Chang & Shaw, 2021).

Tool

A summary of the pipeline is illustrated in Figure 1. The user can specify the contrast (T1w/T2w) of the atlases used, the field strength (3T/7T) and any pre-processing steps. `OSHy-X` utilises Joint Label Fusion (`JLF`; Wang et al. (2013)) from Advanced Normalization Tools (`ANTs`; v2.3.1) for the registration (Avants et al., 2008) of atlases and segmentation of the target image. B1+ bias field inhomogeneity correction is performed using `MriResearchTools` (v0.5.2; Eckstein (2018)). Denoising and cropping are performed using ANTs in Python (`ANTsPy`; v0.2.0).
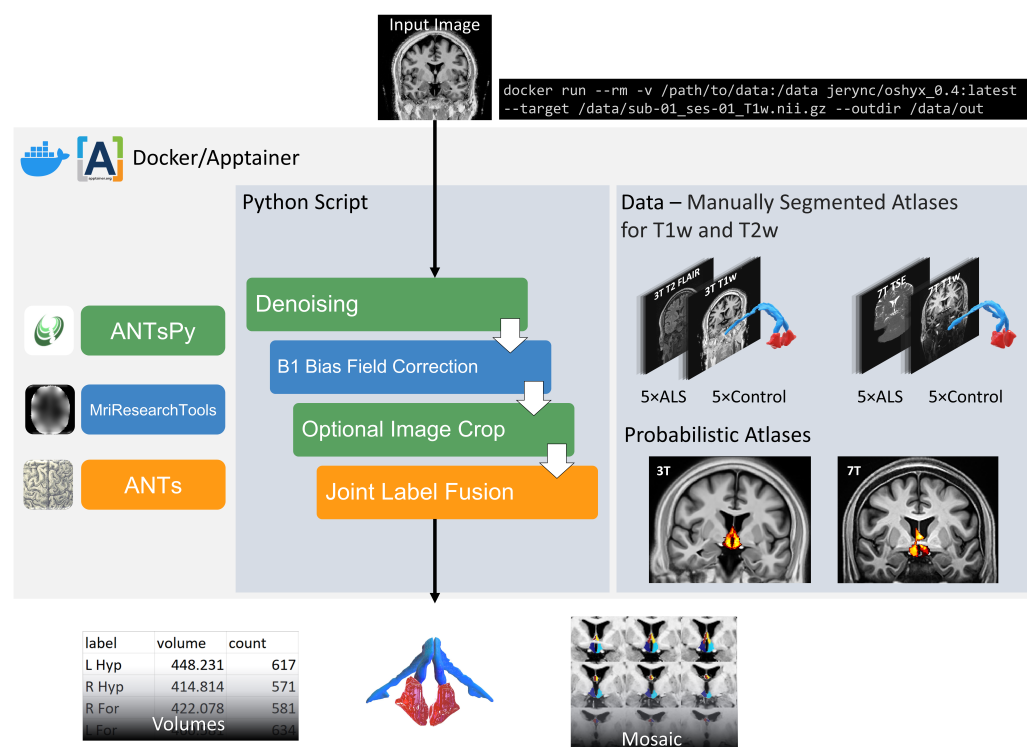

Figure 1: Pipeline overview of the OSHy-X segmentation tool. Users input a target image via an one-line command, and the pipeline produces hypothalamus and fornix labels, their volumes, and a mosaic visualisation of the segmentations. The pipeline and data are encapsulated within a Docker or Apptainer container.

Performance

[Figure 2](#) visually compares the differences in the segmentation of a representative non-neurodegenerative disease participant using manual segmentation and JLF using leave-one out cross validation. Overall, JLF tends to under-segment throughout the hypothalamus and fornix. To a lesser extent, JLF tends to over-segment the anterior and lateral hypothalamus and the body of the fornix.
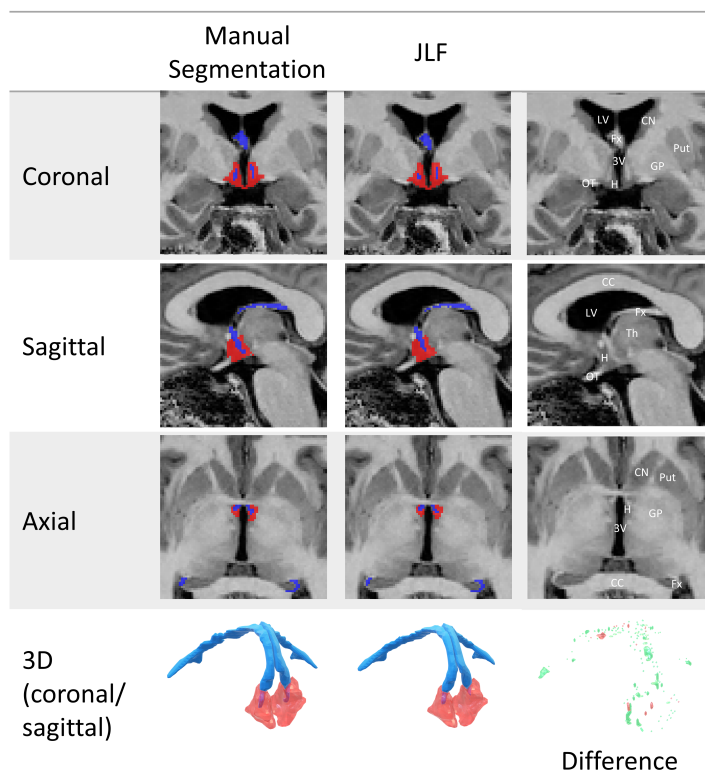

Figure 2: Visualisation of segmentation performance between manual segmentation and JLF. The hypothalamus is shown in red and the fornix in blue. The first three rows show segmentation in coronal, sagittal and axial planes; a 3D rendering of the structures is illustrated in the fourth row. The difference between JLF and manual segmentation illustrates over-segmented (red) and under-segmented (green) areas.

Dice overlaps ([Figure 3](#)) and ICC (Intraclass Correlation; 2-way fixed-rater mixed effects model with single measurement) between the two raters indicate excellent segmentation accuracy. The left and right hypothalamus received scores of 0.90 (0.66-0.98 CI) and 0.91 (0.68-0.98 CI). The left and right fornix received scores of 0.97 (0.87-0.99 CI) and 0.68 (0.13-0.91 CI).
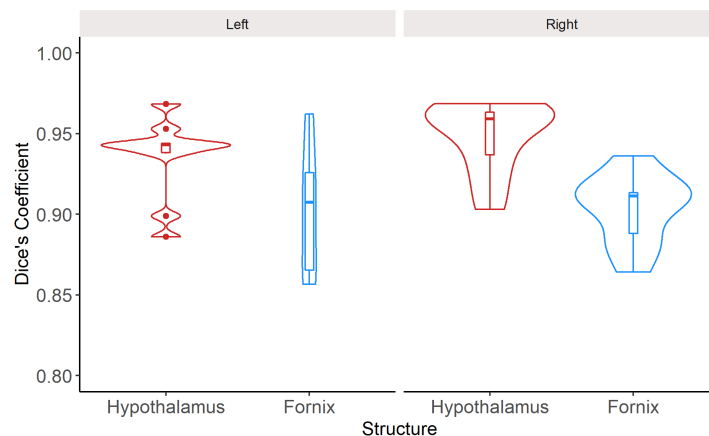
Figure 3: Dice overlaps between two raters for the left and right lobes of the hypothalamus and fornix. The median Dice's coefficient for the left and right hypothalamus is 0.94 (0.01 IQR) and 0.96 (0.03 IQR). The median Dice's coefficient for the left and right fornix are 0.91 (0.06 IQR) and 0.91 (0.03 IQR).

FreeSurfer (v7.2) also offers segmentation of both the hypothalamus (Billot et al., 2020) and fornix (Fischl et al., 2002); however, the segmentation of both structures is not performed by default using the popular `recon-all` command. Overall, we found that JLF has higher Dice overlaps with the manual segmentations at both 3T and 7T (Figure 4). Similarly, Dice overlaps for the fornix are significantly higher for JLF at both 3T and 7T (Figure 4). Additionally, we found that compared to cropped priors, whole-brain priors for JLF offers modest benefits to segmentation accuracy at 3T and 7T field strengths. While whole brain instead of cropped priors for JLF improves segmentation performance, computational time increases prohibitively.
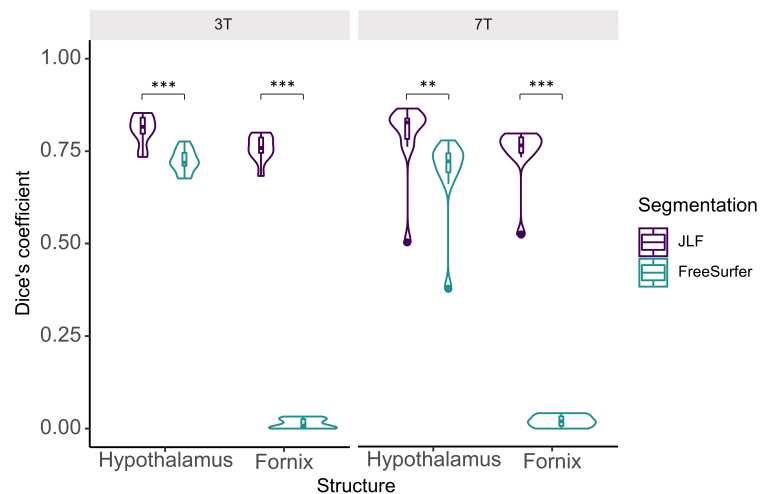

Figure 4: Dice overlaps with manual segmentations for JLF with whole-brain priors, and FreeSurfer segmentations. For hypothalamic segmentation, median Dice's coefficients at 3T and 7T for JLF: 0.82 (0.04 IQR) and 0.83 (0.06 IQR); Freesurfer: 0.72 (0.03 IQR) and 0.72 (0.05 IQR). For fornix segmentation, median Dice's coefficients at 3T and 7T for JLF: 0.76 (0.04) and 0.77 (0.04); FreeSurfer: 0.01 (0.03) and 0.02 (0.03). For both structures at both field strengths, JLF outperforms FreeSurfer (Wilcoxon rank sum test; ***p<0.0005 and **p<0.005).

Availability

The `OSHy-X` atlas is freely available at (https://osf.io/zge9t) and the tool is available via the `Neurodesk` data analysis environment (https://neurodesk.github.io) or as a `Docker`/`Apptainer` container (https://github.com/Cadaei-Yuvxvs/OSHy-X).

Acknowledgements

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