Introduction

Clinical research evaluating changes in neuroanatomical structure volume typically utilize linear registration methods to obtain group statistics. The extent to which these methods alter a structure’s orientation, size, and/or shape is unknown.

Neuroanatomical structure measurements can be acquired in different ways:
1) in natively acquired space
2) to 6 degrees of freedom (linear transformation in x,y,z directions),
3) to 9 degrees of freedom (linear transformation and stretching in x,y,z directions), or
4) to 12 degrees of freedom (linear transformation, stretching, and shearing in x,y,z directions. Figure 1).

Figure 1.

Methods

Participants: 40 Parkinson’s disease (PD) (67.80 ± 5.44) and 40 age matched controls (68.18 ± 4.64) completed a 3T brain MRI that included volumetric measurements and neuropsychological tests.

Native Image Registration. FLIRT, a linear image registration tool, was used to register all brains in each sample into 6, 9, and 12 degree space.

Caudate Nucleus Measurement: An expert rater, using ITK-SNAP (Yushkevich et al., 2006; www.itksnap.org), segmented the caudate nuclei in native space and in all registration spaces (i.e. 6, 9, 12 DOF). Figure 2.

Aims

Aim 1. Examine VOLUME differences by transformation
- Six DOF transformation alters an image in space and the 9 and 12 DOF techniques stretch and shear the image (i.e., warping it).
- We expected 9 and 12 techniques to alter volumetric measurement, whereas the 6 DOF registration technique would result in little or no change as compared to native space.
- We expected PD to have less caudate volume relative to control participants.

Aim 2. Examine differences in volume patterns relative to caudate-behavioral patterns
- Due to known involvement in processing speed and inhibitory functions, we expected increasing volumes to negatively associate with processing speed and positively with better inhibitory functioning (Trail Making Test, Part B).
- We expected strong associations between greater volume and better motor performance.
- We did not expect a strong association to a confrontation naming measure; used as a dissociation variable.

Results

Caudate Nucleus Volumes by Group.

- A bivariate correlation examined associations between processing speed and trail making test while controlling for motor severity as measured by the UPDRS.
- For neuroanatomical-cognitive associations, Fisher’s r-to-z transformation (Fling, Rosenholtz & Rubin, 1996) assessed for statistical differences in native versus 12DOF registration coefficients.

Conclusions

- Volumes were statistically similar for the native and 6 DOF transformed caudate nuclei and similar for the 9 and 12 DOF transformations.
- Transformation approaches alter volumetric and cognitive associations.
- Expected cognitive associations were revealed only with the 9 and 12 DOF transformations.
- On average, the 9 and 12 DOF transformed volumes explained 10.2% of the variance in PSI and 9% of the variance in UPDRS motor score compared to 3.2% and 2% variance explained of the native and 6 DOF volumes.
- It is essential that researchers examine a neuroanatomical structure of interest as a proportion to intracranial volume.
- Only after controlling for total intracranial volume did the native and 6 DOF transformed volumes represent the appropriate volume pattern (i.e., PD < Controls).  
- The inconsistent use of transformations between investigations may account for differences in the results of studies examining brain-behavior relationships.
- It is vital for researchers to communicate effectively and routinely report template registration degree and whether the presented structure volumes were acquired in a specific registration space or from natively acquired scans.

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Warning to Neuropsychologists Examining Structure-Function: Registration Matters

- Use caution when selecting a registration tool.
- Ensure the registration tool is appropriate to the study.
- Use a robust registration tool to minimize bias.
- Consider the impact of registration on the neuroanatomical structure.
- Report the registration method and its impact on the neuroanatomical structure.

Figure 1. Caudate Nucleus Measurement. An expert rater, using ITK-SNAP (Yushkevich et al., 2006; www.itksnap.org), segmented the caudate nuclei in native space and in all registration spaces (i.e. 6, 9, 12 DOF). Figure 2.

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