

Reviewer Report

Title: High precision registration between zebrafish brain atlases using symmetric diffeomorphic normalization

Version: Revision 1 **Date:** 6/15/2017

Reviewer name: Carlos Castro-Gonzalez

Reviewer Comments to Author:

The authors have adequately addressed all my comments and I compliment them on the excellent quality of their work.

I specially appreciated the use of a unified evaluation criteria (MLDS on 6 brains), together with quantitative deformation metrics, which greatly adds robustness and clarity to the paper in my opinion. The flowcharts in Fig. 1, 3, 4 together with the before/after comparison in Additional Fig. 4 greatly help guide the reader. The updated reporting of statistical significance, variability across landmarks and datasets and N was also greatly improved.

I include some minor comments/suggestions below,

- I expect this atlas to become a reference in the scientific community. It is likely that other researchers will try to register their own datasets to the resource following the same methodology. Apart from sharing the individual brain scans and reference brain in "Availability of Supporting Data", would it be possible to share as well the coordinates of the different landmark points and cells used for evaluation? (Additional Figures 1-3) This will allow to easily evaluate the precision of future registered datasets (and perhaps alternative methods) to the results reported in this paper
- Fig. 1b, replace y label "Hausdorff distance" by "Hausdorff distance (um)"
- Fig. 2a, typo on the y label: "Mean Landmark Distance (ANTS)"

Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Yes

Conclusions

Are the conclusions adequately supported by the data shown? Yes

Reporting Standards

Does the manuscript adhere to the journal's guidelines on [minimum standards of reporting?](#) YesChoose an item.

Statistics

Are you able to assess all statistics in the manuscript, including the appropriateness of statistical tests used? Yes, and I have assessed the statistics in my report.

Quality of Written English

Please indicate the quality of language in the manuscript: Acceptable

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