Development of a fully automated method for MRI volumetry in ataxia

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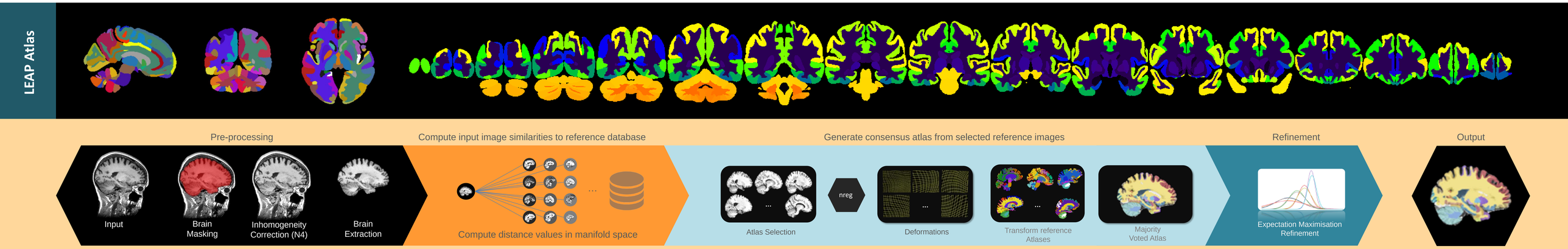
Automated measurement of brain volumes from MRI data can provide an efficient means to assess local brain neurodegeneration, supporting clinical decision making and clinical trial efficacy analysis as well as patient selection. As new therapies in different ataxias are entering clinical development, the development and validation of image analysis pipelines optimized for the specific brain regions affected can critically support trial design and analysis.

We have extended LEAP[1], a fully-automated brain segmentation pipeline, to integrate cerebellar sub-division. A reference database of >800 T1W images was generated by propagating a modified Neuromorphometrics[2] atlas from 15 ground truth segmentations and 19 fine-grain segmentations of the cerebellum provided by Diedrichsen et al[3] enabling automatic parcellation of the whole brain into 159 anatomical regions

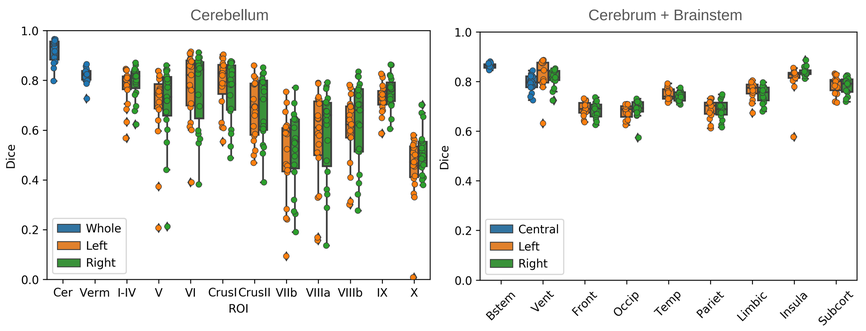
What is LEAP?

LEAP is a fully-automated brain segmentation pipeline employing machine learning and multi-atlas registration. Input T1W images are segmented into 159 anatomical regions where the input is compared against a reference database of previously segmented images. The most similar images are used in multi-atlas registration to generate a majority voted segmentation which is then refined using refinement with expectation maximisation (EM).



To assess the accuracy of segmentations generated by the modified LEAP pipeline, 19 T1 images with ground truth atlases for the cerebellum (provided by Diedrichsen et al[3]) and the 15 T1W images with the gold standard cerebral parcellations were segmented with LEAP.

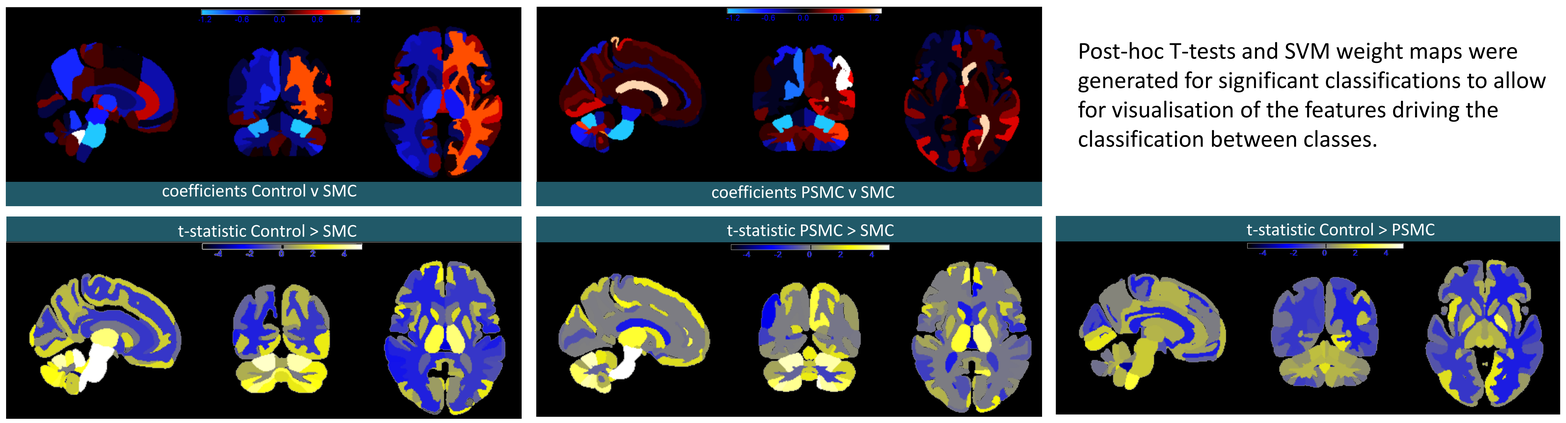
DICE scores were computed and show good agreement between LEAP and the "ground truth", with a mean dice of 0.96 for the overall cerebellum and an average overlap of 0.70+/-0.18 for individual regions. A mean DICE of 0.72 was reported for all cerebrum regions with 0.80 for cortical, 0.78 for sub-cortical, and 0.86 for brainstem areas.



1 - Ledig, C., et al., 2012, May. Multi-class brain segmentation using atlas propagation and EM-based refinement. IEEE ISBI, *2012 9th ISBI*, pp. 896-899.
2 - www.neuromorphometrics.com
3 - Diedrichsen, J. et al, 2011. Imaging the deep cerebellar nuclei: a probabilistic atlas and normalization procedure. *Neuroimage*, *54*(3), pp.1786-1794.

Comparison	Accuracy	Sensitivity	Specificity	F1 –score	p-value
Control v PSMC	64.1	79.17	40.00	0.46	0.129
Control v SMC	84.09	86.21	80.00	0.77	p < 0.005
PSCM v SMC	75.47	75.86	75.00	0.73	p < 0.005

For details of the clinical application see the presentation by Dr Jennifer Faber. Here, volumes were computed for 15 controls, 24 pre-symptomatic mutation carries (PSMC) and 29 symptomatic mutation carriers (SMC). Groups were compared with a linear SVM within a leave-one-out cross validation framework using all features.



Post-hoc T-tests and SVM weight maps were generated for significant classifications to allow for visualisation of the features driving the classification between classes.

A fully automated segmentation tool was developed to provide a sub-division of cerebellar brain regions and compared to gold-standard manual segmentations and validated for its clinical utility in analysis of SCA3 patients. Good agreement was obtained with manual segmentations and relevant clinical trends were measured, strengthening the hypothesis that automated MRI volumetry can support upcoming clinical trials in SCA3 and other forms of ataxia in patient selection and efficacy analysis.