Overt Verbal Responding during fMRI Scanning: Empirical Investigations of Problems and Potential Solutions

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This paper presents a pair of studies designed to empirically explore the severity of potential artifacts associated with overt verbal responding during fMRI scanning and to examine several different solutions to these artifacts. In Study One, we compared susceptibility artifacts, signal-to-noise ratios, and activation patterns when overt versus covert verbal responses were elicited during fMRI scanning, using both individual and group analyses. The results indicated that different patterns of brain activation were elicited during covert as compared to overt verbal responses. This suggests that covert responses cannot be used as a simple substitute for overt verbal responses. Further, the results suggested that the use of overt verbal responses during fMRI scanning can produce interpretable results if: (1) the primary comparison is between two conditions that both use overt verbal responses, and (2) analyses are conducted on pooled group data rather than individual participant data. In Study Two, we evaluated the feasibility and validity of a method for acquiring participants' overt responses during fMRI scanning. The results indicated that our method was very accurate in acquiring the content of participant's responses. Further, inspection of the responses demonstrated that participants do not always comply with task instructions and highlighted the importance of obtaining behavioral performance measures during fMRI scanning. © 1999 Academic Press

INTRODUCTION

Functional magnetic resonance imaging (fMRI) has been used to examine the cortical systems underlying a number of different cognitive functions, including visual perception, working memory, long-term memory, selective attention, and language comprehension. However, fMRI has not been used extensively to study cognitive processes involved in language production, or other cognitive processes that may operate when overt verbal responses are required. The relative lack of research on language production-related processes with

fMRI is due, at least in part, to concerns about artifacts that may occur when overt verbal responses are elicited during fMRI scanning, as well as the difficulty of acquiring the content of verbal responses in the scanner. In the pair of studies presented in this paper, we had the following goals: (1) empirically explore the severity of the potential artifacts associated with overt verbal responding; (2) compare overt to covert verbal responses; (3) explore means of reducing potential artifacts associated with overt verbal responding; and (4) validate a method for acquiring the content of verbal responses during fMRI scanning.

There are two main potential artifacts associated with acquiring overt verbal responses during fMRI scanning. The first one is the possibility that overt verbal responses, as compared to manual responses, will induce an increased, and potentially unacceptable, level of movement into fMRI images. Such movement can have at least two effects. First, if sufficient movement occurs (e.g., 0.5–1 voxel), data for the same voxel may actually be acquired from different cortical locations during the time course of scanning. Second, changes in the position of the head within the scanner may also mean that the spin-excitation history of a voxel (and hence its signal) is nonuniform across time (Friston *et al.,* 1996). Both of these effects of high movement can lead to areas of artifactual activation or can mask the presence of cognition-related activation. Areas of such artifact are most likely to occur at the edges of the brain or at other structural boundaries within the brain (e.g., ventricles). This is because these are regions where even relatively small movements can lead to large changes in the intensity of the fMRI signal, if the location of a voxel moves from one type of tissue to another or from brain to CSF.

A second concern is the possibility that magnetic susceptibility distortions in the fMRI data may be altered and/or worsened during overt speech (e.g., Birn *et al.,* 1998b). One potential source of such effects is changes in the volume of the sinus cavities and the

posterior pharynx during speech. A second potential source is tongue movements that occur during speech. Distortions in the magnetic field can lead to several different artifacts in the fMRI data. One type of artifact is the presence of signal voids in the data. A second type of artifact involves geometric distortions and blurring. Overt speech, via volume and movement changes, may lead to variations in the severity and/or precise location and influence of these artifacts. These types of artifacts can lead to a reduction in the signal-to-noise ratio and impair the interpretability of fMRI data, primarily through an increase in signal variance across time.

An additional problem with acquiring overt verbal responses during fMRI scanning is the difficulty of recording the content of overt verbal responses. This difficulty arises from two sources. First, the presence of recording equipment in the scanner can itself produce distortions in the magnetic field. Second, the noise that occurs during scanning can drown out the content of participants' responses. If one cannot acquire the content of such responses, the usefulness of overt response paradigms is greatly decreased. Without response content, one cannot determine whether the participant is following the task instructions correctly, and one cannot analyze the data according to the actual content of the participant's response.

Potential Methods to Decrease Artifacts

Use covert responses. A relatively frequently employed approach to studying language production with fMRI is to use covert verbal responses, thereby attempting to avoid artifacts associated with overt responding. However, there are at least two problems associated with this approach. First, the use of covert verbal responses does not allow one to determine whether the participant is performing the task as instructed. As such, if one obtains unusual patterns of data, it is impossible to determine whether this is related to participants' failure to follow task instructions. Moreover, without overt responses, one cannot analyze data according to the actual response produced by the participant, eliminating the possibility of testing hypotheses related to individual differences in the type of response produced. Second, it is possible that the cognitive processes operating during covert verbal responding are different, at least in some respects, to those operating during overt verbal responding. Obvious differences between covert and overt responses include processes associated with motor planning and articulation. However, there may also be less obvious differences. For example, some cognitive mechanisms, such as those involved with inhibiting inappropriate responses, are not called into play until overt articulation is required. In fact, data already exists to suggest that covert and overt verbal responses produce different patterns of fMRI (e.g., McCarthy *et al.,* 1993;

Zelkowicz *et al.,* 1998) and PET data (Bookheimer *et al.,* 1995; Price *et al.,* 1996), making it potentially difficult to generalize data acquired from covert response paradigms to overt response paradigms.

Use only data acquired after overt responses have been completed. Movement correction algorithms can help correct for movement that occurs between scans. However, such algorithms cannot correct for the effects of movement that may occur within a single scan (Woods *et al.,* 1992, 1993). The magnitude of within-scan movement will depend upon the length of the image acquisition and the time that it takes participants to respond verbally. Unless one can acquire data very rapidly, some within-scan movement is likely to occur. However, one may be able to take advantage of the relatively slow time course of the hemodynamic response in order to reduce within-scan movement artifacts. Specifically, there is a delay (3–6 s) in the peak of the hemodynamic response associated with the cognitive processes thought to occur upon stimulus presentation (Kwong *et al.,* 1992; Savoy *et al.,* 1995; Vazquez and Noll, 1996). In contrast, signal changes associated with overt response-induced movement occur more rapidly following stimulus presentation. Thus, one should be able to avoid using data acquired during the overt response itself and still detect BOLD responses associated with stimulus processing. This could be done in multiple ways. One way would be to delay the start of the image acquisition until after the overt response is completed. This method has been used in several studies examining auditory processing and may be a useful approach to apply to overt response studies (e.g., Edmister *et al.,* 1999). Alternatively, one could acquire multiple images per trial, and discard those acquired during the overt response itself. For example, imagine a paradigm in which the image acquisition time was 2500 ms, and two images were acquired per trial. Presumably, the majority of the artifacts occur during the first image. Thus, data from the first image of each trial could be discarded, and only the data from the second image analyzed, potentially eliminating or reducing overt response-related artifacts.

Conduct group analyses. Artifactual activation associated with overt verbal responses is most likely to occur at edges and structural boundaries of the brain. However, even within such constraints, the exact location of such artifacts can be somewhat idiosyncratic and vary across individual participants. As such, conducting analyses with the data averaged across a group of participants, rather than analyzing individual participants separately, may help reduce such artifactual activation. This is because group analyses look for areas of activation that are consistent across participants. If the precise location of artifactual activations vary somewhat across participants, these artifacts may not appear in the group-analyzed data.

Avoid scanning in the region of the throat and mouth.
One possible solution to avoiding some of the potential artifacts associated with changes in the volume of the sinus cavities and posterior pharynx, as well as with tongue movements, is to discard data acquired in the regions of the throat and mouth. However, if one acquires data within the region of the throat or mouth, ghosting artifacts (which can result from motion occurring during multishot imaging sequences) may contaminate the data acquired from other regions of the image. To avoid such artifacts, it may be necessary to not acquire any data within the region of the throat or the mouth. Such a solution presents constraints on the plane of scanning, as only scans acquired in the axial plane will allow one to acquire data in frontal regions associated with language production, yet still allow one to avoid scanning through the plane of the throat or mouth. However, scanning in the axial plane during overt responses has associated problems. Movement associated with verbal responses is likely to be greatest in the superior to inferior dimension (i.e., Z and pitch parameters), because of the axis of rotation during overt speech. With axial slices, such movement is between rather than within slice, and between slice movement is more difficult to correct (Noll *et al.,* 1997; Woods *et al.,* 1992, 1993). We should also point out that avoiding scanning through the throat and mouth does not eliminate all possible types of artifact associated with overt speech. For example, some magnetic susceptibility artifacts that could result from mouth and tongue movements may still contaminate other nearby regions of the image even when data is not actually acquired from the throat and mouth region.

The goals of this paper were to empirically explore the presence and severity of several artifacts described above and to examine potential means to reduce or avoid such artifacts. Study One explored methods for reducing artifacts in the fMRI data during overt verbal responding, while Study Two implemented and validated a method for acquiring the content of verbal responses during fMRI scanning. In each study, we used a task that has a long empirical history in the cognitive and neuroimaging literatures, and for which overt verbal responses are typically acquired (a Stroop task in Study One and a verb generation task in Study Two). The choice of tasks was motivated in part by a desire to have an existing set of studies from the PET literature with which to compare the results of the current studies.

STUDY ONE: METHODS

Participants

Informed consent was obtained from nine neurologically normal right-handed participants. Participants were 5 males and 4 females, with a mean age of 24 (range 18 to 36). All subjects were given a pretesting session, in which they briefly practiced the task.

Cognitive Tasks

Participants performed a version of the Stroop color naming task (Stroop, 1935). A factorial design was used, with two tasks (neutral, incongruent) fully crossed with two response types (overt, covert) yielding four conditions. Trials were blocked by condition, and an equal number of blocks (7) were run in each condition. Participants observed stimuli on a visual display controlled by a Macintosh computer in the scanner control room running PsyScope software (Cohen *et al.,* 1993). Trials lasted 5 s, with a stimulus duration of 2.5 s and an intertrial interval of 2.5 s (during which a fixation cross appeared). The neutral stimuli were four "X"s (XXXX) presented in either red, green, blue, or yellow. Incongruent stimuli were the words "red," "green," "blue," and "yellow" presented in one of the three other colors. Subjects performed the task (name the ink color) continuously within a 45-s, 9-trial block. Seven blocks of each of the four conditions were run in a pseudorandom order, such that all conditions were sampled once in every 4 blocks, yielding a total of 28 blocks per subject.

Scanning Procedures

Images were acquired with a conventional 1.5T GE Signa whole body scanner and a standard RF head coil in the UPMC MR Research Center. Sixteen oblique axial slices (3.75 mm^3 voxels) were acquired parallel to the AC–PC line, with the middle of the bottom slice on the AC–PC line, for a total of 60 mm of brain coverage. As discussed previously, axial slices starting at the AC–PC line were chosen to avoid scanning through the plane of the throat and mouth. Functional scans were acquired with a 2-interleave spiral-scan pulse sequence (TR = 1250 ms, TE = 35 ms, FOV = 24 cm, flip = 60°)[1] (Noll *et al.,* 1995). Scanning was synchronized with stimulus presentation so that 2 scans of all 16 slice locations were acquired during each 5-s trial (2.5 s per set of 16 slices). Two images per trial were acquired to determine whether increased movement associated with overt verbal responses occurred primarily during the first scan and, if so, whether better results could be generated by analyzing only the data from the second scan. Nine trials and 18 images were acquired in each block. Anatomical scans (36 slices) were acquired using a standard T1-weighted pulse sequence, with the middle 16 slices placed in the exact same location as the functional slices.

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[1]We also conducted the exact same study using a one-shot EPI sequence, with almost identical results.

Movement Estimation and Correction

Functional images were corrected for movement using a six-parameter 3D automated algorithm (AIR; Woods *et al.,* 1992, 1993). Two sets of estimated movement parameters (pitch, roll, yaw, X, Y, Z) were obtained from AIR. The first set was the difference of the current image from the immediately preceding image, which will be referred to as incremental movement. The second set was the difference of the current image from the reference image (the first image acquired), which will be referred to as absolute movement. For pitch, roll, and yaw, the parameters are expressed in degrees. For X, Y, and Z the parameters are expressed in millimeters. The absolute values of these parameter estimates were used as the dependent measures in the analyses presented below.

Individual Participant Analyses Procedures

This set of analyses used voxel-wise planned contrasts, which are described in more detail below. Voxel-wise statistical maps were generated and then thresholded for significance using a cluster-size algorithm (Forman *et al.,* 1995). This algorithm takes into account the spatial extent of activation to correct for multiple comparisons. A cluster-size threshold of 2 voxels and a per-voxel alpha value of 0.01 was chosen, corresponding to an image-wise false positive rate of 0.01.

## *Group Analysis Procedures*

Images were coregistered and pooled across participants using a procedure similar to one used in PET studies (Woods *et al.,* 1993), which we have employed in several previous studies (Barch *et al.,* 1997; Braver *et al.,* 1997; Cohen *et al.,* 1997). Participants' anatomical images were aligned to a reference brain using a 12-parameter 3D AIR algorithm (Woods *et al.,* 1992). The functional images were then scaled to a common mean (to reduce the effect of scanner drift or instability). The functional images were then registered to the reference brain using the alignment parameters derived for the anatomical scans and smoothed using an 8-mm FWHM Gaussian filter (to reduce effects of anatomic variability across participants). The imaging data, pooled across participants, were then analyzed using voxel-wise planned contrasts, which are described in more detail below. Voxel-wise statistical maps were generated and then thresholded for significance using a cluster-size algorithm (Forman *et al.,* 1995). A cluster-size threshold of 8 voxels and a per-voxel alpha value of 0.01 was chosen, corresponding to an image-wise false-positive rate of 0.01. These regions were overlaid onto the reference anatomical image, which was transformed to Talairach atlas (Talairach and Tournoux, 1988) standard stereotactic space using AFNI software (Cox, 1996).

RESULTS

Estimated Movement Data

We began by examining the estimated movement data obtained from AIR. We used three factor ANOVAs, with response type (overt, covert), condition (incongruent, neutral), and scan (first, second) as within-subject
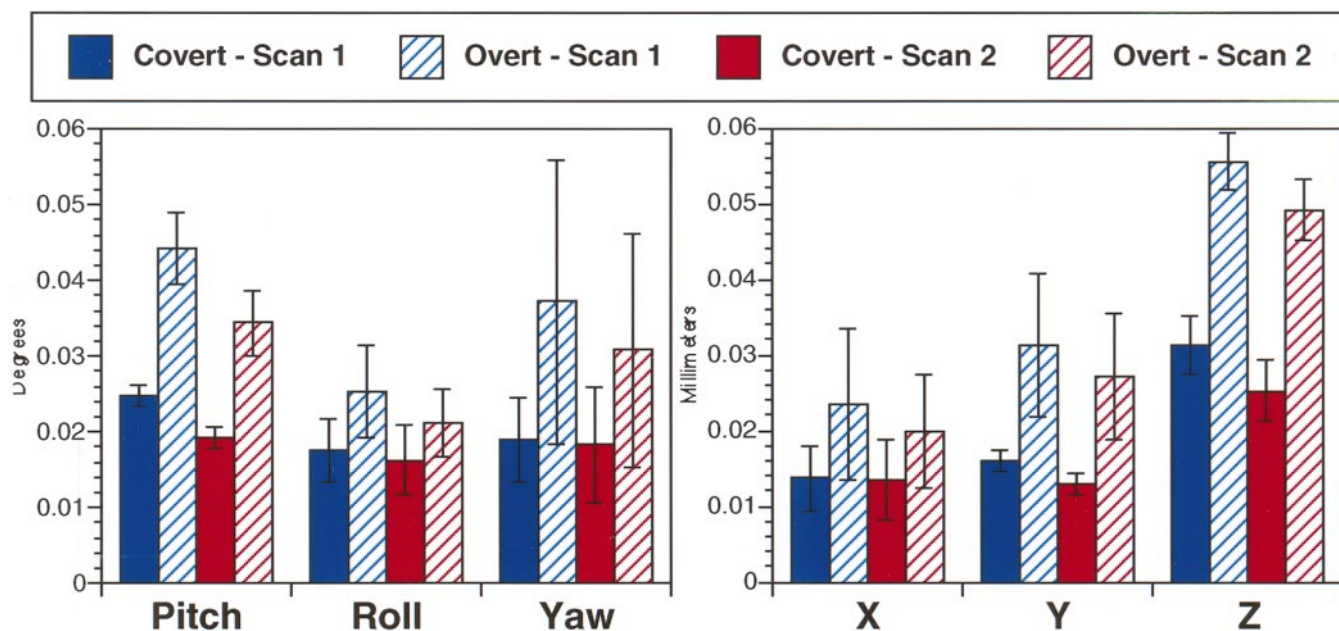
FIG. 1. Graph illustrating the magnitude of increased movement with overt compared to covert responses and with the first as compared to second scan of each trial.

factors and the six movement parameters (pitch, roll, yaw, X, Y, Z) as dependent variables. For incremental movement the ANOVAs demonstrated main effects of response type for pitch ($F(1,8) = 15.46$, $P < 0.01$), roll ($F(1,8) = 20.96$, $P < 0.01$), and Z ($F(1,8) = 22.92$, $P < 0.01$) parameters, all of which showed greater movement with overt than covert responses (see Fig. 1). However, the actual magnitude of the increase in incremental movement with overt responses was surprisingly small (see Fig. 1), with effect sizes ranging from 0.16 to 0.57. There were also significant main effects of scan for the pitch ($F(1,8) = 24.57$, $P < 0.01$), roll ($F(1,8) = 9.41$, $P < 0.05$), yaw ($F(1,8) = 10.35$, $P < 0.05$), X ($F(1,8) = 6.67$, $P < 0.05$), Y ($F(1,8) = 22.05$, $P < 0.01$), and Z ($F(1,8) = 31.26$, $P < 0.01$) parameters, with greater movement in the first than the second scan (see Fig. 1). No other main effects or interactions were significant.

The above analyses indicate significantly greater incremental movement during overt than covert responses and during the first versus second scan. However, such significant results could result from two types of movement. The first possibility is that during overt responses, participants progressively shift away from their initial head positions, such that by the end of the study, their heads are in a different location. Alternatively, during overt responses, participants may be exhibiting movements to and from their initial head position, such that across the course of the study, their head position does not shift dramatically from its initial location. To determine which of these was occurring, we examined the data for absolute movement from the reference image. For these measures, no main effects were significant, and only one interaction with response was significant. For the Z parameter, the response type x scan interaction was significant, ($F(1,8) = 7.833$, $P < 0.05$), with greater movement in the second than the first scan with overt, but not covert, responses. Thus, the analyses of absolute movement suggest that, for the most part, participants were exhibiting small movements to and from their original head position during overt responses and were not progressively shifting away from their initial head position.

Susceptibility Artifacts

To assess potential artifacts and reductions in signal-to-noise (SNR) associated with overt verbal responses, we examined SNR (mean/variance) maps for each individual participant, calculated using the raw data before movement correction was applied. Visual inspection of the SNR maps did not reveal glaring increases in ghosting, geometric distortion, or blurring associated with overt verbal responses. To quantify SNR changes, we calculated the mean SNR for each participant, for each slice location, separately for overt and covert

responses. We then conducted paired-sample t tests to determine if SNR for any of the slices was significantly decreased during overt verbal responses. These analyses indicated a significant reduction in SNR during overt responses for all 16 slices (see Table 1). To determine the magnitude of the SNR reduction, we calculated the average percentage decrease in SNR (((covert SNR − overt SNR)/covert SNR))*100) across participants for each slice. As can be seen in Table 1, the decrease in SNR was relatively small (e.g., less than 10%) in the more superior slices. However, the reduction in SNR did increase in the more inferior slices, which is not surprising given that these slices are closer to the region of the throat and mouth.

Individual Participant Analyses

Each individuals' data were first analyzed using two planned contrasts. The first contrast identified areas of activation greater in the incongruent than the neutral condition for covert responses, and the second contrast identified areas of activation greater in the incongruent than the neutral condition for overt responses. These two contrasts were specifically chosen to compare two different cognitive conditions utilizing the same response modality (i.e., both overt or both covert). As shown in Table 2, there was a great deal of variability in the regions identified in each participant. However, many of the regions were those that have been seen in previous studies of the Stroop task (Carter *et al.*, 1995; Pardo *et al.*, 1990). Relatively few regions of clear movement-related artifact were present, even in the

TABLE 1

Study One: Percentage Decrease in Signal-to-Noise Ratio Associated with Overt Responses

| Slice number | Percentage SNR Decrease | | | |
	Mean	SD	t score	P value
1 (+57 mm Z)	6.0	6.3	2.35	<0.05
2 (+53.2 mm Z)	5.1	6.7	1.99	<0.05
3 (+49.4 mm Z)	4.4	6.9	1.81	=0.05
4 (+45.6 mm Z)	6.8	6.3	2.53	<0.05
5 (+41.8 mm Z)	4.4	6.6	1.90	<0.05
6 (+38 mm Z)	8.1	6.9	2.85	<0.05
7 (+34.2 mm Z)	4.8	6.8	2.01	<0.05
8 (+30.4 mm Z)	9.3	7.6	2.94	<0.05
9 (+26.6 mm Z)	6.0	6.9	2.40	<0.05
10 (+22.8 mm Z)	11.6	10.1	2.83	<0.05
11 (+19 mm Z)	8.2	8.0	2.84	<0.05
12 (+15.2 mm Z)	13.8	11.5	3.21	<0.05
13 (+11.4 mm Z)	11.3	9.3	3.00	<0.05
14 (+7.6 mm Z)	16.3	12.1	3.31	<0.05
15 (+3.8 mm Z)	19.6	12.4	3.24	<0.05
16 (+0 mm Z)	18.6	14.8	3.23	<0.05

TABLE 2

Study One: Regions with Greater Activity in the Incongruent Compared to Neutral Condition[a]

Brodmann area	Both scans				Second scan			
	Covert		Overt		Covert		Overt	
	Right	left	Right	Left	Right	Left	Right	Left
Frontal regions								
46/9	3	2	1	2	2	1	2	3
44/45	2	3	2	2	1	3	1	1
10	4	5	3	2	3	4	2	0
32	2	3	0	1	2	2	1	1
6	1	1	3	1	0	0	1	0
Temporal regions								
22	2	3	1	1	2	2	1	2
37/21	2	0	0	0	0	0	0	1
Parietal/posterior Cingulate regions								
40	0	3	4	3	1	3	1	3
7	1	0	1	1	0	1	0	0
Occipital regions								
17/18/19	3	2	2	0	2	2	0	0

[a] The numbers refer to the number of participants (of 9) that showed activation in this region.

contrast of the incongruent and neutral conditions with overt responses. Comparison of the regions identified in the contrast of the overt responses condition, versus the contrast of the covert conditions, did not reveal strong systematic differences. On visual inspection, more participants showed activity in BA 10 and 44/45 with covert than with overt responses and more participants showed activity in BA 40 with overt than covert responses. However, an ANOVA treating region as a random effect (e.g., "subject") and response (overt versus covert) and hemisphere (right versus left) as within subject factors did not reveal any significant differences in the number of subjects demonstrating activation with overt versus covert responses ($F(1,9) = 2.9$, $P > 0.1$).

We next directly compared overt and covert responses (collapsing across incongruent and neutral conditions), looking for regions with greater activity when overt responses were elicited. As shown in Fig. 2, this comparison was clearly contaminated by movement-related artifacts. This included continuous bands of activation centered around the axis of rotation for speech-related movement, activity in white matter around the ventricles, and activity at the very edge of the brain and outside of the brain. At the same time, some regions of activity were identified that would be expected in a contrast of overt and covert responses, particularly activity in regions associated with motor planning and execution (e.g., BA 6 and BA 8). However, since these regions were embedded in a background of what is likely artifactual activation, it was difficult to

determine which areas represented true cognitive or motor-process-related cortical activation.

We next repeated the above contrasts using only data acquired from the second scan of each trial. As discussed above, the majority of overt-response-related movement likely occurs during the first scan of each trial (e.g., first 2500 ms), while participants are producing the verbal response. Given the delay in the peak of the hemodynamic response associated with cortical activation (3–6 s), one could discard data acquired during overt responses and still detect BOLD responses associated with cognitive processing. Analyzing only the second scan for the two contrasts of the incongruent and neutral conditions (one for overt and one for covert responses) did not have a dramatic impact on the pattern of activity (see Table 2) in individual participants. In fact, analyzing only the second scan decreased the number of participants showing activity in regions that would be expected to be active in the Stroop task. This conclusion was supported by the results of an ANOVA, treating region as a random effect (e.g., "subject") and scan (both, second), response (overt, covert), and hemisphere (right, left) as within-subject factors. This ANOVA revealed a significant main effect of scan ($F(1,9) = 12.1$, $P < 0.01$), with fewer subjects demonstrating activity when only the second scan was analyzed.

Qualitatively analyzing only the second scan did make some improvements for the direct contrast of overt and covert responses. As can be seen in Fig. 2, for a few of the individual participants, analyzing only the second scan reduced some of the activity that appeared related to movement effects (e.g., participant 4). In addition, for a few participants (e.g., 3 and 8), analyzing only the second scan revealed clearer activity in regions associated with motor planning and articulation (e.g., BA 6). However, analyzing only the second scan did not remove all artifacts, for several participants it led to little improvement in the obtained patterns of activity, and an ANOVA did not reveal a significant increase in the number of subjects demonstrating clear activation in regions associated with motor planning and articulation.

Group Analyses

We conducted the same contrasts for the group analyses as we did for the individual analyses. First, we conducted contrasts identifying areas of activation greater in the incongruent than the neutral condition, separately for covert responses and overt responses. The results of these analyses were much more clear-cut than those from the individual participant analyses. For overt responses, several regions were identified that would be expected based on previous studies using the Stroop task (see Table 3 and Fig. 3). All of these regions were ones that were seen in the individual
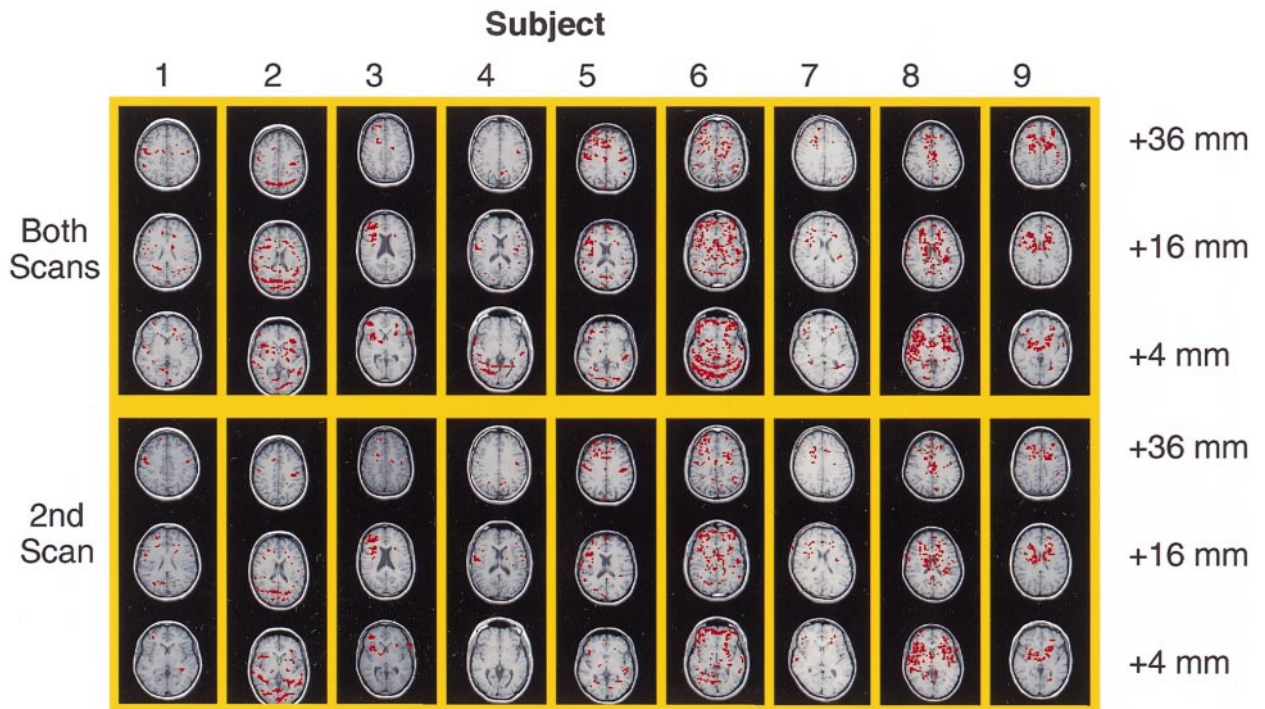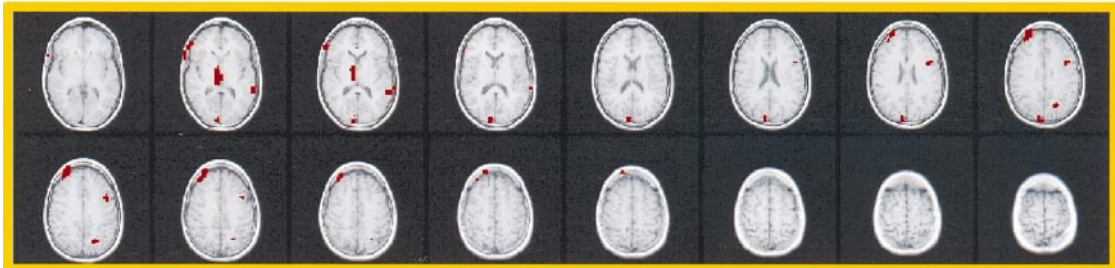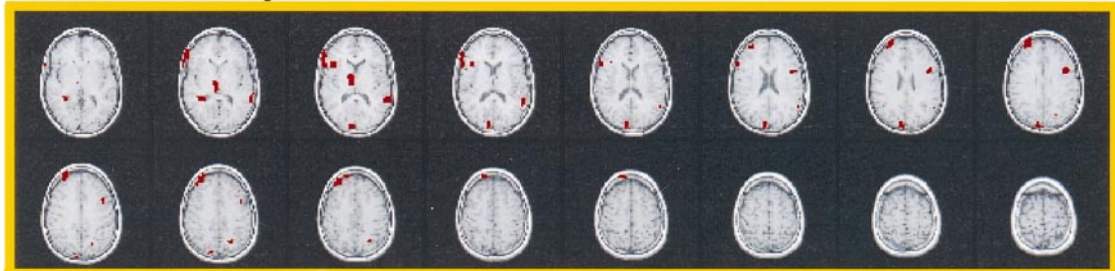
FIG. 2


FIG. 3

FIG. 2. Regions exhibiting significantly greater activation during overt compared covert responses. For each subject, three example slices are shown, one set for results using both scans within a trial and one set for results using only the second scan. The slices are approximately +4 mm *Z*, +19 mm *Z*, and +34 mm *Z*. Regions were identified as described in the text and are shown in axial slices overlaid on corresponding anatomical images. Images are displayed in radiological convention, with the right side of the image corresponding to the participant's left.

FIG. 3. Regions exhibiting significantly greater activation during incongruent than neutral trials during overt responses for the group analysis. All 16 slices are shown. Regions were identified as described in the text and are shown in axial slices overlaid on corresponding anatomical images. Images are displayed in radiological convention, with the right side of the image corresponding to the participant's left.

Both Scans

Second Scan Only

FIG. 4

+ 36 mm   +12 mm

a

+ 40 mm   + 32 mm   + 20 mm   + 16 mm

b
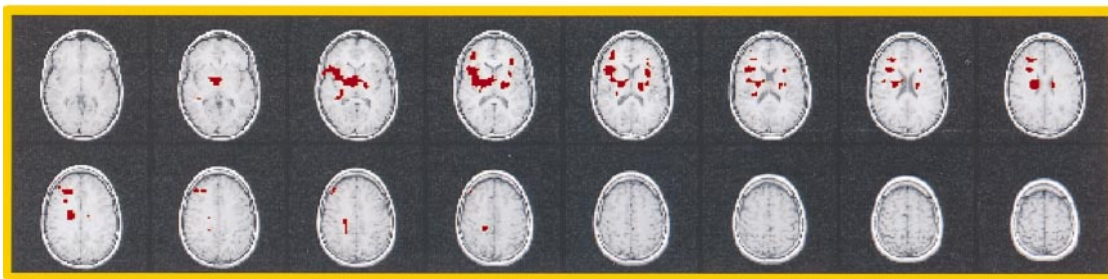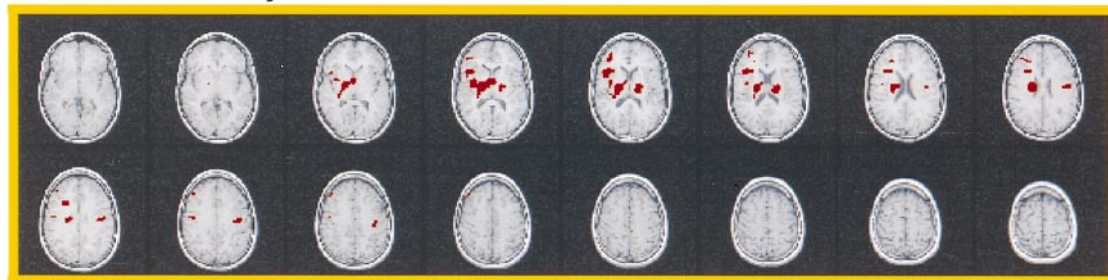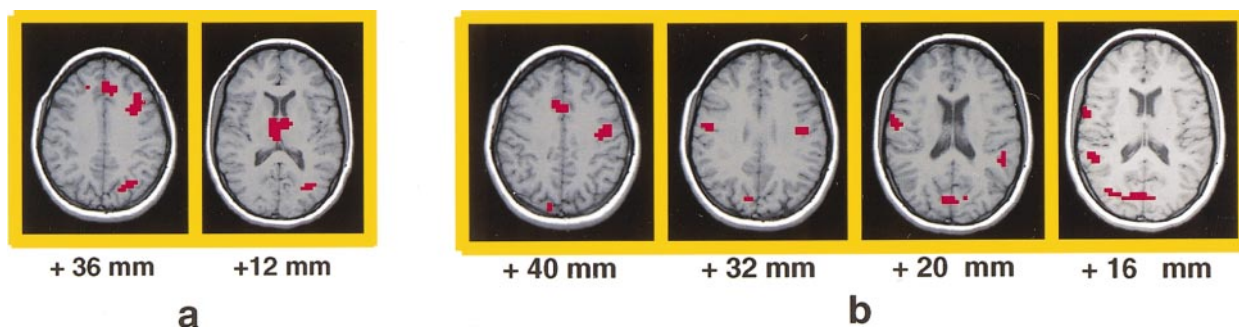
FIG. 6

FIG. 4. Regions exhibiting significantly greater activation during overt as compared to covert responses for the group analysis. All 16 slices are shown. Regions were identified as described in the text and are shown in axial slices overlaid on corresponding anatomical images. Images are displayed in radiological convention, with the right side of the image corresponding to the participant's left.

FIG. 6. (a) Regions exhibiting significantly greater activation during overt verb generation than overt word reading. Regions were identified as described in the text and are shown in axial slices overlaid on corresponding anatomical images. Images are displayed in radiological convention, with the right side of the image corresponding to the participant's left. (b) Regions exhibiting significantly greater activation during overt word reading than covert word reading.

participant analyses, though they were not present in all participants.

In contrast, for covert responses, no regions showed significantly greater activity in incongruent than neutral responses. This result was somewhat surprising, as one might have expected at least BA 44/45 and BA 10 to be active in the group analysis of the incongruent versus neutral comparison for covert responses (since several of the individual subjects showed activity in these regions). To quantitatively compare the results for overt and covert responses, we conducted 2-way

ANOVAs on the regions identified in the contrast of incongruent and neutral conditions for overt responses. We used both response (overt, covert) and condition (neutral, incongruent) as within-subject factors. Three of the eight ROIs (dorsolateral PFC, temporal cortex, and thalamus) demonstrated significant response by condition interactions ($P < 0.05$), such that the difference between incongruent and neutral conditions was significantly greater with overt than covert responses. Further, of the remaining five regions, only two (visual and extrastriate cortex) demonstrated a significant

TABLE 3

Study One: Regions Showing Greater Activation in the Incongruent than the Neutral Condition for Overt Responses for the Group Analysis

Regions of interest	Brodmann area(s)	X^a	Y^a	Z^a	Volume $(mm^3)^b$
Supplementary motor cortex	8	19	54	43	552
Extrastriate cortex	19	−22	−63	34	844
Dorsolateral prefrontal	9	33	52	31	4012
Inferior frontal cortex	44	−42	9	29	1524
Visual cortex	18/19	9	−90	22	1580
Superior temporal cortex	22	−60	−38	11	1048
Thalamus	—	7	−13	9	2048
Inferior frontal cortex	44/45	62	32	7	1292

[a] X, Y, and Z are coordinates in a standard stereotactic space (Talairach and Tournoux, 1988) in which positive values refer to regions right of (X), anterior to (Y), and superior to (Z) the anterior commissure (AC).

[b] Volume refers to the number of voxels (converted to mm³) that reached statistical significance in each region of interest.

increase in activity for incongruent compared to neutral condition for covert responses ($P < 0.05$). The lack of significant activity in the comparison of the two covert response conditions might have been related to threshold effects, in that prior studies suggest that the magnitude of the cortical response is reduced with covert responses. To examine this possibility, we dropped the threshold to $P = 0.10$ and 8 pixels. With this lower threshold, we did see activation in regions similar to those seen in the comparison for overt responses, including BA 46/9, BA 44/45, and BA 18/19.

We next directly compared overt and covert responses. As with the individual participant analyses, there were a few areas of what might be considered movement related activation (Fig. 4). However, with the group analyses, this pattern was much less striking than with the individual participant data. For example, in the group data, we did not see continuous bands of activation centered around the axis of rotation for speech-related movement, and we did not see much activity at the very edge of the brain and outside of the brain. However, the group analysis did not reveal clear activation in some regions that would be expected for a contrast of overt and covert responses, such as activity in primary motor or supplementary motor regions.

We next repeated the above analyses for the second scan of each trial only. For covert responses, the results of these analyses were identical to the analyses of both scans for each trial. No areas of activity were found that demonstrated greater activity in the incongruent than the neutral condition. For overt responses, analyzing only the second scan identified all of the regions found when analyzing both scans (see Fig. 3). However, analyzing only the second scan did identify an additional area of activation in right temporal cortex (BA 22),

an area of activation that had been previously found in the Stroop task (Carter *et al.,* 1995; George *et al.,* 1997; Pardo *et al.,* 1990). To quantify the results for the first and second scans, we conducted 2-way ANOVAs on the regions identified in the contrast of incongruent and neutral conditions for the second scan only. None of these regions demonstrated a significant scan (first versus second) × condition (neutral versus incongruent) interaction. Further, all but one of the regions identified using only the second scan data also showed significantly greater activity in the incongruent as compared to neutral condition when only the data from the first scan was analyzed. The only region not showing such a significant effect was the additional temporal cortex activation newly identified in the analysis using only the second scan. Thus, for overt responses, analyzing only the second scan had a positive, though relatively moderate, impact.

For the direct comparison of overt and covert responses, analyzing only the second scan had a positive impact. As can be seen in Fig. 4, analyzing only the second scan revealed clear bilateral activation of BA 6, activation of right BA 46 and BA 44, and bilateral thalamus activation. However, even when analyzing only the second scan, at least one area of activation remained that appeared to be in white matter near the ventricles. To quantify the comparison of the results for the first and second scans, we conducted 2-way ANOVAs on the regions identified in the contrast of overt and covert responses for the second scan only. None of these regions demonstrated significant scan (first, second) × response (overt, covert) interactions. In addition, 5/7 regions identified using only the second scan data demonstrated significantly greater activity with overt than covert responses when only the data from the first scan were analyzed ($P < .05$). However, interestingly, the two regions in motor cortex that only showed up in the analyses for just the second scan did *not* demonstrate significant effects of response (overt versus covert) when only the data from the first scan was analyzed.

DISCUSSION

The results of Study One begin to shed light on the feasibility of acquiring overt verbal responses during fMRI scanning. The most important result is that when comparing two different cognitive conditions (i.e., incongruent versus neutral), which both utilize overt verbal responses, very little movement-related artifactual activation is apparent. This finding was most striking in the group analysis, where the obtained pattern of activation was much more consistent with true cognitive-related activation than artifactual movement-related activation. We make this claim for two reasons. First, in the group analysis, the regions of activation

were in locations previously seen in PET studies of the Stroop task, including SMA (Carter *et al.,* 1995; Pardo *et al.,* 1990), dorsolateral prefrontal cortex (Derbyshire *et al.,* 1998; George *et al.,* 1997), inferior frontal cortex (Derbyshire *et al.,* 1998), and superior temporal cortex (Carter *et al.,* 1995; George *et al.,* 1997; Pardo *et al.,* 1990). Second, the pattern of activation was very different than that typically found with strong movement-related confounds. For example, we did not find multiple small areas of activation at the edge of the brain, nor did we find activation in either the ventricles or the white matter around the ventricles, both of which are classic signs of movement-related artifacts. The absence of such movement-related confounds in the incongruent versus neutral condition comparison for overt responses is most apparent when contrasted with the results of the overt versus covert response comparison.

In fact, one might wonder why so little movement-related artifact was seen in the analyses comparing the incongruent and neutral conditions for overt responses. The most probable answer is that motion-related effects were occurring in both conditions for these analyses, since both utilized overt responses. As such, when the two overt verbal response conditions were compared, there may not have been consistently greater artifact in one condition versus the other. If so, this result suggests that comparing two conditions that both utilize the same response modality is a feasible experimental strategy, which may generate usable data even without the use the additional techniques to reduce motion-related artifacts.

Susceptibility Artifacts

As discussed previously, in Study One we did not scan through the region of the throat and mouth in order to avoid at least some of the artifacts that could arise from changes in the volume of the sinus cavities and the posterior pharynx, as well as through tongue movements. With this scanning choice, visual inspection of the images did not demonstrate any glaring qualitative evidence of ghosting, geometric distortion, or blurring of the fMRI data associated with overt verbal responses. However, quantitative analyses did indicate significant reductions in SNR associated with overt verbal responses. The magnitude of this reduction was relatively small in more superior regions, but did approach 20% in the more inferior slices, close to the throat and mouth regions. Interestingly, these SNR reductions during overt responses did not appear to impair our ability to detect significant activations associated with cognitive processing in the Stroop task. In fact, if anything, our power to detect cognitive process-related activation appeared greater for overt than covert responses for the group analyses. As such, our results suggest that it is possible to avoid at least

some of the artifacts associated with verbal responses by not scanning through the mouth and throat. However, it should be noted that the tradeoff of this choice is the inability to acquire information about regions of the brain close to the mouth and throat. Given that some of these regions may be involved in language production and processing (e.g., inferior temporal regions), further research is needed on other methods of avoiding susceptibility artifacts that would allow for acquisition of data within these regions.

Covert versus Overt

The analyses of the individual participants did not reveal systematic differences in the regions of activation found for overt versus covert responses when comparing the incongruent and neutral conditions. However, strong differences emerged between covert and overt responses in the group analyses. Specifically, for the comparison of the incongruent and neutral conditions for overt responses, activation was seen in several regions typically found in the Stroop task (e.g., Carter *et al.,* 1995; Derbyshire *et al.,* 1998; Pardo *et al.,* 1990). In contrast, no regions of activation were found in the comparison of the incongruent and neutral conditions for covert responses when the same significance level was used. However, when the significance level was dropped considerably for the covert response comparison, activity was seen in similar regions to those found in the overt response comparison. This result is consistent with the results of previous studies comparing overt and covert responses, many of which have found less activity with covert responses (e.g., McCarthy *et al.,* 1993; Zelkowicz *et al.,* 1998). As such, the findings from our study, as well as those from other studies in the literature (Bookheimer *et al.,* 1995; Price *et al.,* 1996; Rumsey *et al.,* 1997), suggest that the use of covert responses as a substitute for overt responses is problematic. One may miss important areas of activation when using covert responses, and it may not be possible to make firm inferences about the cortical regions engaged when overt responses are required from studies using covert responses.

Use Only Data Acquired after Overt Responses
Have Been Completed

The effects of discarding data acquired during the actual production of overt responses varied according to the type of analyses conducted. For the individual subject analyses, using the data from just the second scan did not have a positive impact on the results. In fact, when looking at the contrasts comparing the incongruent and neutral condition, analyzing only the second scan significantly decreased the number of subjects showing activity across the regions. In the group analyses, the impact of analyzing only the second

scan varied according to the nature of the contrast. For the analyses comparing two cognitive conditions (e.g., incongruent versus neutral) using the same response modality (covert or overt), analyzing only the second scan did not eliminate any regions of activation, and in fact, revealed an additional activation in BA 22 (temporal cortex). Activity in BA 22 has been found in previous studies of performance on the Stroop task. Thus, analyzing only the second scan for the incongruent versus neutral comparison in the group data had a positive, though relatively limited impact.

For the comparisons of the overt and covert response conditions, analyzing only the second scan had a more positive impact in the group analyses. Specifically, analyzing only the second scan revealed bilateral activation in regions involved in motor planning and articulation (i.e., BA 6), areas which would be expected to show greater activity when overt responses are elicited (e.g., Petersen *et al.,* 1989). Activity in these regions was not significantly greater for overt than covert responses when only data from the first scan was analyzed, and no activation in BA 6 was found in the analyses using both scans. However, analyzing only the second scan did not remove all movement artifacts. Thus, additional methods for removing overt response-related movement artifacts may be required, if the contrasts of interest involve comparing an overt response to a covert response condition. For example, Birn *et al.* (1998a), have proposed a method for removing motion-related artifacts in fMRI data that also capitalizes on the delay in the BOLD response to cortical activation. This method requires that paradigms be run in an event-related manner, with relatively long trials (e.g., 15 s) and several scans acquired during each trial. The authors propose removing motion-related effects by orthogonalizing each voxel time-course with respect to a theoretical signal intensity time-course that represents changes due to motion. Preliminary results with this method are promising and may provide an alternative strategy for interpreting data acquired during overt verbal responses.

Group Analyses

Of all the methods explored in this study for reduced movement related artifacts in data acquired during overt verbal responses, the use of a group analyses rather than individual participant analyses clearly had the most uniformly positive impact. Within the individual participant analyses, there was a great deal of variation in the regions activated across participants, and it was not easy to make clear inferences about similarities and differences between overt and covert responses. However, the group results were much more interpretable. For the comparison of the incongruent and neutral conditions for overt responses, the group analyses revealed a very reasonable pattern of activity.

There was no apparent movement-related artifact in the obtained pattern of activity. For the direct comparison of overt and covert responses, the benefit of conducting a group analysis was also apparent, particularly when analyzing only the second scan of each trial. In this latter analysis, relatively little movement-related artifact was apparent (only one region remained that appeared to be in white matter). At the same time, activation was seen in regions that would be expected for a direct comparison of overt and covert responses, including bilateral activation of BA 6 (Herbster *et al.,* 1997; Petersen *et al.,* 1989) and activation of right frontal cortex (Petersen *et al.,* 1989).

As discussed above, the improvement seen in the data with a group analysis is likely due to the fact that a group analysis looks for areas of activation that are consistent across participants. Although motion-related activation has a typical pattern (e.g., more likely at edges of the brain), the exact location and severity of such artifactual activations can vary across participants. Thus, conducting analyses with the data averaged across a group of participants, rather than analyzing each individual separately, may help reduce such artifactual activation. We should note that the positive impact of group analyses was not due to the smoothing used with the group data. We tested this hypothesis by reanalyzing the individual data with a smoothing kernel of 8 mm, with results essentially identically to those seen with the unsmoothed data.

STUDY TWO

The primary goal of Study Two was to evaluate the feasibility and validity of a method for acquiring the content of participants' responses during fMRI scanning. To do so, we used a classic verb generation paradigm (Frith *et al.,* 1991; Petersen and Fiez, 1993; Petersen *et al.,* 1989; Raichle *et al.,* 1994). We chose a verb generation paradigm because it is one that has been extensively studied using PET, but not fMRI, primarily due to the difficulties of acquiring verbal responses during fMRI scanning. Thus, demonstration of the feasibility and validity of acquiring the content of verbal responses in this paradigm seemed particularly appropriate.

METHODS

Participants

Informed consent was obtained from 14 neurologically normal right-handed participants. Participants were 6 males and 8 females, with a mean age of 27.2 (range 18 to 46). All subjects were given a pretesting session, in which they briefly practiced the task.

Cognitive Tasks

Participants performed three conditions: (1) overt verb generation (generate a use or action associated with visually presented nouns); (2) overt noun reading; and (3) covert noun reading. Participants observed stimuli on a visual display controlled by a Macintosh computer in the scanner control room running Psy-Scope software (Cohen *et al.,* 1993). Trials were blocked by condition. Each trial lasted 3.2 s, with a stimulus duration of 2 s and a 1.2-s intertrial interval during which a fixation cross appeared. The stimuli were 192 high frequency nouns, which varied in length from three to six letters. The stimuli used for overt verb generation versus overt word reading versus covert word reading were counterbalanced so that across all 14 participants, each word appeared equally often in all conditions. Participants performed the same task continuously within each 26-s block, and blocks contained 8 trials each. Four blocks of each of the three conditions were run in a pseudorandom order, such that all conditions were sampled once in every set of three blocks, yielding a total of 12 blocks.

Acquisition of Verbal Responses

We used a novel, but relatively simple, method to acquire participants' overt verbal responses during fMRI scanning. Participants' overt verbal responses were acquired through the use of a funnel, a plastic tube, and a condensor microphone attached to a standard tape-recorder. For each participant, an appropriately sized plastic funnel was placed over the region of their mouth and taped to the top of the headcoil. The use of this funnel helped isolate the participants' voices from the background noise of the scanner. We created several different size funnels to accommodate for differences in the size of participants' heads and the closeness of their faces to the top of the head coil. The size of the funnel used for an individual participant was chosen based on which was most comfortable to them and which provided the best fit. A plastic tube was then attached to the small end of the funnel and led out to approximately knee level on each participant. A condensor microphone was taped into the end of the plastic tube, and the microphone was attached to a standard taperecorder within the scanner room. The plastic tube was used to allow placement of the microphone outside the bore of the scanner. In pilot testing, we found that placement of the microphone within the bore of the scanner caused an unacceptable level of interference with the quality of the acquired responses.

Scanning Procedures

All image acquisition procedures were identical to Study One with the exception that a longer TR (1600 s) was used to acquire more slices. Twenty oblique axial slices (3.75-mm^3 voxels) were acquired parallel to the AC–PC line, with the middle of the third slice from the bottom on the AC–PC line. This provided 75 mm of brain coverage. Scanning was synchronized with stimulus presentation by means of a TTL pulse generated by the PsyScope software, which triggered the start of the scanner. One scan of all 20 slice locations was acquired during each 3.2-s trial (1.6 s TR with a 2-interleave Spiral sequence).

Movement Estimation and Correction

All functional images were corrected for movement using a six-parameter 3D automated algorithm (AIR; Woods *et al.,* 1992, 1993), using the same methods employed in Study One. This allowed us to obtain the same two sets of estimated movement parameters as were obtained in Study One.

Group Analysis Procedures

The procedures were identical to the group analysis procedures used in Study One.

RESULTS

Estimated Movement Data

We used one-factor ANOVAs to examine the estimated movement data, with condition (overt verb generation, overt word reading, covert word reading) as the within-subject factor and the six movement parameters (pitch, roll, yaw, X, Y, Z) as the dependent variables. The results of these analyses were very similar to those found in Study One. For incremental movement, the ANOVAs demonstrated main effects of condition for all six parameters (all $Ps < 0.05$; see Fig. 5). For all six parameters, the two overt response conditions (verb generate and word reading) had greater incremental movement that the covert word reading condition. However, overt verb generation and overt word reading did not differ significantly. As in Study One, however, the actual magnitude of the increase in incremental movement with overt responses was surprisingly small, with effect sizes ranging from 0.20 to 0.29 across parameters. For absolute movement from the reference image, there were no significant main effects of condition (all $Ps > 0.30$). Thus, as in Study One, these analyses suggest that participants were exhibiting small movements to and from their original head position during overt responses and were not progressively shifting farther away from their initial head position.

Quality of Response Recording

The audio tapes containing the participants responses were transcribed by a research assistant and
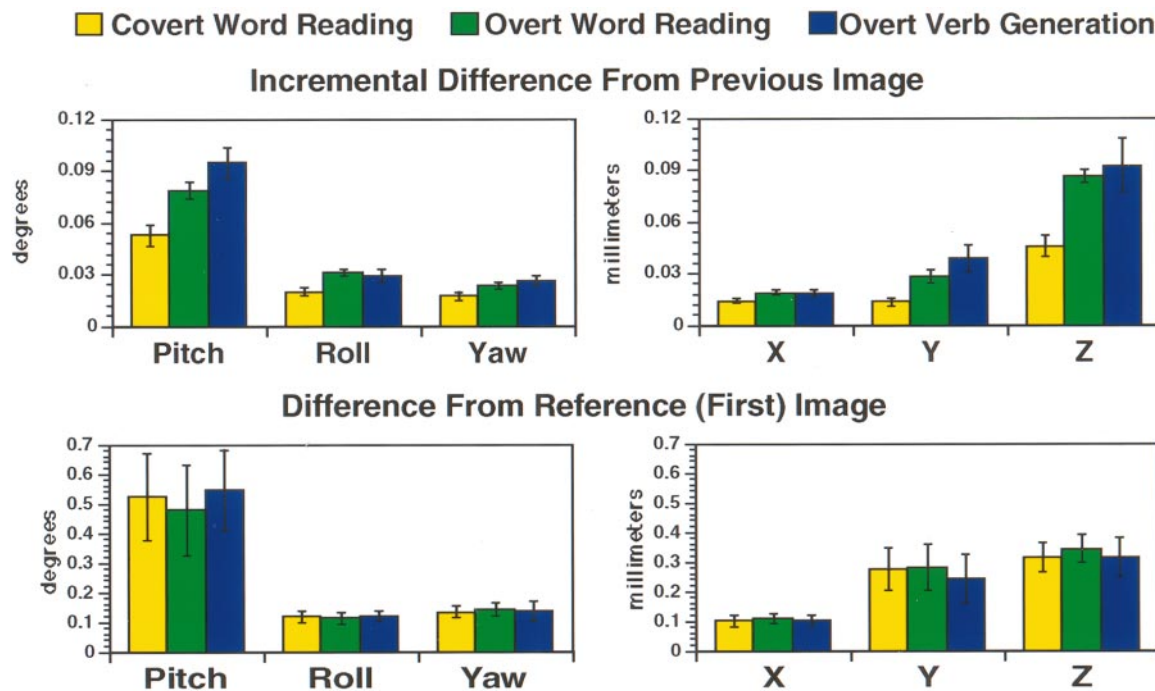
FIG. 5. Graph illustrating the magnitude of increased estimated movement with overt verb generation and overt word reading as compared to covert word reading.

checked for accuracy by the first author. Almost all responses were recorded clearly, and were able to be transcribed. The content of any response was ambiguous for only two participants, and for each of these participants, the ambiguity only occurred on two trials. At the same time, transcribing the content of the participants' responses clarified the importance of having a behavioral measure of participant performance. Specifically, we found three instances of participants *not* performing the task as instructed. One participant performed verb generation when they were supposed to be performing either covert or overt word reading, during two of the four blocks of overt and covert word reading. Another participant read words overtly instead of covertly during one block. Finally, another participant generated verbs covertly rather than overtly during their first block of verb generation. In all analyses presented below, the condition labels for images were corrected appropriately for the task actually performed by the participant.

Susceptibility Artifacts

To assess potential artifacts and SNR reductions associated with overt verbal responses in Study Two, we examined SNR maps for each individual participant, calculated using the raw data before movement correction was applied. We again calculated the mean SNR for each participant, for each slice location, separately for the overt and covert response conditions.

Visual inspection of the SNR maps again did not reveal glaring increases in ghosting, geometric distortion, or blurring associated with overt verbal responses. We then conducted paired-sample t tests to determine if SNR for any of the slices was significantly decreased during overt verbal responses. Similar to Study One, we found significant reductions in SNR associated with overt verbal responses, though not in all slice locations. SNR was significantly ($P \leq 0.05$) decreased during overt responses in slices 1–3 and slices 13–19. As with Study One, the SNR reductions were greater in the more inferior slices than in the more superior slices, although still relatively small. For example, the maximum SNR reduction in the more inferior slices was 14.7% in slice 19, while the SNR reduction was less than 3% for slices 1–12 (except for slice 2, which was 8%).

Verb Generation versus Overt Word Reading

We began by examining activity in regions associated with overt verb generation. To do so, we used planned contrasts that identified regions showing greater activity during overt generation than during overt word reading. An important point about this contrast is that it involved comparing two conditions that both utilized an overt verbal response. As was found in Study One, this contrast did not reveal any clear areas of artifactual activation that might be associated with verbal response-related motion. Instead, as shown in Fig. 6a

TABLE 4

Significant Activations in Study Two

Regions of interest	Brodmann area(s)	X^a	Y^a	Z^a	Volume $(mm^3)^b$
Overt verb generation versus overt word reading					
Anterior cingulate/SMA	8/32	1	27	38	3846
Left prefrontal cortex	46/44	−35	21	24	2951
Left parietal cortex	40/7	−27	−63	38	793
Left temporal cortex	39	−23	−70	9	2168
Thalamus	—	0	−9	16	9056
Overt versus covert word reading					
Supplementary motor cortex	8/32	4	14	35	817
Left motor cortex	6	−41	−9	35	1718
Right motor cortex	44/6	55	−2	18	2380
Left parietal cortex	40	−50	−36	23	601
Right temporal cortex	22	52	−39	17	596
Extrastriate visual cortex	18	11	−76	19	4091
Extrastriate visual cortex	19	14	−73	41	540

[a] X, Y, and Z are coordinates in a standard stereotactic space (Talairach and Tournoux, 1988) in which positive values refer to regions right of (X), anterior to (Y), and superior to (Z) the anterior commissure (AC).

[b] Volume refers to the number of voxels (converted to mm³) that reached statistical significance in each region of interest.

and Table 4, the pattern of activation included only regions that have been identified in previous PET studies of verb generation, including anterior cingulate, middle frontal gyrus, and temporal cortex (Frith *et al.,* 1991; Petersen and Fiez, 1993; Petersen *et al.,* 1989; Raichle *et al.,* 1994).

Overt versus Covert Word Reading

We next conducted planned contrasts that identified regions with greater activity during overt than covert word reading. Based on the results of Study One, we predicted that we would see at least some activation that appeared to be associated with movement-related artifact. This is because a contrast of overt and covert word reading compares a condition using an overt verbal response to a covert verbal response. Consistent with this prediction, we did see an area of activation in this comparison that may have been associated with movement artifact (see Fig. 6b; the most posterior ROI in the +16-mm slice). However, the pattern of activa-

tion (see Table 4 and Fig. 6b) was surprisingly clean, with activation in several regions that might be predicted to be greater during overt word reading, including primary and supplementary motor cortex (e.g., Petersen and Fiez, 1993; Petersen *et al.,* 1989, 1990).

DISCUSSION

We believe that the results of Study Two go far toward establishing the feasibility and validity of acquiring the content of participants' overt verbal responses during fMRI scanning. First, Study Two demonstrated that it is possible to record participants' responses during scanning and then to transcribe the content of such responses with a high degree of accuracy. More specifically, we were able to use a novel, but relatively simple method to acquire the content of participants' verbal responses during fMRI scanning. This method does not require elaborate equipment and can be easily implemented in most scanning environments. Further, this method provided an excellent degree of accuracy for transcribing the content of participants' verbal responses. With this method, future studies can now begin to examine a whole new range of research questions related to individual differences in the type of overt verbal response produced by participants. Further, this method for acquiring verbal responses provides a means to implement validity checks on whether participants are performing verbal response tasks as instructed. As our results demonstrated, even with fairly simple tasks, participants do not always perform as instructed. Thus, it is clearly critical to have a means to check participant compliance and performance. Unfortunately, however, we have not yet established a practical method for acquiring another important behavioral measure during overt response paradigms, namely reaction times. Reaction time information can also provide critical information about participant performance and would provide another valuable means to test hypotheses about the relationships between cognitive functioning and brain activation. We are continuing to work on this issue and are currently developing methods to collect accurate estimates of reaction times.

The results of Study Two also provided a replication of one of the primary results of Study One. Specifically, we again found that one could obtain interpretable patterns of brain activation during cognitive tasks utilizing overt verbal responses. As with Study One, these interpretable patterns of brain activation were achieved by using group analysis procedures, and by comparing conditions that both used overt verbal responses.

CONCLUSIONS

Taken together, the results of Study One and Study Two have several important methodological ramifications. First, we believe that our findings establish the validity and feasibility of using overt verbal response paradigms during fMRI scanning, given that two conditions are met. First, both studies suggest that the best quality data is obtained when one compares two conditions that both use overt verbal responses. As discussed previously, we believe that this is because motion-related effects occur in both conditions, and thus there is no systematically greater artifact in one condition versus the other. Thus, comparing two overt response conditions, when using a group analysis, allows us to generate statistical maps that reflect activity more related to cognitive functions of interest than to movement. Second, the results of Study One suggest that the quality of data obtained is much better with group than with individual subject analyses. Even when comparing two conditions that both used an overt verbal response, the individual participant analyses were still relatively noisy and difficult to interpret. It may be that group analyses are required to increase the signal-to-noise ratio and generate more clearly interpretable patterns of activation.

We also believe that the results of Study Two establish the ability to acquire the content of participants overt verbal responses during fMRI scanning. This has several important consequences. First, it means that investigators can now determine whether participants are performing the task as instructed during verbal response paradigms, providing a critical means to evaluate the source of any unusual or unexpected patterns of data. Second, this method allows for the possibility of testing a whole new domain of hypotheses that related to individual differences in the type of verbal responses produced by participants. We hope that the integration of these methods into future fMRI studies will help advance our understanding of the neurobiological mechanisms underlying a range of cognitive functions.

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