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Assessment and quantification of head motion in neuropsychiatric functional imaging research as applied to schizophrenia

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Abstract

Differing degrees of head motion have long been recognized as a potential confound in functional neuroimaging studies comparing neuropsychiatric populations to healthy normal volunteers, and studies often cite excessive head motion as a possible reason for the different patterns of functional activation frequently observed between groups. We empirically tested the degree of head motion in 16 patients with chronic schizophrenia and 16, age- and education-matched controls during the acquisition of functional magnetic resonance imaging data. We examined the degree of motion across three different indices (total motion, relative motion, task-correlated motion) during a complex attentional task and the effect of entering the motion parameters as additional regressors in a general linear model analysis. Results indicate that individuals with schizophrenia did not exhibit more task-correlated or total motion compared with controls. Moreover, the residual error term from the general linear model analysis was similar for both groups of subjects. In conclusion, current results suggest that stable patients with schizophrenia are capable of controlling head motion compared with matched normal controls. However, a direct comparison of the motion parameters is an essential step for any quality assurance protocol to determine whether additional corrective techniques need to be implemented. (*JINS*, 2007, *13*, 839–845.)

Keywords: fMRI, Motion, Artifact, Neuropsychiatric, Schizophrenia, Quality assurance

INTRODUCTION

The use of functional neuroimaging techniques to investigate brain functioning in neuropsychiatric populations has exploded over the past decade. For example, several studies have now been published investigating functional differences between chronic patients with schizophrenia (SP) compared with healthy normal volunteers (HNV) on a variety of motor, sensory, and higher-order cognitive tasks. Although hyperactivation of brain regions has been reported (Callicott et al., 2000; Manoach et al., 2001; Quintana et al., 2001), recent meta-analyses suggest that the most consistent finding is hypoactivation, or increased variability, in frontal and temporal lobes for SP compared with HNV (Davidson & Heinrichs, 2003; Glahn et al., 2005). Although the exact mechanism or mechanisms producing the hypoactivation in SP are still being debated (Callicott et al., 1998; Callicott & Weinberger, 1999, 2003; Davidson & Heinrichs, 2003; Gupta et al., 2004; Weinberger et al., 1996), possible explanations include disease-related neuronal pathology, neuronal pathology resulting from secondary disease characteristics, inefficient cognitive strategies, medication effects, and differences in behavioral performance.

However, the quality of the imaging data obtained from neuropsychiatric populations and HNV may be inherently different (Bullmore et al., 1999; Seto et al., 2001). Weinberger et al. (1996) were one of the first to recognize that increased head motion during the acquisition of functional data represented a major confound for investigating neuronal functioning in neuropsychiatric populations. Head motion

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is particularly problematic in functional magnetic resonance imaging (fMRI), where it has been shown to reduce inter- and intra-subject reliability (Lund et al., 2005) and increase signal variance (Bullmore et al., 1996, 1999; Friston et al., 1996; Hajnal et al., 1994), both of which will detrimentally impact on the statistical parametric maps in different brain region. Head motion can be either stimulus-correlated (i.e., time-locked with the task) or can occur independent of the task. Although prospective motion correction techniques (Speck et al., 2006) and externally monitored techniques with (Yang et al., 2005) and without (Tremblay et al., 2005) real-time feedback have recently been used to minimize head motion during data collection, retrospective motion correction algorithms are still widely used in neuropsychiatric functional imaging studies.

Retrospective motion correction techniques typically occur in two distinct steps, motion detection and the subsequent correction of this motion (Ardekani et al., 2001; Cox and Jesmanowicz, 1999; Friston et al., 1996). Most three-dimensional motion detection algorithms assume that (1) the basic contrast values between successive images remain relatively stable, (2) movements are relatively small compared with image resolution, and (3) motion can be modeled according to six rigid-body parameters corresponding to the three possible rotations and translations that can occur around the principal axes of Cartesian space (Ardekani et al., 2001; Oakes et al., 2005). In the detection phase, an image of interest (i.e., to be corrected image) is compared with a reference or base image, which typically corresponds to an image that was acquired near the beginning of the experiment following the establishment of T1 equilibrium. Specifically, a cost function, which is posited to be an index of spatial displacement, is calculated between the image of interest and the reference image. An iterative optimization algorithm (typically a least-squares fit) is then implemented to minimize the cost function, thereby reducing the spatial displacement between the two images. During the correction phase, the image of interest is interpolated to a new spatial grid specified by the optimization solution, correcting for the differences in spatial displacement. For an excellent review of current fMRI motion correction programs, the interested reader is encouraged to consult Oakes et al., 2005.

To date, few studies have quantitatively examined the amount of head motion that occurs between SP and HNV. Early studies reported increased signal variance (i.e., poor data quality) or voxel instability in SP compared with HNV, which was partially attributed to excessive head motion in the patient group (Callicott et al., 1998; Weinberger et al., 1996). However, this approach is problematic, because there are many other factors that effect signal variance other than head motion. Another study (Bullmore et al., 1999) reported that SP exhibited greater stimulus-correlated motion during a verbal fluency task, but the sample size in this study was relatively small ($n = 5$). In contrast, more recent studies (Kindermann et al., 2004; McDowell et al., 2002; Yoo et al., 2005) reported reduced motion, similar distributions, or no significant differences for SP compared with HNV, questioning the results of earlier studies. However, the majority of these recent studies did not examine stimulus-correlated and task-independent motion separately, both of which may have differential effects on functional activation. Task-independent, randomly distributed motion is likely to increase overall time-series variance, thereby reducing the magnitude or extent of functional clusters (Oakes et al., 2005). Stimulus-correlated motion may also reduce functional activation, but could also produce false positives in regions of high inherent signal contrast such as the ventricles or the sagittal sinus (Callicott & Weinberger, 1999; Hajnal et al., 1994).

The primary goal of the current study was to perform a systematic investigation of stimulus-correlated and -uncorrelated head motion in a group of SP and demographically matched HNV during a complex sensory–motor/attentional task, which was developed specifically for this study. We hypothesized that SP would exhibit greater motion compared with HNV and that the degree of motion would be greater during the task compared with baseline epochs. We also predicted that SP would exhibit increased signal variance (i.e., residual error) compared with HNV following a general linear model analysis in which motion parameters were entered as additional regressors. Although our sample was limited to SP, the methods used in the current experiment will readily generalize to other patient populations as part of a data quality-assurance protocol.

METHODS

Subjects

All SP subjects were diagnosed by an experienced clinician (J.C.) or team member with the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition Axis-I Disorders, Clinician Version (SCID-CV). Sixteen SP (15 men, 1 woman) and 16 HNV (14 men, 2 woman) participated in the current experiment. To reduce the likelihood of introducing a bias, no subjects were eliminated from the current study. HNV with a history of major medical conditions, neurological disease, major psychiatric disturbance, substance abuse, or psychoactive prescriptive medications were excluded from the current study. SP with a history of other neurological disease, history of psychiatric hospitalizations within the previous 6 months or history of substance abuse within the past year were excluded from the study. SP were also required to be stable on an atypical, antipsychotic medication (aripiprazole 4; ziprasidone: 1; risperidone: 5; quetiapine fumarate: 4; olanzapine: 2) for at least 3 months to be included in the current study. There were no significant differences ($p > .10$ on all t tests) between SP and HNV populations on age (SP, 40.2 ± 7.9; HNV, 39.8 ± 8.3), education (SP, 12.6 ± 2.3; HNV, 13.1 ± 1.3), or handedness (SP, 77.7 ± 54; HNV, 69.4 ± 64) as assessed by the Edinburgh Handedness Inven-

tory (Oldfield, 1971). Informed consent was obtained from subjects according to institutional guidelines at the University of New Mexico and the New Mexico Department of Veterans Affairs.

Task

In the current experiment, participants were requested to simultaneously tap their fingers on both hands to visual (flashing checkerboard; visual angle = 19.42 degrees × 14.88 degrees) and/or auditory (1000 Hz tone) stimuli presented over an 8-s period. A cue preceded the task and indicated whether participants should attend and tap their fingers to the presentation of the visual stimuli, auditory stimuli, or both. The auditory and visual stimuli were presented at the same or at different frequencies at (.5, 1, or 2 Hz) and, therefore, could occur in synchrony or out of phase, dependent on the conditions. Each 8-s block was followed by a baseline period in which a white, visual fixation cross (visual angle = 1.54 degrees) was presented in the center of a black background for 10 to 14 s.

To reduce head motion in the scanner, participants were required to practice the task twice outside of the scanner environment. During the first practice session, participants practiced the task until they were able to demonstrate basic task competency (approximately 5 min of practice). Participants were then instructed to repeat the practice session with the additional requirement of maintaining their head in a fixed position while responding with both hands to task stimuli. All participants were given extensive verbal feedback by one of the investigators on whether they were exhibiting head motion during the second practice session. Finally, participants were encouraged to minimize their movements as much as possible during the acquisition of fMRI data and were instructed that even small motions, such as swallowing, could negatively affect the quality of the data. The functional and behavioral results from this study will be presented in a separate publication.

MR Imaging and Statistical Analyses

High resolution T1-weighted and a gradient echo, echo-planar [echo time = 36 ms; flip angle = 90 degrees; field of view = 256 mm; matrix size = 64 × 64; TR = 2000 ms; 28 sagittal (5 mm) slices; bandwidth = 2442 Hz/pixel; 201 images per run; 6 runs] images were acquired on 1.5 Tesla Siemens Sonata scanner. Foam padding and a strip of tape across the subject's forehead were used to limit the amount of movement during the acquisition of functional data. Time series images were registered in three-dimensional space using the Analysis of Functional NeuroImages (AFNI) software package (Cox, 1996), which has excellent accuracy and efficiency in correcting for simulated motion compared with other freeware algorithms (Ardekani et al., 2001; Oakes et al., 2005). The AFNI motion correction algorithm performs a rigid-body, six-parameter fit based on the image realignment for both translations (units provided in millimeters) and rotations (units provided in degrees) around the three principal Cartesian axes (Cox & Jesmanowicz, 1999). The resulting parameters are estimates of image displacement and subsequent re-alignment to the base image rather than direct indices of head motion. All images from the six runs were registered to a reference image, which corresponded to the second image of the first run. The first image from each run was discarded following registration to establish T1 equilibrium and to eliminate movements that occurred between runs while EPI data were not being acquired. Therefore, movement was assessed over a total of 1200 images. No other postprocessing corrections (i.e., time slice acquisition correction, despiking) or spatial normalization (i.e., Talairach & Tournoux, 1988) procedures were performed on the data to minimize the possibility of increased variability due to interpolation in these steps.

Three separate indices were calculated to assess for differences in task-correlated and overall movement between the groups. First, an average of the total motion (Equation 1) across the entire experiment was calculated separately for each of the six motion parameters by individually summing the six absolute displacement estimates for each image compared with the reference image and then dividing by the total number of images ($n = 1200$).

$$P_{ave\_total} = \frac{1}{N}\sum_{n=1}^{N} |d_P(n)| \tag{1}$$

In Equation 1, d is the rotation and translation displacement estimates and P was equal to one of the six rotational (roll, pitch, and yaw) or translational (I–S, R–L, and A–P) motion parameters.

Second, we calculated an index corresponding to relative motion (Equation 2) by subtracting the displacement estimates from the previous image, summing the absolute difference displacement estimates and then dividing by the total number of images minus one separately for each motion parameter.

$$P_{ave\_relative} = \frac{1}{N-1}\sum_{n=2}^{N} |d_P(n) - d_P(n-1)| \tag{2}$$

This index was posited to represent a more accurate measurement of the motion at each image and to reduce the likelihood of a few large motions biasing the outcome of the results (Yoo et al., 2005). The motion coefficients from the relative motion index were then used to calculate a third index, which measured stimulus-correlated motion. For this calculation, the relative motion coefficients corresponding to images acquired during either the 8-s task or baseline epochs were averaged separately.

Previous research has also reported that the time-series variance is greater for SP compared with HNV (Callicott & Weinberger, 1999; Callicott et al., 2000; Weinberger et al., 1996). One method for accounting for signal variance due to uncorrected motion artifact is to enter the residuals from

the motion correction algorithm into the design matrix of a general linear model (Friston et al., 1996; Rowe & Passingham, 2001; Salek-haddadi et al., 2003). This method has been shown to substantially reduce both intrasubject and intersubject variance in both level 1 and level 2 analyses (Lund et al., 2005), and removing movement-related variance from a fMRI time series should theoretically improve the sensitivity of a test for activated voxels based on a standardized statistic (Bullmore et al., 1999; but see Johnstone et al., 2006). We, therefore, compared the normalized standard deviation from the residual error term across three separate voxel-wise multiple regressions analyses in which (1) only the experimental manipulations were entered as regressors, (2) the six parameters corresponding to total head motion were entered as additional regressors, and (3) the six parameters corresponding to relative head motion were entered as additional regressors. The standard deviation of the residual error term should theoretically be higher in either the population, or the model, where there is more variance (error-related) across the time-series. A mean residual error term was then generated for each of the three models by averaging the normalized standard deviation from the residual error term across all of the voxels within each participant's brain.

RESULTS

Two separate multivariate analyses of variance (MANOVAs) were performed to assess whether the average total or relative motion estimates for the six parameters differed across groups (see Figure 1). Neither the multivariate effects,

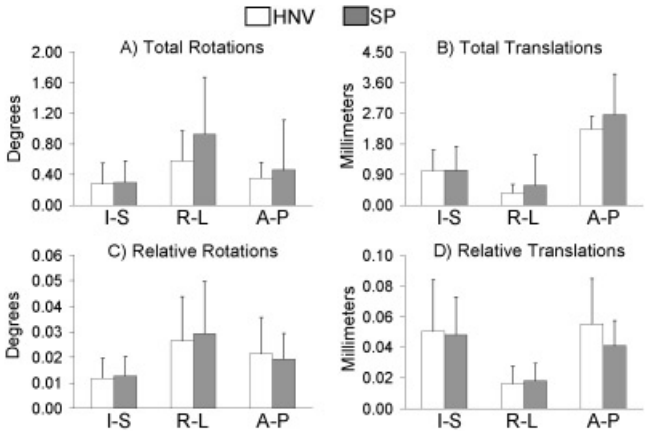

Fig. 1. Displayed are both the average total (A and B) and relative (C and D) motion per image over the course of the experiment for both patients with schizophrenia (SP: gray bars) and healthy normal volunteers (HNV: white bars) in the inferior–superior (I–S), right–left (R–L) and anterior–posterior (A–P) planes. A and C display the rotational displacement (degrees), and B and D display translational displacement (mm). Vertical bars display group means and error bars are equivalent to 1 *SD*. There were no significant differences or interaction effects found for either the average total or relative motion indices between the two groups.

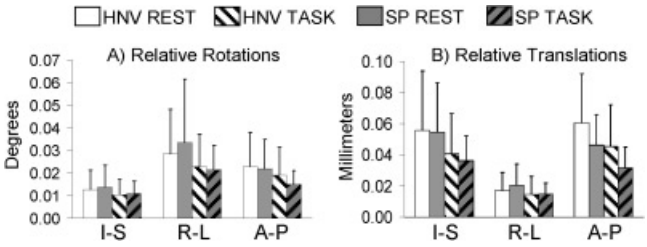

Fig. 2. Displayed are the average relative motion per image separately for the task (striped bars) and baseline (solid bars) periods. Group means for both schizophrenia patients (SP: gray bars) and healthy normal volunteers (HNV: white bars) are presented with error bars equivalent to 1 *SD*. Data are presented separately for the inferior–superior (I–S), right–left (R–L), and anterior–posterior (A–P) planes. There were no group differences in task-correlated motion or motion during the baseline period. However, both groups exhibited increased head motion during the baseline period.

nor the subsequent univariate tests for individual motion parameters, demonstrated a significant group effect (all p values $> .10$). The effect size for the average total motion parameters was medium (Cohen's $d = .62$), whereas, the effect size for the average relative motion parameters was small (Cohen's $d = .14$). We then collapsed across groups and performed six paired-samples t tests to examine axes-related differences in rotational and translational displacement for the relative motion estimates only. A Bonferroni correction value of .008 was adopted to reduce the likelihood of Type I error in these follow-up analyses. Results suggested that greater rotations occurred around the R-L (*mean* = .028 degrees) axis compared with both the A–P (*mean* = .020 degrees) axis ($t_{31} = 3.5$; $p < .001$) and the I–S (*mean* = .012 degrees) axis ($t_{31} = 6.9$; $p < .001$), and also for the A–P compared with the I–S ($t_{31} = 6.4$; $p < .001$) axis. Translational motion was greater along the I–S (*mean* = .049 mm) axis compared with the R–L axis ($t_{31} = 9.0$; $p < .001$) and along the A–P (*mean* = .048 mm) axis compared with the R–L (*mean* = .017 mm) axis ($t_{31} = 7.8$; $p < .001$).

A 2 × 2 [Group (SP *vs*. HNV) × Epoch (Task *vs*. Baseline)] repeated-measures MANOVA was then performed to evaluate the hypothesis that SP would exhibit more stimulus-correlated relative motion compared with HNV. Multivariate results (see Figure 2) demonstrated a significant effect for Epoch ($F_{6,25} = 10.6$; $p < .005$) but not for the group nor for the Group × Epoch terms (all p values $> .10$). Contrary to our hypothesis, subsequent univariate tests suggested that all movement parameters were actually greater during the baseline compared with the task period in both groups for all six motion parameters (all F values$_{1,30} \geq 6.7$, all p values $< .05$).

Finally, a 2 × 3 [Group (SP *vs*. HNV) × Model (Task Regressors, Task + Total Motion Regressors, and Task + Relative Motion Regressors)] mixed-model ANOVA was conducted to examine between group differences in the variation within the normalized residual error term when the

motion parameters were, and were not, entered as regressors in the general linear model. Results indicated a main effect for Model ($F_{2,60} = 89.4$; $p < .001$), but neither the main effect of Group (Cohen's $d = .10$) nor the interaction term was significant ($p > .10$). Follow-up t tests suggested that the residual error term was significantly reduced when either the total (*mean* = 2.79; $t_{31} = -10.6$; $p < .001$) or the relative (*mean* = 2.98; $t_{31} = -10.5$; $p < .001$) motion parameters were entered in addition to task regressors (*mean* = 3.06). Moreover, the total motion parameters reduced the residual error term more compared with the relative motion parameters ($t_{31} = 8.1$; $p < .001$).

DISCUSSION

The primary goal of the current experiment was to conduct a systematic empirical investigation on the prevalence of head motion in chronic SP compared with matched HNV during an fMRI study across three different indices, each of which represents a major concern for data quality assurance. Previous neuroimaging research has hypothesized that increased overall head motion may partially explain the increased variance (i.e., poor data quality), and subsequent decrease in functional activation, that is typically observed in SP compared with HNV (Bullmore et al., 1999; Callicott et al., 1998, 2000; Weinberger et al., 1996). Contrary to our hypotheses, SP neither exhibited greater overall head motion nor exhibited a tendency to move more during the task compared with baseline periods. Moreover, SP did not exhibit increased signal variance, as measured by the normalized standard deviation of the residual error term from a general linear model analysis, compared with HNV.

In the current experiment, there was no difference between SP and HNV on either measure (total and relative) of head motion within the scanner. For both groups, relative rotational motion was greatest around the R–L axis, second largest around the A–P axis, and the least around the I–S axis. In contrast, relative translational displacement was greater along the A–P and I–S compared with the R–L axis, but there was no difference in motion between the A–P and I–S axis. These findings are similar to a previous study examining motion artifact during a visual working memory task in which the largest rotational and smallest translational motion artifacts occurred around the R–L axis (Yoo et al., 2005). The reduced translational motion in the R–L axis may be the result of the additional foam padding or bars that are often placed along the sides of subjects' heads to reduce motion during scanning.

Contrary to our second hypothesis, there were no differences in stimulus-correlated motion between SP and HNV. Moreover, rotational and translational displacements were greater for both groups when participants passively viewed a fixation cross (i.e., baseline) compared with when they performed the sensory–motor task (stimulus-correlated motion artifact). The increase in motion during the baseline task may be a result of participants relaxing more following an extended period of concentration during the task. The lack of group differences in stimulus-correlated motion and the finding of increased motion during baseline are consistent with a recent working memory study (Yoo et al., 2005), but differ from previous results obtained during a verbal fluency task (Bullmore et al., 1999). There are several possible explanations for the discrepancies observed across these experiments, including the use of different paradigms that were more likely to increase head motion. For example, SP may be more prone to head movement during the covert generation of words (Bullmore et al., 1999) due to unconscious vocalizations compared with either a sensory–motor or working memory task (Yoo et al., 2005). Second, other sample characteristics, such as medication profile or disease chronicity, could have also influenced the results. SP in the current and working memory study (Yoo et al., 2005) were on atypical medications, whereas the medication profile was not discussed in the verbal fluency study. Head motion may be greater in patients on typical medications due to the increased likelihood of iatrogenic symptoms such as tardive dyskinesia (Eberhard et al., 2006). Finally, an extensive practice session was administered before the collection of fMRI data in both the current and working memory study (Yoo et al., 2005), which may have reduced head motion during the acquisition of fMRI data. Future neuropsychiatric imaging studies should investigate whether practicing the task and receiving specific feedback about movement before entering the scanning environment can help to reduce motion artifact during the acquisition of fMRI data.

In contrast to previous reports of increased variance across the time series for SP compared with HNV (Bullmore et al., 1999; Callicott et al., 1998, 2000; Weinberger et al., 1996), the variance within the residual error term from a general linear model analysis was not significantly different for SP and HNV. This finding may partially be due to the different methods used to calculate variance, as previous estimates were based on a pooled standard deviation measurement (Callicott et al., 1998) whereas we used the normalized standard deviation of the residual error term from the general linear model. In the current experiment, the variance within the residual error term was significantly reduced when the motion parameters were entered as regressors into the general linear model (Lund et al., 2005). The reduction in the residual error term was greatest when the motion parameters corresponding to total, rather than relative, motion across the course of the experiment were used in the regression. The total motion parameters correspond more closely with the actual experiment, which represents a history of accumulated errors due to motion rather than just representing motion that occurs across subsequent images.

In summary, current and previous results (Kindermann et al., 2004; McDowell et al., 2002; Yoo et al., 2005) question the assumption that differential degrees of head motion contribute to differences in activation or increased variability that are frequently observed in fMRI studies of schizophrenia (Bullmore et al., 1999; Callicott et al., 1998). Results also suggest that practicing the task with feedback about

head motion before the scanning session may also help to reduce head motion. Although these findings may not generalize to other studies given that differences in sample characteristics (i.e., medication profile, disease chronicity) and task requirements (i.e., mode of response, task difficulty) are likely to influence results, these quality assurance measurements should routinely be implemented in all studies until more sophisticated prospective motion correction techniques (Speck et al., 2006) are readily available. Specifically, a comparison of the three types of movement parameters from the different populations should routinely be performed for data quality assurances purposes followed by the consideration of alternative techniques such as slice-by-slice registration (Kim et al., 1999) or entering movement parameters as additional regressors of no interest (Johnstone et al., 2006) dependent on the outcome of the movement analyses. The implementation of these procedures should improve the accuracy of hemodynamic response measurement across different populations and increase the reliability of findings across different neuropsychiatric studies.

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REFERENCES

Ardekani, B.A., Bachman, A.H., & Helpern, J.A. (2001). A quantitative comparison of motion detection algorithms in fMRI. *Magnetic Resonance Imaging*, *19*, 959–963.

Bullmore, E.T., Brammer, M.J., Rabe-Hesketh, S., Curtis, V.A., Morris, R.G., Williams, S.C., Sharma, T., & McGuire, P.K. (1999). Methods for diagnosis and treatment of stimulus-correlated motion in generic brain activation studies using fMRI. *Human Brain Mapping*, *7*, 38–48.

Bullmore, E., Brammer, M., Williams, S.C., Rabe-Hesketh, S., Janot, N., David, A., Mellers, J., Howard, R., & Sham, P. (1996). Statistical methods of estimation and inference for functional MR image analysis. *Magnetic Resonance in Medicine*, *35*, 261–277.

Callicott, J.H., Bertolino, A., Mattay, V.S., Langheim, F.J., Duyn, J., Coppola, R., Goldberg, T.E., & Weinberger, D.R. (2000). Physiological dysfunction of the dorsolateral prefrontal cortex in schizophrenia revisited. *Cerebral Cortex*, *10*, 1078–1092.

Callicott, J.H., Ramsey, N.F., Tallent, K., Bertolino, A., Knable, M.B., Coppola, R., Goldberg, T., van Gelderen, P., Mattay, V.S., Frank, J.A., Moonen, C.T., & Weinberger, D.R. (1998). Functional magnetic resonance imaging brain mapping in psychiatry: Methodological issues illustrated in a study of working memory in schizophrenia. *Neuropsychopharmacology*, *18*, 186–196.

Callicott, J.H. & Weinberger, D.R. (1999). Neuropsychiatric dynamics: The study of mental illness using functional magnetic resonance imaging. *European Journal of Radiology*, *30*, 95–104.

Callicott, J.H. & Weinberger, D.R. (2003). Brain imaging as an approach to phenotype characterization for genetic studies of schizophrenia. *Methods in Molecular Medicine*, *77*, 227–247.

Cox, R.W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, an International Journal*, *29*, 162–173.

Cox, R.W. & Jesmanowicz, A. (1999). Real-time 3D image registration for functional MRI. *Magnetic Resonance in Medicine*, *42*, 1014–1018.

Davidson, L.L. & Heinrichs, R.W. (2003). Quantification of frontal and temporal lobe brain-imaging findings in schizophrenia: A meta-analysis. *Psychiatry Research*, *122*, 69–87.

Eberhard, J., Lindstrom, E., & Levander, S. (2006). Tardive dyskinesia and antipsychotics: A 5-year longitudinal study of frequency, correlates and course. *International Clinical Psychopharmacology*, *21*, 35–42.

Friston, K.J., Williams, S., Howard, R., Frackowiak, R.S., & Turner, R. (1996). Movement-related effects in fMRI time-series. *Magnetic Resonance in Medicine*, *35*, 346–355.

Glahn, D.C., Ragland, J.D., Abramoff, A., Barrett, J., Laird, A.R., Bearden, C.E., & Velligan, D.I. (2005). Beyond hypofrontality: A quantitative meta-analysis of functional neuroimaging studies of working memory in schizophrenia. *Human Brain Mapping*, *25*, 60–69.

Gupta, A., Elheis, M., & Pansari, K. (2004). Imaging in psychiatric illnesses. *International Journal of Clinical Practice*, *58*, 850–858.

Hajnal, J.V., Myers, R., Oatridge, A., Schwieso, J.E., Young, I.R., & Bydder, G.M. (1994). Artifacts due to stimulus correlated motion in functional imaging of the brain. *Magnetic Resonance in Medicine*, *31*, 283–291.

Johnstone, T., Ores Walsh, K.S., Greischar, L.L., Alexander, A.L., Fox, A.S., Davidson, R.J., & Oakes, T.R. (2006). Motion correction and the use of motion covariates in multiple-subject fMRI analysis. *Human Brain Mapping*, *27*, 779–788.

Kim, B., Boes, J.L., Bland, P.H., Chenevert, T.L., & Meyer, C.R. (1999). Motion correction in fMRI via registration of individual slices into an anatomical volume. *Magnetic Resonance in Medicine*, *41*, 964–972.

Kindermann, S.S., Brown, G.G., Zorrilla, L.E., Olsen, R.K., & Jeste, D.V. (2004). Spatial working memory among middle-aged and older patients with schizophrenia and volunteers using fMRI. *Schizophrenia Research*, *68*, 203–216.

Lund, T.E., Norgaard, M.D., Rostrup, E., Rowe, J.B., & Paulson, O.B. (2005). Motion or activity: Their role in intra- and inter-subject variation in fMRI. *Neuroimage*, *26*, 960–964.

Manoach, D.S., Halpern, E.F., Kramer, T.S., Chang, Y., Goff, D.C., Rauch, S.L., Kennedy, D.N., & Gollub, R.L. (2001). Test-retest reliability of a functional MRI working memory paradigm in normal and schizophrenic subjects. *The American Journal of Psychiatry*, *158*, 955–958.

McDowell, J.E., Brown, G.G., Paulus, M., Martinez, A., Stewart, S.E., Dubowitz, D.J., & Braff, D.L. (2002). Neural correlates of refixation saccades and antisaccades in normal and schizophrenia subjects. *Biological Psychiatry*, *51*, 216–223.

Oakes, T.R., Johnstone, T., Ores Walsh, K.S., Greischar, L.L., Alexander, A.L., Fox, A.S., & Davidson, R.J. (2005). Comparison of fMRI motion correction software tools. *Neuroimage*, *28*, 529–543.

Oldfield, R.C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Cognitive Neuropsychology*, *9*, 97–113.

Quintana, J., Davidson, T., Kovalik, E., Marder, S.R., & Mazziotta, J.C. (2001). A compensatory mirror cortical mechanism for facial affect processing in schizophrenia. *Neuropsychopharmacology*, *25*, 915–924.

Rowe, J.B. & Passingham, R.E. (2001). Working memory for location and time: Activity in prefrontal area 46 relates to selection rather than maintenance in memory. *Neuroimage*, *14*, 77–86.

Salek-haddadi, A., Lemieux, L., Merschhemke, M., Friston, K.J., Duncan, J.S., & Fish, D.R. (2003). Functional magnetic resonance imaging of human absence seizures. *Annals of Neurology*, *53*, 663–667.

Seto, E., Sela, G., McIlroy, W.E., Black, S.E., Staines, W.R., Bronskill, M.J., McIntosh, A.R., & Graham, S.J. (2001). Quantifying head motion associated with motor tasks used in fMRI. *Neuroimage*, *14*, 284–297.

Speck, O., Hennig, J., & Zaitsev, M. (2006). Prospective real-time slice-by-slice motion correction for fMRI in freely moving subjects. *Magnetic Resonance Materials in Physics, Biology and Medicine*, *19*, 55–61.

Talairach, J. & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain*. New York: Thieme.

Tremblay, M., Tam, F., & Graham, S.J. (2005). Retrospective coregistration of functional magnetic resonance imaging data using external monitoring. *Magnetic Resonance in Medicine*, *53*, 141–149.

Weinberger, D.R., Mattay, V., Callicott, J., Kotrla, K., Santha, A., van Gelderen, P., Duyn, J., Moonen, C., & Frank, J. (1996). fMRI applications in schizophrenia research. *Neuroimage*, *4*, S118–S126.

Yang, S., Ross, T.J., Zhang, Y., Stein, E.A., & Yang, Y. (2005). Head motion suppression using real-time feedback of motion information and its effects on task performance in fMRI. *Neuroimage*, *27*, 153–162.

Yoo, S.S., Choi, B.G., Juh, R., Pae, C.U., & Lee, C.U. (2005). Head motion analysis during cognitive fMRI examination: Application in patients with schizophrenia. *Neuroscience Research*, *53*, 84–90.