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Assessment and Prevention of Head Motion During Imaging of Patients with Attention Deficit Hyperactivity Disorder

Jeffery N. Epstein^a, B.J. Casey^b, Simon T. Tonev^c, Matthew Davidson^b, Allan L. Reiss^d, Amy Garrett^d, Stephen P. Hinshaw^e, Laurence L. Greenhill^f, Alan Vitolo^e, Lisa A. Kotler^f, Matthew A. Jarrett^c, and Julie Spicer^b

*a*Department of Pediatrics, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, ML 10006, Cincinnati, OH 45229. Phone: (513) 636-8296, Fax: (513) 636-0755, Email: jeff.epstein@cchmc.org.

*b*Sackler Institute and Neuroscience Program, Weill Medical College of Cornell University, New York, NY

*c*Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC

*d*Department of Psychiatry, Stanford University Medical Center, Palo Alto, CA

*e*Department of Psychology, University of California, Berkeley, CA

*f*Division of Child Psychiatry, Columbia University Medical Center/New York State Psychiatric Institute, New York, NY

Abstract

The present study serves to detail the specific procedures for a mock scanner protocol, report on its use in the context of a multi-site study, and make suggestions for improving such protocols based on data acquired during study scanning. Specifically, a mock scanner compliance training protocol was used in a functional imaging study with a group of adolescents and adults with Attention Deficit Hyperactivity Disorder (ADHD) and a matched sample of healthy children and adults. Head motion was measured during mock and actual scanning. Participants across groups exhibited excess motion (>2 mm) on 43% of runs during the mock scanner. During actual scanning, excessive motion was limited to 10% of runs. There was clear task-correlated head motion during a go/no-go task that occurred even after the compliance training: Participants had a tendency to respond with increased head motion immediately after committing an error. This study illustrates the need to (1) report data attrition due to head motion, (2) assess task-related motion, and (3) consider mock scanner training in functional imaging protocols.

Keywords

ADHD; motion; mock scanner

1. Introduction

Functional magnetic resonance imaging (fMRI) is a non-invasive technique that provides researchers and clinicians with information about brain function by mapping activation within the brain. A significant obstacle in implementing this technology is head motion. Slight head motion can produce artifactual patterns of brain activity or can sufficiently increase noise in the data so that activity cannot be accurately mapped (Friston et al., 1996; Hajnal et al., 1994).

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Head motion is often exacerbated in studies of special populations such as children or clinically disordered patients. One patient group that appears particularly prone to head motion is the diagnostic category of attention-deficit/hyperactivity disorder (ADHD).

Most imaging studies conducted with children with ADHD have not reported on movement, and only one study has reported on attrition related to motion (Durstun et al., 2003). In this one study, rates of data loss for this relatively young sample of children (6 years and older) were 50% among the ADHD group and 30% for the normal control group, suggesting the potential magnitude of motion problems for imaging ADHD patients, particularly in young children with the disorder.

Excessive head motion among patients with ADHD poses several methodological and analytical difficulties in the context of fMRI studies. First, excessive head motion can potentially lead to loss of data. Imaging data are often excluded from analyses if head motion exceeds certain thresholds (e.g., less than half a voxel of movement). In addition to the expense involved, loss of data has the potential to skew final samples—i.e., those with valid data—toward less severe patients or those without hyperactivity (i.e., ADHD, Predominantly Inattentive Type).

Common solutions for dealing with head motion include the use of physical restraints (e.g., Green et al., 1994; Menon et al., 1997; Zeffiro, 1996) and/or motion correction algorithms (Woods et al., 1992). Physical restraints can cause subject discomfort, and motion correction algorithms cannot correct motion beyond certain thresholds (Field et al., 2000) sometimes leaving residual motion-related artifact (Friston et al., 1996) and spurious brain activations (Freire & Mangin, 2001).

Given the limitations of physical restraints and motion correction algorithms, compliance training protocols using a mock scanner have been developed to teach subjects to reduce motion prior to actual scanning (Seto et al., 2001; Slifer et al., 1993; Slifer et al., 2002). Mock scanners provide an environment similar to the actual scanning environment. The literature describes several behavioral protocols using operant techniques that reinforce lack of motion while in the mock scanner (Slifer et al., 1993; Slifer et al., 2002) but direct benefits of such protocols with regard to motion in the actual scanner have not been reported.

The current study describes a mock scanner compliance training protocol for minimizing head motion in a cohort of individuals with a current diagnosis of ADHD. In order to determine the success of the mock scanner protocol, motion in the actual scanner is examined. Several indicators (e.g., diagnosis, age, anxiety level, and behavioral performance) are used to assess predictors of motion during scanning.

2. Methods

2.1 Subjects

The participants for this study were parent-child dyads with ADHD and matched control parent-child dyads (Epstein et al., submitted for publication). Selected dyads, recruited from the Multimodal Treatment Study of Children with ADHD (MTA) subject pool, consisted of 12 parents (8 females, 9 right-handed; mean age = 47.8, sd = 8.0, 1 African-American, 1 Asian, 9 Caucasians, 1 Hispanic) and their 12 adolescent offspring (3 females, all 12 right-handed; mean age = 16.9, sd = 1.2, 1 African-American, 9 Caucasians, 1 Hispanic, 1 mixed-race) and comprised the ADHD sample for the present study. Children were recruited from three of the MTA study sites.

At the time of entry into the present study, a Diagnostic Interview Schedule for Children (DISC-P 4.0) was administered. Children were required to meet DSM-IV ADHD diagnostic criteria based on the parent-report of the current DISC included in the study. Biological parents were interviewed to determine if they met DSM-IV ADHD criteria using the Conners Adult ADHD Diagnostic Interview for DSM-IV (CAADID; Epstein et al., 2001). Only biological parents meeting DSM-IV ADHD criteria were included in the study. All youths and parents were required to meet criteria for one of the DSM-IV ADHD subtypes: Predominantly Inattentive (4 youths, 6 parents), Predominantly Hyperactive-Impulsive (2 youths, 1 parent), or Combined Type (5 youths, 5 parents).¹

An age- and gender-matched sample of 11 healthy control dyads was recruited from a Local Normative Comparison Group (LNCG) that was part of the MTA study. LNCG children were living in the same communities and attending the same schools as the MTA children to match the MTA sample in terms of grade, sex, and ethnicity and had to have fewer than 3 ADHD symptoms within each DSM-IV ADHD symptom domain as assessed by the DISC parent report. In addition, a LNCG parent matched on gender to the ADHD parent completed the CAADID and was required to have less than 3 symptoms in each DSM-IV ADHD symptom domain in order to be included. One adult normal control subject was unable to complete the scanning protocol due to having a tattoo above the neckline which is a potential safety issue. The remaining 10 normal control parents (8 females, all 10 right-handed; mean age = 46.9, sd = 3.7, 8 Caucasians, 1 Hispanic, 1 other) and 11 normal control youths (2 females, 9 right-handed; mean age = 17.6, sd = 1.2, 8 Caucasians, 2 Hispanics, 1 other) comprised the normal comparison sample.

2.2 Mock Scanner Protocol

Although there was some variation in apparatuses across the three scanning sites, the mock scanners were designed to resemble a real scanner. The mock scanners were equipped with a manually- or mechanically-operated patient table with a mock head coil to enable the participant to be moved in and out of the bore. Audio recordings of scanner noise were played to the participants through speakers while in the mock scanner.

Participants were told that they were participating in the mock scanner protocol in order to acclimate them to the scanner environment and to ensure that they understood the importance of minimizing head motion in the scanner. Across the scanning sites, head motion was measured either electromagnetically using a magnetic tracking system (Polhemus Fastrak®, Colchester, VT) or mechanically using a potentiometer (custom in-house system). For both methods, motion tracking sensors were applied to the forehead of each participant before entering the mock scanner.

When the equipment was fitted, the participant lay down on the patient table and slid his/her head into the head coil. Vacuum packing or foam padding or plastic “reminder” clamps were used in the head coil to reduce the amount of in-plane motion. The patient table was then moved into the bore in preparation for the first task. A video display was situated behind (or directly above) the participant’s head.

The researcher instructed participants to watch a movie for five minutes, during which head motion data were collected. Head motion was continuously sampled and cumulative head motion was computed from the start of each task. If cumulative head motion in the x, y, or z plane exceeded 2mm, the video immediately paused indicating to the participant that they were moving too much. Head motion would be re-zeroed and a new run of cumulative head motion

¹One of the children with ADHD did not meet full diagnostic symptom criteria for ADHD. The child had 4 Inattentive symptoms and 0 Hyperactive/Impulsive symptoms.

was sampled. If there were more than six of these above-threshold movements within the five-minute span, the task was repeated. This operant feedback during the mock scanning was based upon the prior work of Slifer and colleagues (Slifer et al., 1993; Slifer et al., 2002).

If the participant made six or fewer ($>2\text{mm}$) head movements, he or she moved on to the next task. This task was the same as the first, except that its purpose was to determine whether the first training task was effective. As such, participants' head motion was measured, but no feedback was provided; the video played irrespective of the magnitude of the participants' head motion.

As a final task in the mock scanner, participants practiced minimizing head movements while performing a simple cognitive task similar to the one that they would encounter in the actual scanner. The task was adapted from a procedure used by Huettel, Mack, and McCarthy (2002) in which a circle or square was presented to the participant in the center of the display. Participants were given a two-button response box and instructed to press the left button if they saw a circle and the right button if they saw a square. In all, 180 shapes were presented at two-second intervals, resulting in a 6-minute task. Each $>2\text{mm}$ cumulative head movement was recorded during this interval.

2.3 Scanning Procedure

Prior to entering the scanner and after exiting the scanner, participants indicated their current level of anxiety using a Subjective Units of Distress Scale (SUDS), an analogue scale ranging from 0 (not anxious at all) to 100 (extremely anxious). Although SUDS are commonly used to assess anxiety in research studies (e.g., POTS Team, 2004), the reliability of this scale has not been established.

In the actual scanner, participants performed a go/no-go task. Participants were required to press the response button for each letter that appeared on the screen except for the letter X. The task consisted of five groups (runs) of 128 trials per run. Each run lasted 5 min, 30 sec. Each letter, approximately 1" in size, appeared for 500 ms with an inter-stimulus-interval of 2000 ms. The no-go stimulus (letter "X") occurred at random intervals throughout the run, on approximately 20% of all trials ($n=125$). Other letters (i.e., go stimuli) were randomly selected from the alphabet. Performance measures on the go/no-go task included mean hit reaction times, reaction time standard deviation, errors of omission, errors of commission, and d-prime. The functional images were collected in approximately 30 mins. Results describing between-group differences in behavioral performance and functional activation are reported elsewhere {Epstein et al., submitted for publication}.

2.4 Image Acquisition and Analysis

Subjects were scanned with General Electric 1.5 Tesla fMRI scanners (General Electrical Medical Systems, Milwaukee, Wisconsin) at facilities at Duke University Medical Center, Stanford University, and Weill Medical College of Cornell University. Functional data were collected with a spiral in-and-out sequence ($TR = 2500\text{ msec}$, $TE = 40\text{ msec}$, flip angle = 90° , $FOV = 200\text{ mm}$, 64×64 matrix). Each volume contained 33 oblique slices (3.2 mm thick with 1 mm skip) with an in-plane resolution of $3.125 \times 3.125\text{ mm}$ covering the entire brain.

2.5 Measurement of Motion

During the mock scanner protocol, motion was measured as the number of head movements that exceeded 2 mm. During actual scanning, a center of mass coordinate was estimated for all three dimensions for each functional volume collected. Given that these coordinates could be used to define a single point in three-dimensional space, motion per TR was calculated as the

distance between this point on one TR and the corresponding point on the previous TR. As such, the following equation was used to derive head motion (in mm) from TR $t-1$ to TR t :

$$\sqrt{(x_t - x_{t-1})^2 + (y_t - y_{t-1})^2 + (z_t - z_{t-1})^2}$$

where x , y , and z denote the center of mass coordinates in the x , y , and z dimensions, respectively.

To avoid inflation of overall motion estimates, between-run movement was accounted for by “resetting” motion estimates at the beginning of each run: There was no estimate of motion between the last TR of one run and the first TR of the next; rather, the first trial was always assigned a missing value. The 127 motion values for each run were calculated, totaling 635 values per subject. The mean of these values was calculated for each subject. The test-retest correlation among the LNCG youths and their parents for this motion variable was .79 ($p < .0001$), suggesting adequate reliability.

2.6 Statistical Analyses

Motion during the mock scanner training was compared across ADHD and normal groups using independent sample t -tests. Using an exclusion criterion of any motion greater than 2 mm (Krings et al., 2001), the percentage of excluded runs in both the mock scanner and actual scanner environments was computed and compared using a mixed model ANOVA with scan session (mock vs. actual) as a within-subjects variable and dyad member (parent vs. child) and group status (ADHD vs. LNCG) as between-subjects independent variables.

We were interested in head motion as it corresponds to different trial types (go trials, correct no-go trials, and incorrect no-go trials) as well the temporal properties of this motion. For each trial type, we specified epochs of 7 TRs, which included the three TRs preceding the target, the target TR itself, and the three TRs following the target. These TR-level motion data were analyzed with a 2 (Group: ADHD, control) $\times$ 2 (Dyad Member: Youth, Parent) $\times$ 3 (Trial Type: Go, Correct No-Go, Incorrect No-Go) $\times$ 7 (Epoch TR: $t-3$, $t-2$, $t-1$, t , $t+1$, $t+2$, $t+3$) ANOVA.

In order to determine whether motion during actual scanning could be predicted, correlations were calculated between motion and a variety of predictors including the behavioral variables and pre- and post- SUDS scores.

3. Results

3.1 Motion during the mock scanner protocol

Although both youths with ADHD (mean=5.0, sd=7.6) and parents with ADHD (mean=3.1, sd=3.7) had numerically higher mean levels of head movements during the mock scanner protocol than youths (mean=3.0, sd=4.1) and parents without ADHD (mean=1.4, sd=1.6), ADHD parent-normal parent and ADHD youth-normal comparison youth contrasts did not attain statistical significance (note the high SDs among youths and parents with ADHD; See Table 1).

Another method of examining mock scanner motion, comparable to the way motion is examined during actual scanning, is to assess the percentage of runs with motion exceeding 2mm—often set as a threshold for exclusion of data (Krings et al., 2001). Across all subjects, 42.5% of mock scanner runs would have been so excluded. Normal control parents had the least amount of runs meeting this criterion and youths with ADHD had the most runs. See Table 2.

3.2 Excluded runs due to motion during actual scanning

Of the 45 subjects (23 youths and 22 parents), five runs of functional imaging data were collected for each participant for a total of 225 runs of data. Of these, one run was unavailable for analysis in the present study due to a subject problem (i.e., the participant accidentally pressing a button indicating they needed immediate assistance). The remaining 224 runs were analyzed in the present study.

Data were excluded on a run by run basis based on excessive within- and between-run movement. Movement was judged to be excessive if cumulative motion exceeded 2 mm in any of the three in-plane dimensions (x, y, or z). Rotation was not used as a measure of movement. Using this criterion, 24 runs (10.7% of all runs) were excluded. Among the ADHD patients, 11/119 (9.2%) runs were excluded (7 runs for youths; 4 runs for parents), while 13/105 (12.3%) runs were excluded for the normal control patients (7 runs for youths; 6 runs for parents). See Table 2. The vast majority of excluded runs could be accounted for by motion in the z-direction only (83.3%) or the y- and z-direction together (8.3%). The remaining discarded runs were due to motion in the y-axis (8.3%).

3.3 Excluded run analysis

A mixed-model ANOVA was conducted with diagnostic group (ADHD vs. normal comparison), dyad member (parent vs. youth), and scanning session (mock vs. actual) as independent variables and percentage of excluded runs as the dependent variable. The only significant effect was a main effect of scanning session ($F(1,39)=29.48$, $P<.001$), signifying significantly fewer excluded runs during actual scanning vs. mock scanning across all subjects. No main or interaction effects were observed for the diagnostic group or dyad member variables (all P s $>.15$).

3.4 Random vs. task-correlated motion

The Group $\times$ Dyad $\times$ Trial Type $\times$ Epoch ANOVA analysis revealed a main effect of Trial Type ($F(2,80) = 4.91$, $P = 0.0097$), a main effect of Epoch TR ($F(6,240) = 5.82$, $P < 0.0001$), an Epoch TR $\times$ Dyad Member interaction ($F(6,240) = 4.00$, $P = 0.0008$), and a Trial Type $\times$ Epoch TR interaction ($F(12,480) = 5.83$, $P < 0.0001$). These effects were moderated by a Trial Type $\times$ Epoch TR $\times$ Dyad Member interaction ($F(12,480) = 3.32$, $P = 0.0001$), which is depicted in Figure 1. As the figure shows, this 3-way interaction reflects a relative increase, or “spike,” in head motion when subjects were making incorrect responses to no-go trials. In addition, this motion spike was broader in parents than in adolescents, extending to one TR following the target in the former, but not the latter case. Consistent with the excluded run analyses above, there was no main effect of diagnostic group.

3.5 Predicting motion

Simple correlations between actual scanner motion and behavioral variables (mean RT, SD RT, d' , errors of commission and omission) were performed separately for youths and parents. Correlations were also conducted between motion and both pre- and post- SUDS ratings. No significant correlations were observed (all P s $> .05$).

4. Discussion

Motion compliance training using a mock scanner protocol was used to minimize the motion of youths and adults who met diagnostic criteria for ADHD. Patients with ADHD and as well as normal comparison participants exhibited high levels of motion during the mock scanner training. Using a liberal criterion of run exclusion based on 2 mm of head movement during a run, approximately 42% of runs would have been excluded during mock scanner training across

participants. However, during actual scanning—which occurred after the mock scanner training—data loss due to motion was kept to approximately 10%. Although use of the mock scanner training was not evaluated experimentally, and although different tasks and different measurement techniques were used across mock and actual scanning, the decrease in movement observed between the mock scanner training session and actual scanning suggests that the training protocol may have decreased motion four-fold during actual scanning.

Comparing the rates of excluded runs due to motion in the present study to the previous ADHD imaging research studies is difficult because almost all of the imaging studies of ADHD patients to date have not reported attrition due to motion. The one study that did report data loss due to motion (Durstun et al., 2003) reported a high rate of such data loss (i.e., 50% of the ADHD patients), suggesting that the 10% rate of data loss in this study was minimal. The lower attrition rates in the current study may be due to the use of the mock scanner training protocol in this study. Another explanation for reduced data loss in the present study compared to Durston et al. may be the age of subjects, as Durston et al. included children as young as 6 years of age, whereas the youngest participants in the current study were 15 years of age.

Analyses of motion during scanning were quite interesting on several accounts. First, there were no differences in head motion between the patients with ADHD and the normal comparison participants even though clear differences were observed between these groups on a wide variety of other outcomes including behavioral performance and patterns of functional brain activation (Epstein et al., submitted for publication). Given the hyperactivity problems that define ADHD as a disorder, it is remarkable that between-group differences in motion were not observed. The lack of between-group differences in motion is also inconsistent with increased scanner-related motion among other patient populations (e.g., patients with schizophrenia and stroke patients, Bullmore et al., 1999; Seto et al., 2001). A possible explanation for the lack of differences is the high degree of inter-subject variability seen in the ADHD group on measures of mock scanner movements and motion during actual scanning. Patients with ADHD were widely variable in the amount of motion that they exhibited. Some moved comparably to normal controls while others were highly active. This high variability observed in the ADHD groups decreased power to detect between group differences. Another explanation may be that between-group differences were attenuated by the operant training. Patients with ADHD may have responded well and learned from the immediate contingent feedback during the mock scanner training.

Second, the form of the motion evidenced across the groups was not random. The participants, except for the ADHD youths, presented with a distinct pattern of task-correlated motion. Interestingly, the motion was specific to no-go trials on which the participant made an incorrect response. It seems that after making an incorrect response, the participant immediately moved his/her head primarily in the inferior-superior direction. Given the spike-like properties of this task-correlated motion, the risk of falsely inferring an error-linked BOLD activation response is greatly increased, particularly around grey-white matter borders and parenchyma-CSF borders. This finding points to the importance of using an event-related design that can independently examine the hemodynamic response function during incorrect no-go trials, so that these trials can either be removed or accounted for in the data analyses.

A third point of interest in our study is that, similar to Seto et al (2001), we found that the majority of motion during scanning was motion in the inferior-superior direction (i.e., z-direction) suggesting that the head restraint systems employed across sites were effective at reducing in-plane (i.e., right-left and anterior-posterior) head motion but ineffective at reducing inferior-superior head motion. Based on the design characteristics of the vacuum packs and cushions that were placed on the side of the participants' heads, the lack of in-plane motion is not surprising. Perhaps consideration should be given to placing additional restraints at the top

of the head and/or under the chin to reduce inferior-superior participant motion. Another implication pertains to selecting a scan plane. Because realignment algorithms have more difficulty coping with through-plane vs. in-plane motion (Cox, 1996), perhaps the scan plane should be set to coronal or sagittal so that inferior-superior motion becomes in-plane motion and can be corrected more easily through preprocessing. Additional research is needed to determine if the inferior-superior motion observed in this study is specific to tasks that promote error responses or generalize to a wider variety of imaging tasks.

Finally, the task-correlated motion present during scanning was not correlated with patient anxiety or overall behavioral performance. As stated above, it also was not correlated with ADHD status. This task-correlated motion artifact appears to be the normal response to making an error (e.g., a “whoops” phenomenon). The one variable that did predict this task-related motion was age. This effect was much larger among adults than youths irrespective of diagnostic status. It could be that adults were more conscientious of their performance or that they showed a more pronounced reaction, because of the lower frequency of errors made in adults (Epstein et al., submitted for publication).

The primary limitation is that the study was not designed to test the effectiveness of a mock scanner protocol to reduce motion relative to a control condition. The study design required all patients to receive the mock scanner protocol training. Hence, there is no control group to which we can compare the amount of lost data runs and objective motion related to the mock scanner protocol. The present study thus primarily serves to detail the specific protocol procedures for a mock scanner protocol, report on its use in the context of a multi-site study, and make suggestions for improving such mock scanner protocols based on data acquired during study scanning.

In summary, the present study suggests that (1) task-correlated motion is a universal problem and likely needs to be addressed even among healthy participant populations; (2) there is a need for standards in imaging research to report attrition due to movement, which has not been done consistently in the existing research; (3) when comparing brain activation across groups, it is important to test for differences in movement to ensure that motion is not causing artifactual activations; and (4) when possible, a mock scanner compliance training protocol prior to scanning should be considered in order to reduce motion during actual scanning. Reducing motion before scanning is likely to be the most effective technique for acquiring valid functional imaging data.

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Figure 1.

Graphical depiction of head motion occurring after the presentation of a no-go stimulus (time t) and an error response. Parents and children, irregardless of ADHD status, seem to demonstrate increased head motion immediately after making an error.

Table 1

Mock and actual scanner motion for youths and parents with and without ADHD

	ADHD	Normal Controls	T-test values
Youths	Mean (SD)	Mean (SD)	
Mock Scanner Motion	5.0 (7.6)	3.0 (4.1)	0.76
Actual Scanner Motion	0.10 (.06)	0.07 (.04)	1.50
Parents			
Mock Scanner Motion	3.1 (3.7)	1.4 (1.6)	1.38
Actual Scanner Motion	0.08 (.03)	0.07 (.04)	0.49

Note: Mock scanner motion measured as the number of head movements greater than 2 mm; Actual scanner motion measured as mean motion (in mm) per image acquisition (i.e., 2.5 secs)

Table 2

Percentage of runs with more than 2mm of motion during mock and actual scanning for youths and parents with and without ADHD

		ADHD	Normal Controls
	Youths		
Mock Scanner		51%	39%
Actual Scanner		12%	13%
	Parents		
Mock Scanner		41%	31%
Actual Scanner		7%	12%