# Quantifying Head Motion Associated with Motor Tasks Used in fMRI

E. Seto,\*'<sup>†</sup> G. Sela,\*'<sup>†</sup> W. E. McIlroy,<sup>‡</sup>'§ S. E. Black,\*'<sup>1</sup>|| W. R. Staines,\*'§'|| M. J. Bronskill,\*'<sup>†</sup> A. R. McIntosh,<sup>‡</sup>'<sup>1</sup> and S. J. Graham<sup>\*,†'<sup>1</sup></sup>

\*Imaging/Bioengineering Research and ‡Centre for Studies in Aging, Sunnybrook & Women's College Health Sciences Centre; ||Rotman Research Institute, Baycrest Centre for Geriatric Care; and †Department of Medical Biophysics, §Graduate Department of Rehabilitation Therapy, ||Department of Medicine (Neurology), and <sup>§</sup>Department of Psychology, University of Toronto, Toronto, Ontario, Canada M4N 3M5

Received September 18, 2000

In functional magnetic resonance imaging (fMRI) studies, long experiment times and small intensity changes associated with brain activation frequently lead to image artifacts due to head motion. Methods to minimize and correct for head motion by restraint, fast imaging, and retrospective image registration are typically combined but do not completely solve the problem, particularly for specific patient populations. As an initial step toward optimizing future designs of head restraints and improving motion correction techniques, the head motion characteristics of groups of stroke subjects, age-matched controls, and young adults were investigated with the aid of an MR simulator and a highly accurate position tracking system. Position measurements were recorded during motor tasks involving either the hand or the foot. Head motion was strongly dependent on the subject group and less upon the task conditions based on ANOVA calculations (P < 0.05). The stroke subjects exhibited approximately twice the head motion compared to that of age-matched controls, and the latter's head motion was about twice that of young adults. Moreover, the range of head motion in stroke subjects over all tasks was approximately  $2 \pm 1$  mm, with the motion occurring predominantly as translation in the superior-inferior direction and pitch rotation (nodding). These results lead to several recommendations on the design of fMRI motor experiments and suggest that improved motion correction strategies are required to examine such patient populations comprehensively. © 2001 Academic Press

*Key Words:* fMRI; motion; simulator; position tracking; stroke recovery.

# **INTRODUCTION**

Functional magnetic resonance imaging (fMRI) has been shown to be a powerful tool in neuroscience research (Cohen and Bookheimer, 1994; Kim and Ugurbil, 1997; Le Bihan and Karni, 1995; Orrison et al., 1995). The technique is still comparatively new, however, and is not without methodological deficiencies that limit clinical applications. In particular, head motion is a frequent problem in fMRI due to long examination times (typically, multiple fMRI scans of several minutes within a session of approximately 1 h) and the small intensity changes from the BOLD effect (several percent; Gati et al., 1997). Head motion is detrimental to fMRI because it leads to false positive and false negative inference of neuronal activation (Bullmore et al., 1999; Friston et al., 1996; Hajnal et al., 1994). Motor tasks, a major avenue of research, compound the problem because the motion associated with the task (e.g., finger tapping) can translate to the head. Methods to minimize and correct for head motion using restraints (Fitzsimmons et al., 1997: Green et al., 1994: Ruttimann et al., 1995; Zeffiro, 1996), fast imaging (Glover and Lee, 1995; Nishimura et al., 1995; Yang et al., 1998), and retrospective image processing (Biswal and Hyde, 1997; Friston et al., 1996; Ostuni et al., 1997; Zeffiro, 1996) are currently used in combination, but do not always provide sufficient compensation. When this happens, fMRI data are inevitably discarded (Righini et al., 1996).

The little quantitative literature on head motion has been reported on healthy young adult volunteers, mainly in the context of PET (Green *et al.*, 1994; Ruttimann *et al.*, 1995; Zeffiro, 1996). Given the differences in the underlying imaging physics, as well as the temporal and spatial resolution between PET and fMRI, the requirements of head restraint are more stringent in the fMRI context and necessitate additional investigations. Furthermore, it is expected that many patient populations, particularly those with motor control difficulties, will exhibit greater head motion than that of young healthy adults. Although this is an obvious problem, it has been investigated quantitatively only in schizophrenics (Bullmore *et al.*, 1999) and



requires additional investigation in other patient populations. Such experiments could be a useful first step in designing new strategies for improving the clinical robustness of fMRI.

In this study, the head motion characteristics of subjects recovering from stroke are investigated, compared, and interpreted with respect to those of agematched controls and young healthy adults for the performance of simple motor tasks. These particular subject groups were chosen because understanding stroke recovery mechanisms (Cramer et al., 1997; Johansson, 2000; Weiller, 1998) and changes in brain function with normal aging (D'Esposito et al., 1999) are active areas of fMRI research. Furthermore, the hemiparesis commonly associated with stroke can make the performance of motor tasks involving the hand or foot (of particular interest for fMRI because of their large cortical representation in primary sensorimotor cortex and their important role in quality of life and functional independence) extremely difficult without the corecruitment of proximal muscles. These cocontractions suggest that the problem of head motion is likely to be significant in such patients.

The experimental component of this work includes measurement of head motions associated with two representative motor tasks involving hand gripping and ankle flexion. The resulting data are analyzed to test the hypothesis that statistically significant differences in motion are produced by these tasks in the three groups of subjects. As the primary focus of this paper involves providing initial estimates of typical head motions in the three groups, measurements were performed using a highly accurate position tracking system and an fMRI simulator. This apparatus offered several direct advantages over performing real fMRI: (a) motion data were acquired efficiently and rapidly, versus much more lengthy measurements and computer-intensive calculations utilized in fMRI studies; (b) motion data were highly accurate over a wide range of displacements and rotations, compared to the estimates provided by image coregistration algorithms used in fMRI (typically accurate only for subvoxel motions); and (c) population data were acquired without wasting valuable scanner time (from the standpoint of cost and availability). Furthermore, use of a simulator allows the large question of functional image interpretation in these populations to be deferred to future work. The heterogeneous presentation of motor deficits in stroke patients, as well as the multiple patterns of brain reorganization that characterize the recovery process, remain to be categorized in detail and compared with normal aging. The experiments described here, together with discussion of their methodological implications for actual fMRI studies, represent initial groundwork toward tackling this question.

### **METHODS**

### *Subjects*

Eight stroke subjects (three females and five males, average age 58 years, range 22–78 years) were recruited that represented the population of interest for fMRI motor recovery research. Selection criteria included intermediate hemiparesis measured by the Chedoke-McMaster Stroke Assessment (CM) (Gowland et al., 1993), used clinically on site, and the ability to lie reasonably still for several minutes. The CM has been validated against other diagnostic classification schemes, contains an comprehensive impairment inventory to determine the presence and severity of common physical impairments associated with stroke, and was originally designed to classify patients when planning and selecting interventions and evaluating their effectiveness (Gowland et al., 1993). As part of the CM, the hand and foot are evaluated on a seven-point scale corresponding to the seven stages of motor recovery, with a score of 1 indicating little or no motor control and a score of 7 indicating normal motor function. Based on the CM, two stroke patients were discarded: one that could not perform the necessary fMRI hand and foot motor tasks (score = 1, hand and foot) and one with full recovery (score = 7, hand and foot) whose ability to remain still would not be a particular concern. The remaining six subjects were investigated and had intermediate scores (hand, average score 3.0, range 2-5; foot, average score 3.7, range 3-5), representing the characteristic heterogeneous presentation of spastic motor deficit typically found with stroke. The anatomical locations of the lesions for these individuals were as follows: right MCA territory—frontal, parietal, temporal, putamen; left putamen, posterior limb internal capsule; right corona radiata; left parietal/occipital. Lesions for two subjects could not be localized beyond hemisphere (one left, one right) as anatomical imaging had not been performed at the time of diagnosis. Seven controls age matched to the stroke subjects (5 females and 2 males, average age 59 years, range 25–71 years), and 10 young healthy adults (4 females and 6 males, average age 28 years, range 25-38 years) were recruited for comparison.

## Tasks

Subjects performed a battery of hand gripping and ankle flexion motor tasks according to Table 1. All unilateral motor tasks were performed using the stroke subject's affected side. Although finger-tapping tasks could result in less head motion than hand gripping tasks in healthy subjects, the latter were investigated in this study because in our experience more stroke subjects can grip effectively than can tap their fingers on their affected side. Each task was performed at approximately 0.5 Hz, depending on each subject's capability, for 15 s followed by 15 s of rest. This cycle

**TABLE 1** 

Battery of Six Motors Tasks Performed by All Subjects

Task	Unilateral (U)/ bilateral (B)	Variation
Hand gripping	U	No restraint
Hand gripping	В	No restraint
Hand gripping	U	Forearm restraint
Ankle flexion	U	Device + pelvic restraint
Ankle flexion	U	Device alone
Ankle flexion	U	No device or restraint

was repeated twice, such that each trial in the experiment lasted 1 min. The start of the task and rest phases was verbally cued. All subjects were instructed to perform the tasks while keeping their head as still as possible. Gripping involved the metacarpalphalangeal and interphalangeal joints of the hand, whereas the foot task involved plantar flexion and dorsiflexion of the ankle joint.

The battery of motor tasks was chosen for three reasons: (1) the importance of unilateral and bilateral hand gripping for the fMRI study of stroke recovery (Staines et al., 2001), (2) to investigate the effects of restraining limb movement with straps, and (3) to investigate the potential benefit of using an ankle flexion device designed to decouple distal movements from movement of the trunk and head. The ankle flexion device consisted of a wooden pedal attached to a support stand at the pedal's pivot point. The pivot point was located such that when each subject placed their foot on the pedal, the ankle was coaxial with the pivot point, allowing free dorsiflexion and plantar flexion. The device also included two Velcro straps to stabilize the foot. One strap bound the subject's foot to the pedal. The other was used in conjunction with two plastic bars that were attached to the pivot point on either side of the pedal. The other ends of these bars were strapped to the medial and lateral aspect of the subject's calf. With the subject lying supine, plantar flexion of the ankle produced flexion of the knee, whereas dorsiflexion of the ankle produced extension of the knee. It was hypothesized that this knee motion would limit substantial motion in the superior-inferior direction through the pelvis.

To verify that each subject executed all motor tasks, hand gripping was monitored using force-sensing resistors (FSRs) mounted on the outside surface of two hollow plastic cylinders. The subject's palm was positioned over an FSR. When a cylinder was squeezed, the resistance of the FSR decreased and was recorded via a laptop computer running Labview software (National Instruments, Austin, TX). Ankle flexion was monitored with a fiber-optic Shape Sensor (Measurand, Fredericton, New Brunswick, Canada) and dedicated software. The 10-cm active region of the fiber, located near the tip of the optical fiber, was strapped to the ventral aspect of the foot and lower leg and the flexion angle was recorded.

# Experimental Setup

MR scanner simulator. The MR scanner simulator consisted of a hospital gurney lined with a thin foam sheet for comfort. A surplus MRI head coil (General Electric Medical Systems, Waukesha, WI) was mounted securely onto the gurney. A vacuum pillow (Par Scientific Inc., Odense, Denmark) was used to help stabilize the head and represented a typical restraint technique used in current fMRI examinations. A thin opaque sheet of flexible plastic was folded over the subject and fixed to the gurney, creating a tunnel (60 cm across, 40 cm high, 122 cm long) with bore dimensions similar to that of the local MRI scanner operating at 1.5 T (General Electrical Medical Systems, NV/i hardware platform, LX 8.25 software) available for fMRI research (Fig. 1a). For simplicity, recorded sound from the MR scanner was not presented to the subjects while inside the simulator, as well as because these sounds appear not to affect head motion strongly (Rosenberg et al., 1997).

Polaris tracking system and initial evaluation. Head motion was measured using an active Polaris tracking system (Northern Digital Inc., Waterloo, Ontario, Canada). The system consists of two chargecoupled device (CCD) cameras that detect infrared light from at least 3 of 12 infrared-emitting diodes (IREDs) contained in a precisely machined tracking tool (Traxtal Technologies Inc., Toronto, Ontario, Canada). Movement is tracked with six degrees of freedom (three orthogonal translation directions and three rotations) by parallax calculations. The tool was fixed to a cap strapped to the top of each subject's head prior to positioning the subject supine in the simulator. This ensured that the tool was in each CCD camera's line of sight (Fig. 1b). Tracking data were recorded onto a laptop computer by RS232 interface. Figure 2 displays the entire experimental setup and the tracking coordinate system.

The manufacturer's specifications of the Polaris system stated a root mean square accuracy of 0.35 mm, based on a single IRED marker stepped through 1269 positions over a specified measurement volume (slightly less than 1 m<sup>3</sup>). For our purposes, the Polaris tool would be expected to deviate maximally by about only 1 cm while tracking head motion, such that measurement accuracy would be significantly improved. Therefore, the accuracy and stability of the Polaris system were determined over this range prior to measuring subjects. The Polaris tool was tightly clamped onto a stage capable of translating in three orthogonal directions (accurate to 0.002 mm) and rotating in two orthogonal orientations (accurate to 0.2° for roll and 0.4° for pitch) on an optical bench. By conducting multiple repeated measurements of the stage at precise



**FIG. 1.** Subject in simulator: view inside simulator (a) and view from Polaris camera of cap with attached Polaris tool and vacuum pillow (b).

angular and position increments over a 1.5-cm-diameter volume, the anterior-posterior (A-P) and right-left (R-L) accuracy (averaged maximum difference between true and measured positions) were each found to be 0.03 mm, and the accuracy in the inferior-superior (I-S) direction was 0.12 mm. The angular accuracy in pitch and roll was 0.23° and 0.09°, respectively. These accuracy measurements were all much smaller than the magnitude of head motion that was expected, establishing that the Polaris camera was sufficiently accurate for the subsequent experiments.

To determine the stability of the Polaris system, the position of a stationary object was recorded from system start-up for 1.5 h. The resulting measurements drifted significantly (up to 1 mm) over this time. This drift is a thermal effect produced as internal components in the camera warm-up and starts to level off after 30 min. Importantly, the short-term (1.5 min)



FIG. 2. Experimental set-up showing MR simulator and Polaris tracking system (coordinate system also indicated: A-P, anterior-posterior; R-L, right-left; I-S, inferior-superior).

stability of the Polaris system was determined to be much less than 0.1 mm even when the system was immediately turned on. The stability of the system therefore sufficed for this study. To achieve maximal stability, the Polaris system was turned on at least 1 h prior to use.

To assess the validity of using the simulator by comparing head motion data from subjects inside the simulator and inside the MR scanner, the compatibility of the Polaris system with the MR scanner's high magnetic field was first tested. The camera unit functioned properly in the magnetic field once the unit's power supply was located outside the magnet room with the appropriate cabling. The Polaris tool interface unit (TIU) and the laptop computer were similarly located outside of the MR scanner room. A wooden frame was constructed such that the Polaris camera straddled the patient table track at the back of the MR scanner, providing approximately the same distance and orientation from the tracking tool as achieved with the simulator system.

Although position measurements were reliably obtained inside the MR scanner, MR images could not be obtained due to magnetic field distortion during data collection because of the interference of the ferromagnetic leads inside the Polaris tool. Use of a passive Polaris tracking system without ferromagnetic leads (IREDs are mounted surrounding the CCD cameras, which image infrared light bouncing off MRI-compatible reflective plastic spheres) would circumvent this problem although such a system was unavailable during these experiments.

With the Polaris system well characterized, head motion data were collected for all subjects. The 10 young control subjects were measured both inside the simulator and inside the MR scanner for all six tasks. Data were acquired with a 17-ms sampling period (6 Hz), ensuring that four data samples were acquired within 80 ms, the typical time scale of individual image acquisition during fMRI.

## Analyses

Three different metrics were used to interpret the head motion data: (1) the sample standard deviation of the head motion (with linear drift detrended)  $(M_{sd})$ ; (2) the cumulative motion (the sum of all the distances between each position measurement over time)  $(M_c)$ ; and (3) the range of the head motion with linear drift detrended  $(M_r)$ . The metric  $M_{sd}$  is described by the formula

$$M_{\rm sd} = \sqrt{\frac{\sum_{i=1}^{N} (X_i - \bar{X})^2}{N - 1}},$$
 (1)

where  $X_i$  is the head position measurement at a particular time *i*,  $\overline{X}$  is the mean of all the head position measurements, and N is the total number of data points.  $M_{\rm c}$  was calculated as

$$M_{\rm c} = \sum_{i=1}^{N-1} |X_i - X_{i+1}|.$$
 (2)

 $M_{\rm r}$  is described as

$$M_{\rm r} = X_{\rm max} - X_{\rm min},\tag{3}$$

where  $X_{\text{max}}$  was the maximum and  $X_{\text{min}}$  was the minimum head position measurement. The metrics were calculated separately for both task and rest conditions.

These metrics were applied to both the translation and the rotation of the head, with the three degrees of translation (anterior–posterior, inferior–superior, and right–left) added in quadrature to provide a single distance measurement to facilitate data interpretation. The main focus was directed on  $M_{\rm sd}$  because of the obvious physical meaning of the values.  $M_{\rm c}$  was used as a cruder confirmation of whether head motion increased or decreased during different tasks. For brevity, the analyses of  $M_{\rm c}$  are not extensively discussed below except when a significant difference was found between  $M_{\rm c}$  and the  $M_{\rm sd}$ .

Statistical analyses were performed using SPSS (Statistical Package for the Social Sciences, version 10.0, Chicago, IL). A repeated-measures two-way analysis of variance (two-way RANOVA) of the subject groups and four of the total six tasks (unilateral hand gripping, unilateral hand gripping with restraint, ankle flexion with device, and ankle flexion with device and restraint) was performed for all three metrics.  $M_{\rm sd}$  and  $M_{\rm c}$  values used for the analyses were the average of the two task periods for each subject.  $M_{\rm r}$  values used were the larger of the two ranges of the task periods for each subject (rest periods were ignored).

Other analyses included a comparison of task-correlated motion by a three-way RANOVA of the subject groups, task vs rest periods, and the unilateral hand gripping without restraint vs ankle flexion without foot device or restraint. The mean head positions during the task and rest periods were also examined to determine if there was a positional shift during the transition between task and rest. Directional dominance was analyzed separately for translation and rotation of the head during the unilateral hand gripping without restraint and ankle flexion without the foot device or restraint through 4 two-way RANOVAs of the subject groups and directions. The question of how bilateral vs unilateral hand gripping affected head motion was examined by a two-way RANOVA of the subject groups and the unilateral and bilateral hand gripping data. Repeated-measures t tests were also performed for each group. Finally, the usefulness of the foot device was determined by the analogous assessment procedure used for the unilateral vs bilateral hand gripping data.

0.5

The data variance from the three subject groups were often significantly different, with the largest variance observed in the stroke subject group and the smallest variance observed in the young controls. Where indicated, a linear (square root) transformation was first applied to bring the variances of the groups closer together to allow parametric testing.

## RESULTS

#### Initial Observations

Behavioral monitoring data indicated that the subjects in all three groups executed the motor tasks correctly. No correlation between the extent of motor activity and head motion was found with respect to data from the FSR or shape sensor or with respect to CM score (P > 0.05). Such correlations are likely to be observed only by electromyography experiments involving proximal and distal muscle groups. Although all subjects were able to perform the tasks during the correct time intervals, the phenomenon of extinction was observed in two of four stroke subjects, which manifested as an approximately twofold reduction in force of the affected side during bilateral versus unilateral gripping.

A two-way RANOVA of the data from the young adult group showed a statistically significant difference in the amount of head motion during different tasks (P < 0.01), but no significant difference between being in the MR scanner versus being in the simulator (P = 0.37) in terms of head movement. This latter finding validates the experimental approach and confirms that the simulator data generally reflect what would be observed during actual fMRI examinations over similar time intervals.

Prior to presenting results that involve significant data reduction and calculation of motion metrics, an example of raw head position data for a stroke subject, showing all three directions of translation, is plotted in Fig. 3, to highlight interesting features observed in the stroke group. Clearly, head motion increased during ankle flexion compared to rest and was correlated with the subject's behavior. The subject's head moved to a different position during dorsiflexion and then returned to the original position after plantar flexion, as can be seen during the task phases. Periodic respiratory motion was dominant, in this example, during the rest phases. Although breathing was not monitored, head motion from respiration can be confidently inferred because the cyclic pattern disappears in healthy subjects when they are instructed to suspend breathing (data not shown). Similar head motion characteristics were observable during hand gripping tasks.

Summary bar plots of the average  $M_{sd}$  and  $M_r$  for the three groups of subjects are shown in Fig. 4 for all task conditions. As indicated by the error bars, there were large differences in the 95% confidence intervals between the groups, which motivated linear (square root)



ankle flexing with foot device, exhibiting larger motion during task intervals compared to rest intervals and a shift in the mean head position between the first task and first rest periods. Note also the periodic head motion during the task periods due to ankle flexion and the cyclic motion during the rest periods due to breathing (p, plantarflexion; d, dorsiflexion).

transformations of the data. The average variance across all tasks for  $M_{\rm sd}$  was 0.026 mm<sup>2</sup> for the stroke group. The age-matched and young controls had much smaller variances of 0.007 and 0.001 mm<sup>2</sup>, respectively.

The predominant subsequent observations are: (1) stroke subjects exhibited more head motion than the age-matched controls, and the latter exhibited more head motion than the young adults; (2) ankle flexion resulted in more head motion than the hand gripping tasks, except for the stroke group; (3) use of limb restraints did not alter head motion; (4) head motion was larger during the task intervals compared to the rest phases; (5) head motion in the anterior-posterior and inferior-superior directions was larger compared to the right-left direction for the foot task, but no preferential translational direction was observed for the hand task; (6) pitch and roll rotations were larger than the yaw rotation for both hand and tasks, and the pitch rotation was larger than the roll for only the hand task; (7) bilateral hand gripping increased head motion compared to unilateral hand gripping for the stroke group only; and (8) the foot device did not reduce head motion for any of the groups, but was helpful for the stroke subjects to perform effective ankle flexion. The statistical significance of these trends was investigated by subsequent RANOVAs (see below).

## *Comparison of Groups, Hand vs Foot Tasks, and Efficacy of Restraints*

A two-way RANOVA of the  $M_{sd}$  data across the three groups and four task conditions, chosen for comparison of hand and foot tasks (hand gripping, hand gripping with forearm restraint, ankle flexion, and ankle flexion with pelvic restraint), omitting all rest periods, found that there was a strong statistically significant differ-



**FIG. 4.** (a) Standard deviation of head motion  $(M_{sd})$  and (b) range of head motion  $(M_r)$  with linear drift detrended for stroke subjects, age-matched controls, and young adults during six different motor task conditions. Error bars indicate 95% confidence intervals. Note difference in vertical scales. (r), restraint; (no d), no device; (d), device; (d+r), device + restraint.

ence in head motion between the groups (P < 0.001) and the task conditions (P < 0.01), which is suggested in Fig. 4. The age-matched controls had much more head motion than the young adults (P < 0.01), and the stroke subjects had increased head movement over the two other groups (P < 0.001 for both comparisons). Ankle flexion resulted in significantly larger head motion than hand gripping for the age-matched and young controls (P < 0.05 and P < 0.001, respectively), but not for the stroke group. For all three groups, the forearm and pelvic restraints did not significantly alter the head motion.

The same analysis was repeated with the  $M_c$  data and yielded similar results, except that the stroke sub-

ject and age-matched control groups showed similar head motion, and the use of the hand restraint notably decreased head movement (P < 0.01).

## Task-Correlated Motion

Comparing the task and rest periods of the head motion  $(M_{\rm sd})$  pooled for all subjects (for hand and foot tasks without restraints) revealed that (1) much more head movement occurred during the task intervals (P < 0.01), and (2) there was a significant interaction between the task–rest differences and group (P < 0.001). These effects can be seen in Fig. 5, where it is apparent that there is a larger difference between task and rest interval head motion for stroke subjects than the controls and is also suggested in the representative data of Fig. 3.

There was a substantial difference between taskcorrelated motion associated with the hand and foot tasks for the pooled data from all subjects (P < 0.05). The hand data showed no significant difference between the task and rest intervals, but the foot data showed a meaningful increase in head motion during the task period (P < 0.001).

Another type of task-correlated motion, a *shift* in the mean head position, was also analyzed. A comparison of the mean head position for task versus rest intervals, after taking out any linear head motion trends, showed that this type of task-correlated motion was not common enough to show statistically significant differences in mean position shifts for either the hand or the foot tasks (P > 0.05).

# Directional Dominance of Head Motion

The translational head motion data from the hand gripping task without restraint generally did not reveal any preferential direction of head movement, but a very significant interaction between the direction of the head motion and the group was observed (P < 0.01, Fig. 6a). This was also observed for foot task (P < 0.01), as well as an interaction between the direction of head motion and the group (P < 0.05, Fig. 6b). Head motion in the A-P and I-S directions was larger compared to the R-L direction (P < 0.05 and P < 0.01, respectively).

An analysis of the rotational head motion revealed differences for the hand task (P < 0.001) and the foot task (P < 0.01) and strong interactions between the directions and groups (P < 0.001, P < 0.01 for hand and foot tasks, respectively, Figs. 6c and 6d). Pitch (nodding) and roll (ear to shoulder) rotations were significantly larger than the yaw (indicate no) direction (P < 0.05). The pitch movement was larger than the roll (P < 0.001) for the hand task, but was not significantly different for the foot task.

**FIG. 5.** Standard deviation of head motion with linear drift detrended  $(M_{sd})$  under task and rest conditions for stroke subjects, age-matched controls, and young adults. The two tasks shown are unilateral hand gripping without restraint and ankle flexing with device but no restraint. Error bars indicate 95% confidence intervals.

# Comparison of Unilateral vs Bilateral Hand Tasks

Unilateral hand gripping compared to bilateral gripping resulted in a strong significant difference in  $M_{\rm sd}$  when the data from all the subjects were pooled (P < 0.001). There was also a substantial interaction effect between the unilateral vs bilateral gripping and the group (P < 0.01). Specifically, gripping with one hand or two hands did not result in a significant difference for the young or age-matched controls, but bilateral hand gripping caused an increase in head motion for the stroke subjects (P < 0.05). Analyses with  $M_c$  and  $M_r$  supported these findings.

## Comparison of Foot Tasks with vs without Foot Device

The use of the foot device did not reduce head motion for any of the groups on the basis of both  $M_{sd}$  and  $M_c$ . Importantly, effective unilateral ankle flexion, however, was often not achieved by the stroke subjects without the apparatus. This is further discussed below.

#### DISCUSSION

The findings reported in this study significantly extend and corroborate the small existing scientific literature devoted to quantifying the characteristics of head motion in different subject populations. Knowledge of the range of head motion in these populations is important because it provides a reference criterion for designing new motion correction methods to perform fMRI of a larger proportion of patients more reliably. Before entering a detailed discussion of the results, however, it is necessary to place these findings in appropriate perspective.





**FIG. 6.** Graphical representation of RANOVA results depicting task and group effects on head motion. Values plotted are mean fitted parameters calculated using SPSS, including square root transformation of the motion standard deviation metric  $M_{sd}$  to improve uniformity of variance across each group. Translational motion versus group is shown in (a) for unilateral hand gripping without restraint and in (b) for ankle flexion without restraint (b). Analogous plots for head rotation are shown in (c) and (d), respectively.



**FIG. 7.** Translational head motion of a stroke subject performing the hand gripping task during a training session in the simulator. Compared to the first run in (a), much less head motion occurred during a subsequent run (b) after more instruction and practice.

First, the simulator experiments were designed to yield comparatively quick, highly accurate measurements of head motions up to several centimeters, generating data over the range of motions expected in stroke patients. The motor tasks were of shorter duration than those typically performed in actual fMRI experiments (1 min vs approximately 5–10 min, respectively) and were not performed in randomized order because completion of the testing in the shortest time led to a natural sequence. Thus, the effects on head motion of habituation to the tasks and loss of vigilance to remain still during the course of an actual fMRI examination remain unresolved directly. Habituation, if present, would probably manifest as a decrease in head motion between the first and second repetition cycle of each task; this effect was not observed, however. Habituation could also make detecting differences in head motion increasingly more difficult across tasks; in practice, foot tasks were performed after hand tasks and still showed increased head motions. Although the data likely were not substantially biased by task order, they do not include effects due to loss of vigilance and thus represent a "best-case" estimate of the motion exhibited over longer task durations. Notwithstanding this fact, the observation of different amounts of head motion in the three subject groups even over short task durations has important implications for performing fMRI in patients.

Consequently, it is natural to ask what is the quantitative impact of specific amounts and types of motion on fMRI data quality. However, the relationship between head motion and corruption of fMRI data is complex and depends on multiple variables. It is well known that motion causes a spatial misregistration of image voxel locations with brain anatomy, leading either to false positive activation (stimulus or task-correlated motion) or to false negative activation (random motion that increases the noise variance in fMRI signals). The associated erroneous variations in signal intensity occur from partial voluming, spatial variation in static magnetic field strength, and disruption of the equilibrium magnetization if there is significant motion through the imaging plane (Cox, 1996).

What constitutes a tolerable amount of motion is difficult to define, however, and depends additionally on the behavioral task and the distribution and intensity of the associated activations, the nature of the motion (e.g., the effect of extremely transient motions can be suppressed simply be deleting the associated fMRI data), the type of motion correction strategy adopted, magnetic field strength, and imaging spatial resolution. From our experience at 1.5 T performing fMRI of patient and control subjects using the motor tasks described in this study, however, the usual range of head movement that results in reliable fMRI data after image coregistration is about 1 to 0.5 mm or less (single shot spiral imaging protocol (Glover and Lai, 1998), 64 by 64 acquisition matrix at 20 cm field of view (FOV), coregistration performed using AFNI, Analysis of Functional Neuroimages freeware (Cox and Jesmanowicz, 1999)). Others have made similar observations (Breiter *et al.*, 1997). As the head movement increases above 1 mm, the severity and spatial distribution of characteristic motion artifacts rimming the brain or at sharp contrast interfaces increases. When head motion becomes comparable to the size of a voxel, unrecoverable image corruption occurs. These observations are supported by a recent study (Field *et al.*, 2000) indicating that submillimeter in-plane motion and only weakly to moderately task-correlated motion (correlation coefficient > 0.52) could cause false fMRI activation.

Given the above considerations, the results reported here are evaluated qualitatively with respect to a threshold of 1-mm range of motion, above which fMRI data are assumed significantly contaminated by motion artifact, as well as the presence of significant task-correlated motion. The findings of the study are first compared to the pertinent existing scientific literature, followed by a series of recommendations.

# Differences of Head Motion Characteristics between Subject Groups

The age-matched controls (average age 59 years old) exhibited a large increase in the amount and range of head motion compared to the young subjects (average age 28) (P < 0.001), as can be observed in Fig. 4. For instance,  $M_r$  for the hand gripping task without restraint for age-matched and young controls was 0.7  $\pm$  0.2 mm (average  $\pm$  confidence interval of 95%) and 0.4  $\pm$  0.05 mm, respectively, and  $M_{\rm sd}$  was 0.12  $\pm$  0.02 and 0.08  $\pm$  0.01 mm, respectively. These findings are similar to those reported in a previous fMRI study based on image coregistration data (D'Esposito *et al.*, 1999). Specifically, the median head motion of elderly subjects (61–82 years old) was found to be 1.8 times larger than the median motion of the young group (18–32 years old).

A comprehensive study on the head motion of stroke patients during fMRI had not been performed prior to this study. It was found that the stroke subject group (average age 58 years) produced more head motion, and more variation in head motion, than the agematched controls. For example, when performing ankle flexion with the foot device,  $M_{\rm sd}$  for the stroke subjects and the age-matched controls were 0.35  $\pm$  0.24 and 0.18  $\pm$  0.07 mm, respectively (Fig. 4). The increase in amount and variability of head motion found with the stroke subjects was expected, given their hemiparesis.

From Fig. 4b, the range of motion for the control groups is usually well below 1 mm, which would indicate little if any significant motion-induced artifacts in actual fMRI data. The stroke subjects, however, had an average  $M_{\rm r}$  of 1.5 ± 1.0 and 2.0 ± 1.4 mm for the hand

and foot tasks without restraints, respectively. It is therefore not surprising that fMRI data from stroke subjects are often plagued by motion artifacts. For the stroke subjects who participated in this study, improved head motion correction methods would probably greatly reduce motion-induced corruption of fMRI data.

Through the RANOVA analysis, the head motion of the stroke subjects was found to be significantly more task-correlated than that of the age-matched controls, which is also of concern regarding fMRI data quality (Fig. 5). These results are analogous to motion characterization data reported for schizophrenics performing a silent verbal fluency task (Bullmore et al., 1999). Schizophrenics produced more stimulus-correlated motion than control subjects, who produced motion dominated by linear trends. The young adults and agematched controls measured in the simulator also exhibited little task-correlated head motion, with approximately half of these individuals exhibiting head motion data characterized simply by random noise. The other half showed head motion predominated by linear trends (slow drift) and head motion arising from respiration. Respiratory-induced motion is often difficult to observe using coregistration methods, particularly if fMRI is performed with insufficient temporal resolution. This is one possible reason for the failure previously to see this motion in schizophrenics (Bullmore et al., 1999).

#### Translational and Rotational Motion

Both new results and those that support previous studies were obtained that highlight differences in translational and rotational head motion during fMRI tasks. For example, translational head motion was produced in a preferred direction for foot tasks but was not statistically significant for the hand tasks (Figs. 6a and 6b). This could be explained by the hand tasks producing too little head motion to distinguish the preferential directions in a statistically significant manner. For the foot tasks, there was significantly more motion in the A-P and S-I directions compared to the R-L direction. Although the vacuum pillow used in this work is particularly good at restricting R-L motion, and not as good for restricting S-I and A-P motion, there is evidence that this result cannot be completely attributed to the vacuum pillow. A previous analysis during frameless stereotaxic radiosurgery (Kai et al., 1998) also used an optical tracking system (Optotrak, Northern Digital, Inc.) to assess the head motion of young adults for 30 min while they remained at rest. The largest motion was produced in the S-I direction (1.44 mm maximum amplitude, attributed to swallowing). This agreement between the two studies suggests that translational motion in the S-I direction is most problematic, regardless of the influence of the vacuum pillow. This has implications for choosing scan plane orientation for fMRI, as coregistration algorithms have more difficulty coping with through-plane vs in-plane motion (Cox, 1996). Scan plane orientation is also influenced by other factors, however, such as volume of coverage and temporal resolution of time series data and sensitivity to magnetic field distortion in-plane due to magnetic susceptibility differences at air-tissue interfaces.

Concerning rotational motion, both the hand and the foot tasks produced preferred rotational components (pitch greater than roll, roll greater than yaw) (Figs. 6c and 6d). The pitch versus roll difference for the foot task, however, was not statistically significant. This is consistent with the characteristics of the vacuum pillow, which restrained pitch rotations less than yaw and roll rotations. It is also in accordance with a previous PET study using a laser-based system to measure head motion for subjects wearing thermoplastic molds (Ruttimann *et al.*, 1995). Rotations up to 4.1° and 2.4° in the pitch and roll directions occurred in 130 min, respectively, again suggesting the preferential nature of pitch rotation.

The translational and rotational head motion information obtained in this study will be useful in designing new head restraints. Special attention to immobilize the head in the directions associated with the most severe motion could be helpful, perhaps while somewhat relaxing the restrictions to directions associated with intrinsically smaller head movement. These potential design considerations should also be considered together with the ergonomics of patient restraint. The restraint should sufficiently maintain head immobilization to an adequate threshold such that coregistration and fast imaging are effective, while attempting to maintain an open structure that can accommodate a variety of stimulus presentation and response devices (e.g., auditory headphones). These issues are especially challenging for subjects with large head motion, such as the stroke group, but with knowledge of the expected magnitude of motion in different directions, real-time and retrospective motion correction techniques could be optimized together. Optimization can be particularly important for prospective motion compensation techniques because execution of real-time motion minimizing and correction algorithms are under a tight time constraint (Korin *et al.*, 1995). There is clearly much research in these areas that can be undertaken in the future.

## Head Motion Differences Due to Tasks and Restraints

Head motion is highly dependent on the motor task that is being used for the fMRI study. Most fMRI motor studies use hand tasks (Cramer *et al.*, 1997) because of the large cortical representation of the hand primary sensorimotor area, and translation of motion from the hand to the head is minimal. Quantitative head motion characterization enables the assessment of other tasks

to be used for fMRI. The study of head motion translation from ankle flexion is of particular interest because foot function is very important for stroke recovery and it is highly probable that there would be increased head motion compared to hand tasks. Our data indicate that although the foot task did produce larger head motion in young adults and age-matched controls, in both cases the motion was likely within acceptable limits (i.e., under 1 mm). In the stroke subject group, however, little difference in head motion was observed when comparing hand and foot tasks. This could have been because the inherently large head movements for the stroke group obscure the more subtle differences in motion produced by these specific tasks. Nevertheless, fMRI of the lower limb appears feasible for carefully selected stroke subjects based on this study, suggesting new research opportunities.

Of the restraints investigated, none significantly improved the head motion characteristics associated with the three groups. The foot device had additional merit, however, because well-controlled unilateral ankle flexion was much more achievable for many of the stroke subjects when using the device. This could have been due to the additional somatosensory and proprioceptive input provided by the wooden pedal versus the unaided condition, which tended to produce smaller extent of flexion or severe mirror motion of the contralateral leg. The attenuation of these unwanted motor components, which can influence the intensity and location of brain activations, has important implications for interpreting fMRI of motor recovery. In the case of the pelvic and forearm restraints, their ineffectiveness could be due to the inability to reduce the predominant translational motion of the head (S-I direction). The use of additional restraints requires further consideration.

## Simulator

In addition to the data reported in this study, it is important to emphasize that the MR scanner simulator is a potential tool for familiarizing, training, and screening future fMRI subjects, as well as developing and testing behavioral tasks designed for fMRI.

As an example, a stroke patient in the acute phase of recovery (several days poststroke) who was suspected of having difficulty keeping his head still was trained on the MR simulator before performing fMRI. The subject was trained on a number of hand tasks that were to be performed for the fMRI exam (unilateral and bilateral gripping and finger-tapping with the affected hand) and instructed to lie as still as possible without speaking during the practice runs as positional data were acquired. Head motion is plotted in Fig. 7a for unilateral gripping and clearly indicates unacceptable movement: the second task interval exhibits head motion ranging from 3 to 6 mm associated with three hand grips, the second rest interval contains a large head movement (>8 mm), and the subject also started speaking during the last rest interval. (Excessive speech was subsequently verified as one aspect of the subject's neurological deficit.) On the basis of these data, the subject was instructed to concentrate on lying even more still and keeping his arm and hand from moving any more than necessary during the hand gripping task. Second, the subject was instructed to squeeze the hand grips much less tightly to eliminate movement of the entire body associated with the effort of the gripping action. As can be seen from Fig. 7b. subsequent head motion was mostly much smaller (<0.5 mm) compared to the previous run. There was, however, a large head movement during the first rest interval from the subject speaking even though he was instructed to remain silent several times. The reduction in head motion during the second run is very compelling and exemplifies the potential usefulness of an extended training session as one of a combination of strategies to improve the quality of fMRI data.

The biggest advantage of the simulator is that it frees up valuable scanning time on the MR scanner. Our simulator was very low cost because it was constructed in-house with materials found mainly on site. The MR simulator used in a previous study was found to be a useful alternative to sedating children during MR scans and was built using a genuine scanner patient tube (Rosenberg *et al.*, 1997). Commercial MRI simulators are now available that feature internal lights and cooling system, motorized table, and a speaker and amplifier and are substantially less costly than MR scanners.

Nevertheless, no matter how closely a simulator resembles an MR scanner, it is not the real thing and likely does not provoke the same level of anxiety subjects. This could result in more movement than expected after training sessions in the simulator. It is worth noting, however, that this effect was not observed for the measurements of young adults in the scanner and the simulator.

Coupling a simulator with a position tracking system has numerous uses (e.g., for training subjects) and has not been reported prior to this study. The inclusion of additional equipment to deliver sensory stimuli and monitor behavioral responses to a variety of cognitive tasks would complete an experimental system to quantify the benefits of simulators carefully, which would be an important future endeavor.

### **RECOMMENDATIONS AND CONCLUSIONS**

Quantification of head motion in different subject groups is an important practical consideration when comparing brain activations measured using fMRI. This study has indicated that young, elderly, and stroke subject populations have different head motion characteristics and that fMRI of recovering stroke patients is challenging on this basis. It is promising,

REFERENCES

however, that at least a subset of such patients may ultimately yield acceptable fMRI data quality solely through careful practice, training, and repetitive prompting as they perform behavioral tasks.

Although this study was performed with fMRI applications in aging and stroke recovery in mind, the trends observed in this study are likely to extend to patient populations with other pertinent neurological deficits, such as Alzheimer's disease, traumatic brain injury, multiple sclerosis, Parkinson's disease, and cerebral palsy. Beyond head restraint, imaging pulse sequence, and postprocessing issues, general recommendations are provided for performing practical scientific fMRI examinations of such patients:

a. Subject selection for any fMRI study is an important factor. Subjects, especially those with diminished motor control, should be screened for excess motion and trained carefully either before fMRI using a simulator or during fMRI examination. A similar study to the one presented here could be performed to investigate the head motion of specific patients to optimize correction techniques and head restraints during other specific behavioral tasks.

b. Choose behavioral tasks such that they minimize head motion. This study suggests that ankle flexion tasks are practical for fMRI studies in young adults and the elderly, but only in a fraction of stroke recovery patients. In addition, event-related designs may be more practical for some subjects that are incapable of sustained repetitive motor function.

c. Behavioral monitoring should be implemented to verify task compliance.

d. Assistive devices, such as the one used in this study to facilitate ankle flexion, can improve behavioral performance without introducing additional head motion. Use of simple straps to restrain limbs and reduce motion translated to the head are likely to be ineffective.

Finally, the findings of this study require further interpretation and evaluation through new experiments that include the acquisition of actual fMRI data in patients. Given the above recommendations, and use of stand-alone position tracking systems for assessing patient motion during fMRI and in fMRI simulators, such a study will be the subject of future reports from our laboratory.

## ACKNOWLEDGMENTS

This work was supported by the Canadian Institutes of Health Research (CIHR), Sunnybrook Trust for Research, General Electric Medical Systems Canada, the Heart and Stroke Foundation of Ontario, and the Natural Sciences and Engineering Research Council of Canada. The authors thank Cynthia Danells and Cathy Nangini for their assistance with subject management and data acquisition, respectively.

- Biswal, B. B., and Hyde, J. S. 1997. Contour-based registration technique to differentiate between task-activated and head motion-induced signal variations in fMRI. *Magn. Reson. Med.* **38**: 470–476.
- Breiter, H. C., Gollub, R. L., Weisskoff, R. M., Kennedy, D. N., et al. 1997. Acute effects of cocaine on human brain activity and emotion. *Neuron* 19: 591–611.
- Bullmore, E. T., Brammer, M. J., Rabe-Hesketh, S., Curtis, V. A., Morris, R. G., Williams, S. C. R., Sharma, T., and McGuire, P. K. 1999. Methods for diagnosis and treatment of stimulus-correlated motion in generic brain activation studies using fMRI. *Hum. Brain Map.* **7**: 38–48.
- Cohen, M. S., and Bookheimer, S. Y. 1994. Localization of brain function using magnetic resonance imaging. *Trends Neurosci.* 17: 268–277.
- Cox, R. W., and Jesmanowicz, A. 1999. Real-time 3D image registration for functional MRI. *Mag. Reson. Med.* **42:** 1014–1018.
- Cox, R. W. 1996. Workshop on Functional MRI, Boston, MA.
- Cramer, S. C., Nelles, G., Benson, R., Kaplan, J. D., Parker, R. A., Kwong, K. K., Kennedy, D. N., Finklestein, S. P., and Rosen, B. R. 1997. A functional MRI study of subjects recovered from hemiparetic stroke. *Stroke* 28: 2518–2527.
- D'Esposito, M., Zarahn, E., Aguirre, G. K., and Rypma, B. 1999. The effect of normal aging on the coupling of neural activity to the BOLD hemodynamic response. *NeuroImage* **10**: 6–14.
- Field, A. S., Yens, Y. F., Burdette, J. H., and Elster, A. D. 2000. False activation on BOLD fMRI caused by low-amplitude motion weakly correlated to stimulus. In *Proceedings of the 8th Scientific Meeting* of *ISMRM*, No. 1005.
- Fitzsimmons, J. R., Scott, J. D., Peterson, D. M., Wolverton, B. L., Webster, C. S., and Lang, P. J. 1997. Integrated RF coil with stabilization for fMRI human cortex. *Magn. Reson. Med.* **38**: 15– 18.
- Friston, K. J., Williams, S., Howard, R., Frackowiak, R. S. J., and Turner, R. 1996. Movement-related effects in fMRI time-series. *Magn. Reson. Med.* 35: 346–355.
- Gati, J. S., Menon, R. S., Ugurbil, K., and Rutt, B. K. 1997. Experimental determination of the BOLD field strength dependence in vessels and tissue. *Magn. Reson. Med.* **38**: 296–302.
- Glover, G. H., and Lai, S. 1998. Self-navigated spiral fMRI: Interleaved versus single-shot. *Magn. Reson. Med.* **39**: 361–368.
- Glover, G. H., and Lee, A. T. 1995. Motion artifacts in fMRI: Comparison of 2DFT with PR and spiral scan methods. *Magn. Reson. Med.* **33**: 624–635.
- Gowland, C., Stratford, P., Ward, M., Moreland, J., Torresin, W., Van Hullenaar, S., Barreca, S., Vanspall, B., and Plews, N. 1993. Measuring physical impairment and disability with the Chedoke-Mc-Master stroke assessment. *Stroke* **24:** 58–63.
- Green, M. V., Seidel, J., Stein, S. D., Tedder, T. E., Dempner, K. M., Kertzman, C., and Zeffiro, T. A. 1994. Head movement in normal subjects during simulated PET brain imaging with and without head restraint. *J. Nuclear Med.* **35**: 1538–1546.
- Hajnal, J. V., Myers, R., Oatridge, A., Schwieso, J. E., Young, I. R., and Bydder, G. M. 1994. Artifacts due to stimulus correlated motion in functional imaging of the brain. *Magn. Reson. Med.* 31: 283–291.
- Johansson, B. B. 2000. Brain plasticity and stroke rehabilitation. *Stroke* **31**: 223–230.
- Kai, J., Shiomi, H., Sasama, T., Sato, Y., Inoue, T., Tamura, S., and Inoue, T. 1998. Optical high-precision three-dimensional position measurement system suitable for head motion tracking in frameless stereotactic radiosurgery. *Comput. Aided Surg.* 3: 257–263.
- Kim, S. G., and Ugurbil, K. 1997. Functional magnetic resonance imaging of the human brain. J. Neurosci. Methods 74: 229–243.

- Korin, H. W., Felmlee, J. P., Riederer, S. J., and Ehman, R. L. 1995. Spatial-frequency-tuned markers and adaptive correction for rotational motion. *Magn. Reson. Med.* 33: 663–669.
- Le Bihan, D., and Karni, A. 1995. Applications of magnetic resonance imaging to the study of human brain function. *Curr. Opin. Neurobiol.* 5: 231–237.
- Nishimura, D. G., Irarrazabal, P., and Meyer, C. H. 1995. A velocity k-space analysis of flow effects in echo-planar and spiral imaging. *Magn. Reson. Med.* 33: 549–556.
- Orrison, W. W., Lewine, J. D., Sanders, J. A., and Hatshorne, M. F. 1995. *Functional Brain Imaging: Functional Brain Imaging*, pp. 239–326. Mosby–Year Book, St. Louis.
- Ostuni, J. L., Santha, A. K., Mattay, V. S, Weinberger, D. R., Levin, R. L., and Frank, J. A. 1997. Analysis of interpolation effects in the reslicing of functional MR images. *J. Comput. Assist. Tomogr.* 21: 803–810.
- Righini, A., de Divitiis, O., Prinster, A., Spagnoli, D., Appollonio, I., Bello, L., Scifo, P., Tomei, G., Villani, R., Fazio, F., and Leonardi, M. 1996. Functional MRI: Primary motor cortex localization in patients with brain tumors. *J. Comput. Assist. Tomogr.* **20**: 702–708.

- Rosenberg, D. R., Sweeney, J. A., Gillen, J. S., Kim, J., Varanelli, M. J., O'Hearn, K. M., Erb, P. A., Davis, D., and Thulborn, K. R. 1997. Magnetic resonance imaging of children without sedation: Preparation with simulation. *J. Am. Acad. Child. Adolesc. Psychiatry* **36**: 853–859.
- Ruttimann, U. E., Andreason, P. J., and Rio, D. 1995. Head motion during positron emission tomography: Is it significant? *Psychiatry Res.* 61: 43–51.
- Staines, W. R., McIlroy, W. E., Graham, S. J., and Black, S. E. 2001. Bilateral movement enhances ipsilesional cortical activity in acute stroke: A pilot functional MRI study. *Neurology* 56: 401–404.
- Weiller, C. 1998. Imaging recovery from stroke. *Exp. Brain Res.* **123**: 13–17.
- Yang, Y., Glover, G. H., van Gelderen, P., Patel, A. C., Mattay, V. S., Frank, J. A., and Duyn, J. H. 1998. A comparison of fast MR scan techniques for cerebral activation studies at 1.5 Tesla. *Magn. Reson. Med.* **39:** 61–67.
- Zeffiro, T. 1996. Clinical functional image analysis: Artifact detection and reduction. *NeuroImage* **4**: S95–S100.