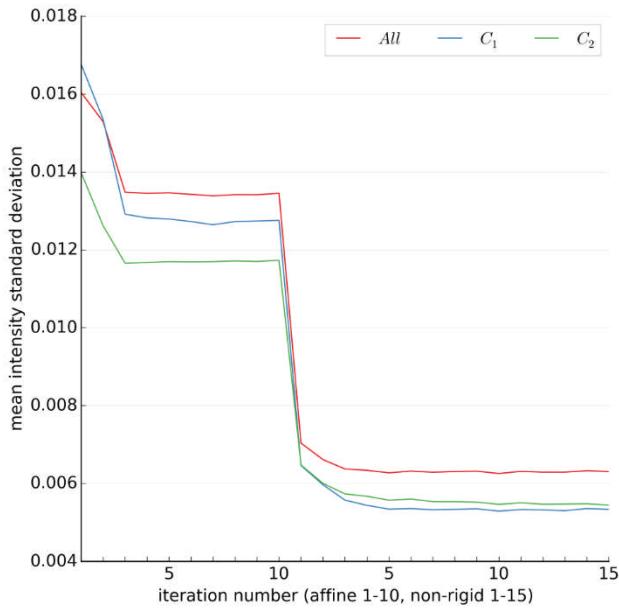


1 **S1. Group-wise registration assessment**

2 We quantified the progressive improvement in image alignment at each iteration of group-wise
3 registration (GWR), and justified the number of iterations, by measuring the intensity standard
4 deviation σ_I between resampled images at every voxel within the brain. Inter-image intensities in
5 equivalent aligned regions should have low standard deviation, thanks to standardisation prior to
6 GWR. Fig A shows the mean σ_I over all voxels, at each iteration, within the brain mask, for all brains,
7 and for C_1 and C_2 . After a dramatic decrease with the first iteration of NRR, σ_I reaches a plateau after
8 5-10 iterations.

9 We sought to assess whether the difference in SNR and CNR between cohorts affected the precision
10 of spatial alignment. We resampled each binarised brain mask into the final GWR average space. For
11 each resampled mask, we computed the Jaccard index with every other resampled mask in the cohort,
12 and calculated their mean and standard deviation. We compared cohorts' mean Jaccard indices with
13 a t-test. There was no appreciable difference ($p>0.9$; Cohen's $d = 0.0065$): GWR performed similarly in
14 aligning brain masks from each cohort.

15 We also used the per-voxel standard deviation to compare cohorts' alignment (Fig A). Deviation in
16 voxel intensities should arise from alignment offset, natural variations in local tissue intensity, and
17 noise. Fig A illustrates that after NRR, C_1 and C_2 had similar mean standard deviations, over the whole
18 brain.



19

20 Fig A: **Group-wise registration assessment:** Mean standard deviation of brain voxels in resampled
21 images, within the brain mask, for all brains and each cohort individually.