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# Motion and morphometry in clinical and nonclinical populations

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ABSTRACT

*Introduction:* The relationship between participant motion, demographic variables and MRI-derived morphometric estimates was investigated in autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), schizophrenia and healthy controls. Participant motion was estimated using resting state fMRI and used as a proxy measure for motion during T1w MRI acquired in the same session. Analyses were carried out in scans qualitatively assessed as free from motion-related artifact.

*Methods:* Whole brain T1-weighted MRI and resting state fMRI acquisitions from the ABIDE, ADHD-200 and COBRE databases were included in our analyses. Motion was estimated using coregistration of sequential resting state volumes. We investigated if motion is related to diagnosis, age and gender, and scanning site. We further determined if there is a relationship between participant motion and cortical thickness, contrast, and volumetric estimates.

*Results:* 2141 participants were included in our analyses. Participant motion was higher in all clinical groups compared with healthy controls. Younger (age < 20 years) and older (age > 40 years) people move more than individuals aged 20–40 years. Increased motion is associated with reduced average cortical thickness (−0.014 mm thickness per mm motion, $p = 0.0014$) and cortical contrast (0.77% contrast reduction per mm motion, $p = 2.16 \times 10^{-9}$) in scans that have been qualitatively assessed as free from motion artifact. Volumetric estimates were also associated with motion, however the relationships were generally weaker than cortical thickness and contrast and were dependent on the segmentation method used.

*Conclusions:* Participant motion is increased in clinical groups and is systematically associated with morphometric estimates. These findings indicate that accounting for participant motion may be important for improving the statistical validity of morphometric studies.



## Introduction

Movement artifact is a potential source of error for morphometric analysis of structural MRI. In this study we quantitatively assessed the relationship between participant motion during MRI acquisition and morphometric estimates in clinical populations, comprising autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD) and schizophrenia, and healthy controls. MRI data was obtained from the ABIDE, ADHD-200, COBRE databases respectively. Participant motion was estimated using resting state fMRI (rsfMRI) data acquired in the same session as the whole brain T1-weighted MRI acquisition. After determining the validity of rsfMRI-based motion as a proxy measure of motion during the structural MRI scan, we investigated if participant motion was related to diagnosis, participant age, gender and scanning site. We then investigated the effect of motion on many widely used morphometric estimates, including cortical thickness, contrast between white and cortical gray matter, voxel-based gray matter volume, and whole brain and subcortical volumes. In order to determine if a visual quality assurance rating can adequately control for motion effects, analyses were carried out on scans that had been qualitatively assessed as free from motion-related artifact.

If motion has a systematic effect on morphometric estimates, and also varies between subject groups, then participant motion may be a source of bias in morphometric brain analyses and a potential source of false positive findings. A recent prospective study in which participants were instructed to move during MRI acquisition demonstrated that participant motion is correlated with reduced cortical thickness and volume (Reuter et al., 2015). Our study extends this analysis to investigating participant movement in a 'natural' setting in which participants were not instructed to move, as well as investigating how motion varies between clinical and nonclinical groups and with demographic variables.

Motion was quantified using resting state fMRI (rsfMRI) that was acquired in the same session as the volumetric T1-weighted acquisitions that were used to obtain morphometric estimates. The rsfMRI-derived motion estimate was used as an explanatory variable in subsequent analyses of morphometric data. An assumption of our study is that individuals that move during the resting state fMRI also move during the T1-weighted MRI. In order to determine if this assumption is valid, we

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investigated if there is a relationship between the rsfMRI-based motion estimate and qualitative estimates of scan quality obtained by visual inspection of the T1-weighted MRI.

Specific hypotheses investigated in this study were:

1. Participant motion, estimated from resting state fMRI, will be related to qualitative estimates of scan quality of volumetric T1-weighted MRI.
2. Participant motion is related to diagnosis, age, gender and scanning site in ASD, ADHD, schizophrenia and healthy controls.
3. Participant motion is related to cortical thickness, contrast between cortical gray matter and underlying white matter, voxel-based estimates of gray matter volume, and whole brain and subcortical volumetric estimates.

## Methods

### *Participant and MRI acquisition details*

#### *Autism spectrum disorder (ASD)*

T1 weighted whole brain and resting state fMRI data of subjects with ASD and healthy controls from the Autism Brain Imaging Data Exchange (ABIDE) database were used for our analyses (Di Martino et al., 2013). Typical voxel resolutions for T1 weighted MRI were 1 mm isotropic or similar. Image acquisition parameters for both the whole brain T1 weighted acquisition and the resting state acquisition varied by site (see Table 1 in Kucharsky Hiess et al. (2015) for a summary of T1w image acquisition parameters for the ABIDE study). Scan time for rsfMRI varied from 3:32 s to 10 min. A summary of ABIDE rsfMRI acquisition parameters is provided as Supplementary material. Importantly, quality assurance (QA) protocols for image acquisition also varied by site. Nine sites stated that they did not remove scans that had motion or poor image quality, five sites stated that QA procedures were applied with a relative lack of information regarding the QA protocol, and three sites applied specific criteria for QA processing. Further information about the study can be found at the ABIDE website (http://fcon_1000.projects.nitrc.org/indi/abide/).

#### *Attention deficit hyperactivity disorder (ADHD)*

T1-weighted MRI and resting state fMRI data of subjects with ADHD and healthy controls from the ADHD-200 sample were used for this analysis (The ADHD-200 Consortium, 2012). Image acquisition parameters are provided as Supplementary material. T1 weighted whole brain MRI had voxel resolution of 1 mm isotropic for 5 sites, $1.3 \times 1 \times 1.3$ mm for two sites and $1 \times 1 \times 1.1$ mm for one site. Further information about the study, including diagnostic criteria, can be found at the ADHD-200 website (http://fcon_1000.projects.nitrc.org/indi/adhd200/). QA procedures for the ADHD-200 study were not explicitly provided to the best of our knowledge.

#### *Schizophrenia*

The COBRE dataset, comprising individuals with schizophrenia and healthy controls, was used for our analysis (http://fcon_1000.projects.nitrc.org/indi/retro/cobre.html). COBRE whole brain T1-weighted MRI was acquired on a 3T Siemens Trio scanner using a multi-echo MPRAGE acquisition. Voxel resolution was 1 mm isotropic. Other acquisition parameters were: TE = 1.64, 3.5, 5.36, 7.22, 9.08 s, TR = 2530 ms, TI = 900 ms, flip angle = 7°. Recruitment information and image acquisition parameters are found at the COBRE website.

No identifying information was provided with the MRI scans in accordance with HIPAA guidelines. Each institution's human subject research board established the criteria of informed consent. All available data from each study was used for our analyses.

### *Image processing*

Subject motion was estimated using two methods; (i) coregistration of sequential image volumes obtained during resting state fMRI acquisition, and (ii) qualitative assessment of structural MRI quality by a reviewer blind to participant demographic and phenotypic information (RKH).

#### *Motion assessment using rsfMRI*

The primary rsfMRI-based participant motion estimate used in our study was the average Root Mean Square (RMS) estimate obtained using the software tools *MCFLIRT* and *rmsdiff* provided as part of the FSL neuroimaging analysis software package (Jenkinson et al., 2002). *MCFLIRT* was used to estimate linear registrations between successive rsfMRI volumes. The transformation matrix describing the transformation between subsequent volumes was used as input to the *rmsdiff* program. The program *rmsdiff* calculates the root mean square deviation of rigid body alignment of successive image volumes obtained during an rsfMRI acquisition. It therefore provides a composite estimate (in mm) of both translation and rotation needed to align the two volumes. Rotations, which would typically be measured in radians or degrees, are converted to distance measures using an analytic formula that is applied over a sphere with a radius of 80 mm. After calculating the root mean square deviation for each sequential pair of images within the rsfMRI acquisition, these values were averaged to obtain an estimate of subject motion during the scan.

#### *Qualitative assessment of structural MRI*

Qualitative assessment of T1-weighted volumetric image quality was determined by a single reviewer for the ABIDE, ADHD-200 and COBRE datasets (RKH). T1 weighted images were rated on a scale between 1 and 5, with 1 indicating the lowest quality images with severe motion artifact, and 5 indicating images with no detectable motion artifact. Example images for each category, and more detailed explanations of criteria for assigning each rating are provided as Supplementary material.

The quantitative rsfMRI motion estimates (mm), and qualitative structural MRI assessments (rating 1–5) were compared using a linear model with the qualitative assessment as the explanatory ordinal variable and the quantitative assessment as the response variable.

#### *The relationship between motion, diagnosis and demographic parameters*

The relationship between quantitative rsfMRI-derived motion estimates and diagnosis, age, gender and site was investigated using a general linear model, with participant motion as the response variable and diagnosis, age, gender and site as explanatory variables. Statistical analyses were carried out for each study (ABIDE, ADHD-200, COBRE) independently. For the purposes of visualization of the relative magnitude of the effects of diagnosis, age and gender across clinical populations, figures will be presented with combined data from the three subject groups. For visualization of the relationship between participant motion and age, the function *stat_smooth* provided with the R package ggplot2 was used (Wickham, 2009).

#### *Morphometric measurements*

Morphometric estimates investigated in our analysis included cortical thickness, contrast between the cortical sheet and underlying white matter, voxel-based assessment of gray matter volume using voxel-based morphometry, and subcortical volume estimates. Cortical thickness was measured using two methods, Freesurfer (Fischl and Dale, 2000) and Advanced Normalization Tools (ANTs, (Tustison et al., 2014; Das et al., 2009)). Brain volumes, including measures of total brain volume and subcortical brain volume estimates were obtained using Freesurfer (Fischl et al., 2002) and FSL software packages Brain Extraction Tool (BET, (Smith, 2002)), FMRIB's Automated Segmentation Tool (FAST, (Zhang et al., 2001)). Average whole brain cortical thickness