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| <b>14. ABSTRACT</b><br>Recent evidence suggests that underlying patterns of cortical activation may partially account for individual differences in susceptibility to the effects of sleep deprivation. Here, functional magnetic resonance imaging (fMRI) was used to examine the activation of military pilots whose sleep-deprivation vulnerability previously was quantified. A Sternberg Working Memory Task (SWMT; S. Sternberg, 1966) was completed alternately with a control task during a 13-min blood oxygen level-dependent fMRI scan. Examination of the activated voxels in response to SWMT indicated that, as a group, the pilots were more similar to fatigue-resistant nonpilots than to fatigue-vulnerable pilots. Within the pilots, cortical activation was significantly related to fatigue vulnerability on simulator-flight performance. These preliminary data suggest that baseline fMRI scan activation during a working memory task may correlate with fatigue susceptibility. |                               |                                |                                                  |                                                                          |                                                                    |
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## Are Individual Differences in Fatigue Vulnerability Related to Baseline Differences in Cortical Activation?

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Recent evidence suggests that underlying patterns of cortical activation may partially account for individual differences in susceptibility to the effects of sleep deprivation. Here, functional magnetic resonance imaging (fMRI) was used to examine the activation of military pilots whose sleep-deprivation vulnerability previously was quantified. A Sternberg Working Memory Task (SWMT; S. Sternberg, 1966) was completed alternately with a control task during a 13-min blood oxygen level-dependent fMRI scan. Examination of the activated voxels in response to SWMT indicated that, as a group, the pilots were more similar to fatigue-resistant nonpilots than to fatigue-vulnerable nonpilots. Within the pilots, cortical activation was significantly related to fatigue vulnerability on simulator-flight performance. These preliminary data suggest that baseline fMRI scan activation during a working memory task may correlate with fatigue susceptibility.

**Keywords:** functional magnetic resonance imaging, individual differences, sleep deprivation, aviation, fatigue

Fatigue and sleepiness from inadequate sleep are associated with generalized decrements in performance (Caldwell, Caldwell, Brown, & Smith, 2004; Dement & Vaughn, 1999), increased safety risks (Dinges, 1995; Leger, 1994; Mitler et al., 1988; Webb, 1995), and adverse health consequences (Briones et al., 1996; Buysse & Ganguli, 2002). On average, it has been estimated that

every 24 hr without sleep leads to performance declines of approximately 25%–30% (Angus & Heslegrave, 1985; Belenky et al., 1994). However, recent reports have made it clear that what is known about the average response to sleep loss obscures the fact that there are wide variations in individual responses to fatigue (Balkin et al., 2000; Van Dongen, Baynard, Nosker, & Dinges,

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2002; Van Dongen, Maislin, Mullington, & Dinges, 2003). Little is presently known about the magnitude of these between-individual variations in fatigue susceptibility. Also, the factors that underlie individual differences in fatigue vulnerability are presently unknown.

Although vast differences in the more general characteristics of individuals have long been recognized (Tyler, 1965), Wilkinson (1974) was evidently the first to make note of the fact that average group responses to stressors, such as sleep deprivation, do not accurately convey the impact of these stressors across different individuals. Since the time of Wilkinson's (1974) study, few other scientists have focused research on variations in individual responses to sleep loss. Morgan, Winne, and Dugan (1980) substantiated the presence of striking individual differences in the responses to acute sleep deprivation (44 hr of continuous wakefulness). In their study, the synthetic-work performance of some participants was degraded by as much as 40%, whereas the performance of others was essentially unaffected. Balkin et al. (2000) reported that systematic sleep restriction (chronic sleep deprivation) also produced differential amounts of degradations in different participants. Such divergent effects were observed on basic vigilance tasks as well as driving simulations. Caldwell et al. (2004) showed that even well-trained, fully experienced, military fighter pilots were not uniformly affected by fatigue. Although the flight-simulator performance of the group declined an average of 52% as a result of 26–37 hr of sleep deprivation, individual impairments ranged from 135% in one case to only 0.6% in another.

The factors underlying such differences in fatigue vulnerability have yet to be determined, but Mallis et al. (2001) and Van Dongen et al. (2002) have indicated that whatever accounts for individual variations in the responsiveness to fatigue is a relatively stable, trait-like characteristic. In other words, an individual who is fatigue resistant on one occasion likely will be fatigue resistant on others and vice versa. Van Dongen et al. (2002) found that participants who were exposed to two 36-hr sleep-deprivation periods were similarly affected on both occasions even though the periods were separated by 2–4 week intervals. Morgan et al. (1980) likewise found that participants who were subjected to four different 44-hr periods of sleep deprivation responded consistently on each occasion despite the fact that each sleep-loss period was separated by a 1-week interval. Thus, fatigue tolerance/vulnerability seems to be a relatively stable individual trait. However, it remains to be determined whether this trait can be predicted and used for practical purposes such as to select people who are particularly well suited for fatigue-inducing jobs.

There is limited evidence that the vulnerability to sleep loss may be related to overtly observable characteristics such as personality makeup, age, or measurable sleep needs, and such associations might help to identify fatigue-resistant individuals. For instance, neurotic extroverts appear to be more affected by sleep loss than nonneurotic extroverts (Blagrove & Akehurst, 2001); younger people seem somewhat less tolerant to sleep deprivation than their older counterparts (Belenky, Bliese, Wesensten, & Balkin, 2003); and participants who have greater sleep needs are often less fatigue resistant than those with lesser sleep needs (Blagrove & Akehurst, 2001; Van Dongen, Maislin, et al., 2003). However, none of these characteristics serve as an accurate litmus test for the presence or

absence of fatigue susceptibility, and for this reason, other possibilities, such as measurable physiological markers, are being explored.

The electroencephalogram (EEG) often has been used in an attempt to explain the changes in behavioral performance capacity known to occur during periods of sleep deprivation (Lorenzo, Ramos, Arce, Guevara, & Corsi-Cabrera, 1995; Pigeau, Heslegrave, & Angus, 1987; M. E. Smith, McEvoy, & Gevins, 2002), but no published documentation was found of successful efforts to use presleep-deprived EEG evaluations to predict individual susceptibility to sleep loss. In fact, even though low-frequency EEG activity has been used as a marker for the increased homeostatic sleep pressure that often adversely affects behavioral performance (Cajochen, Brunner, Krauchi, Graw, & Wirz-Justice, 1995; Cajochen, Khalsa, Wyatt, Czeisler, & Dijk, 1999), such data do not accurately predict individual susceptibility to fatigue. In fact, Aeschbach et al. (2001) found that although the kinetics of the homeostatic sleep drive (as measured via EEG) were similar in short sleepers and long sleepers, short sleepers were simply better able to tolerate higher homeostatic pressure than their longer sleeping cohorts. Thus, sleep needs alone (and by inference, electrophysiological measures of sleep pressure) are not sufficient to account for the trait-like interindividual differences in how individuals will respond to sleep loss (Van Dongen, Rogers, & Dinges, 2003).

Perhaps the underlying determinants of fatigue vulnerability will be found in the types of brain imaging studies in which researchers have begun to more precisely characterize the effects of sleep deprivation on global and regional central nervous system changes using positron emission tomography (Thomas et al., 2000) and blood oxygen level-dependent (BOLD) functional magnetic resonance imaging (fMRI; Allen, 2000; Drummond & Brown, 2001; Mu et al., in press-b). In fact, recent work by Mu et al. (in press-a) indicated that individual differences in fatigue vulnerability may be related to trait-like differences in global brain activation that are detectable prior to an episode of sleep loss. After conducting baseline fMRI scans on participants who were alternately performing a Sternberg Working Memory Task (SWMT; Sternberg, 1966) and a control task in the scanner, Mu et al. (in press-a) discovered that the fatigue-resistant participants had more global cortical activation (number of activated voxels) even in the non-sleep-deprived state than did the fatigue-vulnerable participants. This suggested an association between fatigue vulnerability and baseline brain activity that could be exploited in a selection context.

In the current research, we sought to determine whether baseline fMRI data could be used to predict fatigue susceptibility in a group of volunteers known to commonly encounter job-related sleep loss. To accomplish this objective, we merged performance data from a group of military pilots who had recently undergone sleep-deprivation testing during 37-hr periods of continuous wakefulness (Caldwell et al., 2004) with non-sleep-deprived fMRI data collected from these same pilots approximately 3–6 months after their period of sleep deprivation. The two data sets were examined for the presence of statistically significant correlations. Results from Mu et al.'s (in press-a) study led to the hypothesis that the baseline BOLD fMRI activation during the SWMT (Sternberg, 1966) would vary as a function of sleep-deprivation vulnerability, with

more resilient individuals having more baseline activation. This study was thus an attempt to test and extend the earlier work (Mu et al., in press-a).

## Method

### General

This research consisted of three phases. During the first phase, simulator-flight performance of 10 active-duty Air Force pilots was evaluated during 37 hr of continuous wakefulness. Testing was performed in an operational F-117 simulator-testing environment at Holloman Air Force Base (AFB), New Mexico. This phase quantified the impact of fatigue on piloting skills and characterized the extent of individual differences in fatigue vulnerability. During the second phase, 8 of these 10 pilots traveled to the Medical University of South Carolina (MUSC) in Charleston to participate in fMRI evaluations conducted under non-sleep-deprived conditions. This phase provided information about how the pilots' baseline cortical activation compared with the cortical activation of the fatigue-resistant versus fatigue-vulnerable nonpilots that were earlier assessed in Mu et al.'s (in press-a) study. During the third phase of the research, the fMRI data on the pilots (obtained at MUSC) were combined (in masked or blinded fashion) with the earlier-obtained flight-performance data, and correlational analyses were performed. This phase yielded information about the degree to which individual differences in fatigue vulnerability could be predicted by fMRI-derived differences in brain activation.

### Participants

**Pilot participants.** There were 10 F-117 fighter pilots who participated in the first phase of the study. The average age of this group was 35.7 years (range = 27–43 years). The participants were enrolled after signing an informed consent agreement (approved by the Air Force Institutional Review Board) and after passing a medical prescreen. For the second phase of the research, 8 of these 10 participants (mean age = 35.9 years; range = 30–43 years) agreed to participate in the fMRI imaging that was conducted at MUSC. These volunteers were enrolled after signing additional informed consent agreements (approved by the Air Force Institutional Review Board and the MUSC Institutional Review Board). In the third phase of the research, 1 of these 8 pilots was excluded from the correlational data analysis because of the fact that his performance (from the flight-simulator phase of the research) was found to be two standard deviations below the performance of the group as a whole, and this raised concerns about the motivational level of this particular individual. Data from the remaining 7 participants were retained for correlational analysis. The mean age of the participants who made up the correlational data set was 36.1 years (range = 30–43 years).

All of the pilots were in good health as evidenced by the fact that they all possessed recent flight physicals (F-117 pilots are required to pass physical examinations every 6 months to maintain their flight status). None were taking any type of medication known to have an impact on mental alertness. In addition, none of the pilots were working a nonstandard work schedule during any phase of the research. Thus, circadian factors would not have confounded their responses to sleep deprivation (in the first phase) or the validity of their fMRI data (in the second phase). As a group, the 7 pilots who made it into the third phase of the research reported an average of 7.7 hr ( $SD = 0.517$ ) of sleep prior to the flight-simulation testing at Holloman AFB and 6.7 hr ( $SD = 1.011$ ) of sleep prior to the fMRI scanning at MUSC. Their reported habitual sleep averaged 7.8 hr ( $SD = 0.424$ ) per night.

No data were collected on habitual caffeine consumption. Although caffeine use was restricted during the first phase of the research (the flight-simulation phase), no such restrictions on caffeine or other charac-

teristic preferences or behaviors were instated during the second phase of the research (the fMRI scan).

**Nonpilot participants.** For part of the purposes of the second phase of the research, 10 fatigue-vulnerable nonpilots and 10 fatigue-resistant nonpilots were identified from a large sample who had participated in a previous fMRI study on working memory following sleep deprivation conducted at MUSC. The demographics and brain imaging results of this full cohort have been reported elsewhere (Mu et al., in press-a); however, in general, the original sample of nonpilots consisted of 43 healthy male participants between the ages of 18 and 45 years, with no history of medical, neurologic, psychiatric, or sleep disorders. Participants who abused alcohol or drugs were excluded. These participants were recruited and participated in a MUSC study, approved by the MUSC Institutional Review Board, after providing a written informed consent. They habitually maintained normal sleep schedules of 7–9 hr per night, between 10:00 p.m. and 8:00 a.m. During the study, participants followed their regular sleep schedules to avoid circadian-related confounds. All participants performed the SWMT in the mornings after a normal night of sleep and again following 30 hr of sleep deprivation. The SWMT was chosen because it has been widely used as a verbal working memory task (Rypma & D'Esposito, 1999; Rypma, Prabhakaran, Desmond, Glover, & Gabrieli, 1999; Veltman, Rombouts, & Dolan, 2003) and has shown changes following sleep deprivation (Elkin & Murray, 1974; Polzella, 1975).

During the SWMT, participants were asked to judge whether a test letter was contained in a previously memorized short sequence of letters. Reaction times (RTs) and number of errors were recorded for each stimulus. The participants were presented with random sets of 1, 3, or 6 letters as a recognition set. Following a blank screen that represented a retention period, the participants were expected to recall whether a test letter was present within the recognition set. The SWMT lasted for 6 min, 24 s, not including a control task. The RTs were defined as the time from start of the presentation of the test letter to the occurrence of the response.

Of the original 43 nonpilot participants, 33 underwent fMRI scanning during the SWMT following both a normal night of sleep and following 30 hr of sleep deprivation. Following inspection of the changes in individual RTs from the SWMT after 30 hr of sleep deprivation relative to a normal night of sleep, 10 participants were classified as *fatigue resistant* because their RTs were shorter and their performance contained no more errors following sleep deprivation than during their non-sleep-deprivation baseline. A second age-matched and education-matched group of 10 participants was classified as *fatigue vulnerable* because their RTs were longer and their performance contained more errors following sleep deprivation than during their baseline. There was no significant difference between the two groups in age ( $28.2 \pm 6.0$  years in the fatigue-vulnerable group;  $27.8 \pm 5.3$  years in the fatigue-resistant group;  $p > .1$ ) and in education years ( $16.6 \pm 3.6$  years in the fatigue-vulnerable group;  $16.5 \pm 1.8$  years in the fatigue-resistant group;  $p > .1$ ).

### Apparatus

**Flight-simulator testing.** We conducted the first phase of the research at Holloman AFB (New Mexico) using the F-117 Weapon Systems Trainer (WST; L-3 Communications/Link Training and Simulation, Binghamton, NY) that is typically used as a training device and as one method for sustaining pilot proficiency in the actual F-117 aircraft. The WST is a stationary digital-device that simulates the characteristics and operations of the F-117A stealth fighter aircraft currently in the U.S. Air Force inventory. It provides a fully functioning replica of the interior cockpit of the actual aircraft, including all primary and secondary flight controls, aural cues (engine sounds), and cockpit lighting (L-3 Communications, 1993). The components of the WST include the simulator itself, as well as an instructor/operator station, a computer complex that includes an Alpha Server 8200 (Digital Equipment Corporation, Nashua, NH) and input/output cabinets, and the equipment necessary for the generation of out-of-the-window

visual scenes. We collected objective flight-performance data using the Coherent Automated Simulation Test Environment (L-3 Communications/Link Training and Simulation) tool—a set of software routines that normally provide the capability to evaluate simulator performance, display/manipulate various data from simulator data pools, and/or trace and correct problems. The trace use of the Coherent Automated Simulation Test Environment tool was used to capture various parameters of flight-performance data at a rate of 2 Hz throughout each flight.

**Neuroimaging.** The second phase of the research was conducted at the MUSC Imaging Center (Charleston, South Carolina). We acquired all images with a 3T MRI scanner (Intera, Philips Medical System, Andover, Massachusetts) using a send/receive single channel head coil. We acquired a set of T<sub>1</sub>-weighted axial structural images that encompassed the whole brain using the following parameters: return time (TR) = 625 ms, echo time (TE) = 20 ms, slice thickness = 5 mm, interslice gap = 1 mm, field of view (FOV) = 25.6 cm, number of slices = 24, matrix = 256 × 256. With the same slice coverage as with the structural scans, a whole brain gradient echoplanar imaging sequence was used to acquire data continuously on 24 slices in an ascending fashion in the axial plane for each functional scan. The parameters used were TR = 2,670 ms, TE = 40 ms, FOV = 25.6 cm, image matrix = 64 × 64, in-plane pixel size = 4 × 4 mm<sup>2</sup>, slice thickness = 5 mm, interslice gap = 1 mm. A total of 160 contiguous axial, high-resolution, 1-mm anatomical images were also acquired for each participant (matrix = 256 × 256, FOV = 25.6 cm). Functional analyses were conducted with statistical parametric mapping (SPM) software (Wellcome Department of Cognitive Neurology, London, England).

**Correlational analyses.** The third phase of the research did not involve additional participant testing but rather involved the merging and further analysis of data that had already been collected. The fMRI data analysis was performed at MUSC, where no personnel knew of the prior sleep-deprivation results. These blinded data were then shipped to the U.S. Air Force Research Laboratory (Brooks City-Base, Texas), where they were matched with the corresponding simulator-flight-performance data.

## Procedure

**Flight-simulation testing.** The first phase of the research was designed primarily to assess the impact of fatigue associated with 37 hr of continuous wakefulness on basic piloting skills. Secondly, we sought to examine the range of individual differences in susceptibility to fatigue in a group of well-trained, experienced pilots who were often required to work long hours on nonstandard (evening or night) schedules. The simulator flights in this phase of the research (at Holloman AFB, New Mexico) were set up for night-illumination conditions with zero visibility and no visible lighting on the horizon. In addition, the simulation environment was programmed to generate zero air turbulence with no wind gusts to prevent nonpilot-related flight-path deviations. The auto-throttle and auto-pilot modes (which can automatically maintain designated flight paths) were disengaged to force all participants to “hand fly” the simulator. Flight performance was monitored with a computer system that sampled headings, altitudes, air speeds, bank angles, and vertical velocities at a rate of 2 Hz throughout each flight.

This fatigue-susceptibility phase of the research involved a 3-day time commitment from each participant. During this phase, there were few restrictions on the participants' activities and schedules on the 1st day (a training day), but more structure was imposed on the 2nd day (this was the beginning of the sleep-deprivation period). For Day 2, the pilots were instructed to awaken at 0700 after obtaining approximately 8 hr of sleep. They also were instructed to refrain from napping between the wake-up time and the time at which they reported for testing. Compliance with both of these instructions was facilitated by requiring the pilots to wear wrist activity monitors. The data from these monitors also offered an objective estimate of sleep-duration times that could later be factored into the data

analysis. Participants were asked to refrain from caffeine consumption after 1000 in the morning on Day 2 (the 1st day of the sleep-deprivation period) and for the remainder of the testing period (until the conclusion of 37 hr of continuous wakefulness).

The schedule was as follows: On the 1st day, there were three training/familiarity sessions, and over the next 2 days, there were five testing sessions that covered the final 23 hr of the sleep-deprivation period. Training flights were conducted at 1400, 1700, and 2000 on Day 1. Testing flights were conducted at 2300 on Day 2 and at 0400, 0900, 1400, and 1900 on Day 3.

During each flight, participants completed 13 standardized maneuvers (2 right 360° turns, 1 left 360° turn, 5 straight-and-level segments, 1 climb and descent, 1 right-descending and 1 left-climbing turn, and 1 720° left turn) to assess the impact of fatigue on basic flight skills. The pilots were instructed when to begin each of the flight maneuvers by a console operator seated outside of the simulator. This console operator ensured that the correct flight parameters were being maintained before each maneuver was started, but no performance feedback was provided during the individual maneuvers. The exact same flight profile was flown on each of the three training sessions and each of the five testing sessions. In between the flights, participants were given rest breaks or administered other tests (Caldwell et al., 2003). They were released from the test facility following the 1900 flight on Day 3.

Analysis of the flight-performance data (performed on the data derived from all 10 of the participants) began by converting the raw flight data into root-mean-square errors to objectively quantify deviations from assigned flight paths. Next, the root-mean-square-error data were converted into scores that represented the percentage of change from baseline, with the last training session used as baseline. The following formula was used, which allowed decreases in performance to be represented by negative percent changes as well as changes greater than 100%:

$$\text{Percent change} = [(\text{baseline} - \text{score})/\text{baseline}] \times 100.00.$$

These data were analyzed with BMDP4V (BMDP Statistical Software, Version 7.0, Los Angeles) repeated measures analysis of variance (ANOVA) for time (2300, 0400, 0900, 1400, and 1700) and maneuver (right turn, left turn, climb, descent, left-climbing turn, right-descending turn, left 720° turn, and straight and level). Follow-up tests on the time main effect consisted of regression evaluations for the presence of linear, quadratic, and cubic trends (also calculated with BMDP4V). The maneuver main effect was not explored further for the purposes of this report, and in fact, the flight data used in the correlational analyses reported here were derived from composite scores (averaged across the various maneuvers—yielding one flight score per participant per session).

**Neuroimaging.** The second phase of the testing was designed to determine whether individual differences in fatigue susceptibility (noted from the first phase of the research) might be associated with differences in the brain activation that could be detected in the non-sleep-deprived brains of the pilots. For this part of the research, the fMRI data from the pilots were compared with fMRI data from fatigue-vulnerable and fatigue-resistant nonpilots. The fMRI scans conducted during this part of the research were performed at MUSC approximately 3–6 months after the pilots had completed the flight-performance evaluations discussed above. Eight of the 10 pilots agreed to participate in this second phase of testing. Five of the pilots were imaged in the morning, and 3 of the pilots were imaged in the afternoon (all on Thursdays).

Each of the pilots spent approximately 2 hr at the imaging center during which time they completed (a) a questionnaire regarding their previous night's sleep and their usual (habitual) amount of sleep, (b) a Visual Analog Scale that described their current level of sleepiness, and (c) an Epworth Sleepiness Scale that described their usual level of sleepiness. Following the collection of these data, each pilot completed an fMRI evaluation.

At the MUSC Brain Stimulation Laboratory, following the orientation and prior to scanning, the pilots practiced the SWMT task described earlier. Later, while they were being oriented to the fMRI scanner section, they again practiced the task a couple of times until they felt comfortable with the task prior to scanning. The SWMT performed during the fMRI scan was modified to fit an imaging design and to enable the acquisition of behavioral data within the scanner. Briefly, each functional scan consisted of 12 blocks. Each block included a control task (32 s) with an alternative Sternberg task (32 s), starting from control task. Each task contained two trials, with each trial lasting 16 s. The entire functional scan lasted 12 min, 48 s.

For the implementation of the SWMT in the scanner, an Integrated Functional Imaging System (IFIS; Gainesville, Florida) was used to display the letters and asterisks that allowed participants to view the stimuli on a liquid crystal display screen positioned in front of their eyes. Participants were instructed to hold two hand pads with their hands and to respond with their thumbs (left or right) to "yes" or "no" (this order was randomized between individuals). The control trial consisted of a 3-s viewing of 6 asterisks in 2 rows, followed by a 7-s delay, and then a 3-s viewing of either "yes" or "no" presented at the center of the screen. During the control trial, each participant was asked to press the appropriate button for "yes" or "no" when "yes" or "no" was presented on the IFIS screen in a randomized order. During the SWMT trial, arrays of either 1, 3, or 6 letters were randomized to display on the IFIS screen. Participants viewed the set of letters for 3 s (recognition). They then maintained this set in mind during a 7-s delay (retention). Subsequently, a probe letter was presented on the screen for 3 s, and participants responded either "yes" or "no" according to whether the probe letter had been included in the previously viewed set (recall). There was a 1.5-s time-out interval (rest) that followed presentation of the probe and another 1.5-s time-out interval before the display of the recognition letter(s). Participants were instructed to respond as accurately as possible. RTs and the number of errors were recorded within IFIS.

Functional analyses were conducted with SPM software. Echoplanar imaging scans (pilots and nonpilots) were corrected for motion and coregistered to the  $T_1$ -weighted structural images. After motion correction, all functional scans were found to contain residual motion movement that was less than 1 mm in any of the three planes and were thus included for further analysis. The functional images were then spatially normalized to SPM template and resampled with a voxel size of  $2 \times 2 \times 2$  mm<sup>3</sup> (Ashburner & Friston, 1999). After normalization, we spatially smoothed functional images using a Gaussian kernel with 6 mm of full width at half maximum to condition for random field theory that was applied to correct for multiple comparisons in SPM (Worsley & Friston, 1995). For creating individual  $t$  maps, the block design was convolved with a hemodynamic response function that approximated the activation patterns. We estimated effects at each and every voxel using the general linear model at the first statistical level. A box-car reference function modeled the activation blocks. The motion-recorded parameters generated during the realign process were applied to reject the motion-related activation at six user-specified regressors. A high-pass filter (cutoff frequency = 128 s) was used to remove possible effects of low-frequency changes. The activated and deactivated  $t$  maps were generated by defining the contrast  $(-1 \ 1 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0)$  and  $(1 \ -1 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0 \ 0)$ , where  $-1, 1$  represented the contrast of Sternberg task versus control task;  $1, -1$  represented the contrast of control task versus Sternberg task; and  $0$  indicated that the activation or deactivation associated with the motion movement would be rejected. Voxel values for the contrasts of interest yielded a statistical parametric map of the  $t$  statistic (SPM  $T$ ), subsequently transformed to the unit normal distribution (SPM  $Z$ ).

Eight individual contrast images generated at the first statistical level were used to create a group  $t$  map in a random-effects model (Friston & Frackowiak, 1997). In addition, 10 fatigue-vulnerable and 10 fatigue-resilient nonpilot group maps were created in the same way. Cluster analyses were performed on each group map at an identical threshold at

$p < .01$ . To protect against Type I error and correct for multiple comparisons across voxels, cluster thresholding was used to determine significant regions (Forman et al., 1995). Areas of significant activation were reported and compared only if they contained at least  $70 \times 2 \times 2$  contiguous voxels (cluster volume = 560 mm<sup>3</sup>), each individually activated at an a priori  $p < .01$ .

On the basis of the results of the cluster analysis, the number of activated voxels that passed  $p < .01$  were calculated from each individual  $t$  map in each selected region of interest (ROI) and were used to compare global and regional activation across three groups. ROIs were focused on the well-established brain regions involved in verbal working memory from previous imaging studies (E. E. Smith & Jonides, 1997, 1998), including the left dorsolateral prefrontal cortex (LDLPFC), the left posterior parietal cortex (LPPC), and the left ventrolateral prefrontal cortex (LVLPFC). The Sternberg task (Sternberg, 1966) used in the current study is a verbal working memory task (Rypma & D'Esposito, 1999; Rypma et al., 1999; Veltman et al., 2003). The functional anatomy involved in verbal working memory has been well investigated by researchers using neuroimaging approaches (Andreasen et al., 1995; Awh et al., 1996; Cohen et al., 1997; Jonides et al., 1998; Paulsen, Frith, & Frackowiak, 1993; Petrides, Alivisatos, Meyer, & Evans, 1993; Rypma & D'Esposito, 1999; Rypma et al., 1999; E. E. Smith & Jonides, 1997, 1999; E. E. Smith, Jonides, Marshuetz, & Koeppel, 1998; Veltman et al., 2003; Walter et al., 2003). Most of these studies have provided evidence that the left hemisphere is dominant for verbal processes (Jonides et al., 1998; Rypma & D'Esposito, 1999; Rypma et al., 1999; E. E. Smith et al., 1998; E. E. Smith & Jonides, 1998; Veltman et al., 2003). As a result, many related studies have focused the ROIs on the LDLPFC, LVLPFC, or LPPC. The right hemisphere has been demonstrated to be activated during spatial working memory, which is not an interest in the current study. It is still a matter of scientific debate whether the right hemisphere involves verbal working memory.

Regional hemodynamic time courses were individually extracted for each participant in the selected ROIs, first averaged across cycles within scan and then converted to percentage of signal change for each functional scan (Mu et al., 2004). In addition, global activated voxels were calculated on the basis of the group statements and individual  $t$  maps. Correlational analyses were conducted between participants' performance and brain activation (global activation in number of activated voxels, regional activation in number of activated voxels, and percentage of signal change).

*Pilot versus nonpilot group comparisons.* In the second phase of the research reported here (using the identical threshold mentioned above), data analysis consisted of comparing the global number of activated voxels from the 8 pilots who agreed to be imaged with the global number of activated voxels from two groups of nonpilots who had been evaluated during a previous investigation at MUSC. This was accomplished with a one-way, between-groups ANOVA (using BMDP4V univariate and multivariate ANOVA and analysis of covariance, including repeated measures). We further examined a significant overall group effect using pairwise contrasts. When the assumption of compound symmetry was violated in the ANOVA, Huynh-Feldt adjusted degrees of freedom were used.

*Within-pilots correlational analyses.* The next phase of the research involved merging the fMRI data from the 8 pilots who were imaged (excluding the 1 who was found to be a two standard deviation outlier in terms of simulator-flight performance) with the flight-performance data that were collected 3–6 months earlier at Holloman AFB. Therefore, 7 participants were included in this analysis. The brain activation included the global number of activated voxels as well as the activated voxels in the LDLPFC, the LPPC, and the LVLPFC. In addition, information about (a) the amount of sleep prior to the flight-simulation testing (based on actigraphy data), (b) self-reported habitual nightly sleep, (c) self-reported pilot flight experience (hours of flight time), and (d) the individual ages of each of the pilots was examined (correlated with the flight-performance data) to determine whether these could have confounded correlations between the

fMRI results and the performance results. Stepwise regression analyses, which provided simple and partial correlations, were conducted with BMDP2R (BMDP Statistical Software, Version 7.0, Los Angeles).

## Results

### *Effects of Continuous Wakefulness on Flight Performance (Phase 1)*

As noted above, the simulator-flight performance (measured 5 times during the final 23 hr of a 37-hr period of continuous wakefulness) was evaluated to determine the effects of fatigue on the group as a whole and on the individuals within the group.

**The overall group effect.** The two-way ANOVA that examined the impact of both testing time and flight maneuver on basic piloting skill revealed a time main effect,  $F(2.44, 21.93) = 10.72$ ,  $p = .0003$ , which was a function of significant linear ( $p < .05$ ), quadratic ( $p < .05$ ), and cubic ( $p = .05$ ) trends in the data. As can be seen in Figure 1, group flight performance degraded from 2300 to 0900, remained consistently poor from 0900 to 1400, and then recovered slightly (although not to predeprivation levels) at 1900. In addition to these effects, there was an overall difference among the individual maneuvers,  $F(4.79, 43.10) = 3.83$ ,  $p = .0064$ , but this finding was not considered worthy of follow-up because it is well known that some maneuvers are more difficult to perform than others. There was no Time  $\times$  Maneuver interaction, indicating that none of the maneuvers were more sensitive to the effects of fatigue than the others.

**The extent of individual differences.** There is no universally agreed on method for analyzing the magnitude of individual differences in the presence of a statistically significant group effect.

However, the data were visually inspected in an effort to gauge the extent of individual differences in the current research. Figure 2 shows that one of the pilots was largely unaffected by the sleep loss imposed in this investigation, whereas another was degraded by a full 135%. Although this most affected pilot was later excluded from the correlational analyses between flight-performance and fMRI data (for reasons described earlier), large individual differences nevertheless remained.

### *Similarities Between the Pilots (From Holloman AFB) and the Nonpilots From MUSC (Phase 2)*

Eight of the pilots who were evaluated in the continuous-wakefulness study subsequently agreed to participate in the fMRI component of this research, which resulted in three groups for comparison—pilots, fatigue-vulnerable nonpilots, and fatigue-resistant nonpilots. On completion of the imaging, the number of activated voxels from these individuals was statistically compared with the data collected from nonpilots who were earlier classified as fatigue resistant and as fatigue vulnerable (Mu et al., in press-a). The results of the one-way, between-groups ANOVA on the global number of activated voxels indicated that there was a statistically significant difference among the groups,  $F(2, 25) = 36.20$ ,  $p < .0001$ . Subsequent pairwise contrasts revealed that this overall effect was attributable to the fact that all of the groups differed from one another ( $p < .01$ ). As shown in Figure 3, upper left panel, the pilots were characterized by the greatest amount of global activation, the fatigue-resistant nonpilots were next, and the fatigue-vulnerable nonpilots evidenced the least amount of global activation.

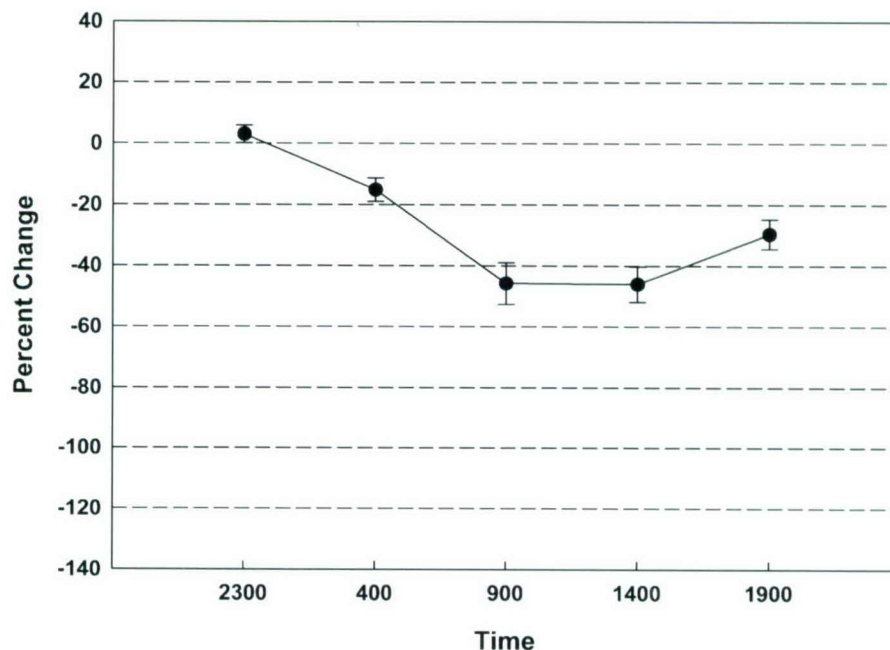


Figure 1. The overall group effects of continuous wakefulness on the accuracy with which the flight maneuvers were performed.

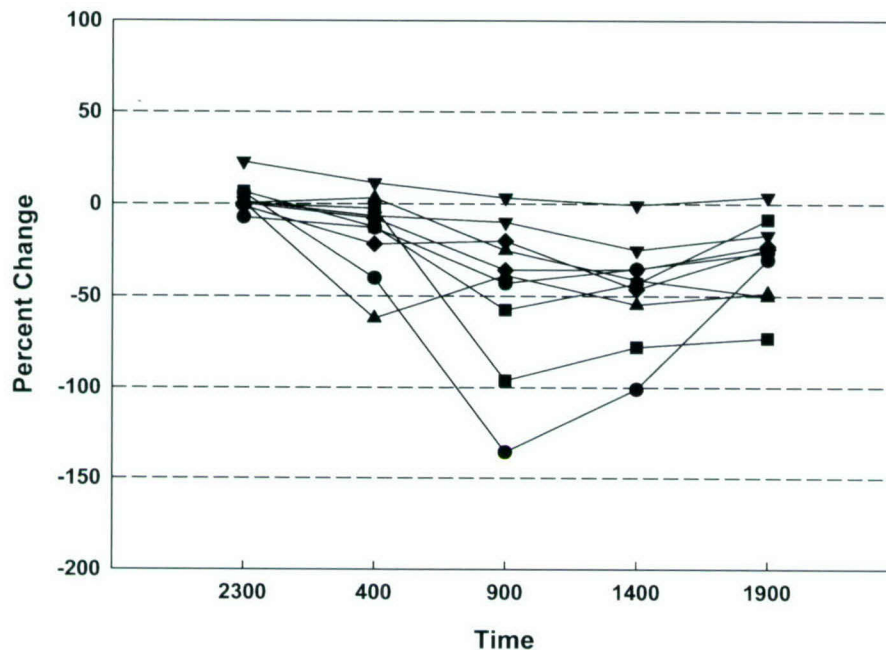


Figure 2. Individual variability in the effects of continuous wakefulness on the accuracy with which the flight maneuvers were performed. Each line represents one pilot's data.

In addition to the global number of activated voxels, brain activation in other brain regions involved in verbal working memory was analyzed. The results of the between-groups ANOVA on the number of activated voxels at these brain sites indicated a statistically significant difference among the groups at each of the sites: LDLPFC,  $F(2, 23) = 33.06$ ,  $p < .0001$ ; LPPC,  $F(2, 23) = 23.97$ ,  $p < .0001$ ; and LVLPFC,  $F(2, 23) = 3.44$ ,  $p = .0494$ . Contrasts between the groups indicated that more activation occurred in both the pilots and the fatigue-resistant nonpilots than in the fatigue-vulnerable nonpilots at areas LDLPFC and LPPC. In addition, the fatigue-resistant nonpilot group showed more activation in the LVLPFC than did the fatigue-vulnerable nonpilot group. These effects are shown in Figure 3. The results of the cluster analyses on the three groups are presented in Table 1, with comparison maps displayed in Figure 4.

In addition to the analysis of the number of activated voxels, analyses were conducted on the averaged percentage of signal change in the LDLPFC, LVLPFC, and LPPC of each of the participants. The ANOVA to determine differences among the groups indicated statistically significant effects for the LDLPFC,  $F(2, 23) = 11.92$ ,  $p = .0003$ ; the LVLPFC,  $F(2, 23) = 8.02$ ,  $p = .0023$ ; and the LPPC,  $F(2, 23) = 11.97$ ,  $p = .0003$ . Subsequent analyses indicated that the pilots had significantly greater percentage of signal changes in all three areas than did the fatigue-resistant and fatigue-vulnerable nonpilots ( $p < .01$ ). The two nonpilot groups did not differ from each other ( $p > .05$ ).

#### *Relationship Between fMRI Data and Fatigue Vulnerability in the Pilots (Phase 3)*

After the 8 pilots were imaged at MUSC, data on global and regional activation were correlated with data that showed the

average flight-performance decrement (each participant's average flight-performance data averaged across the five test sessions) and the maximum flight-performance degradation (each participant's lowest average flight-performance score from the five sessions, regardless of the time of day) recorded earlier from the continuous-wakefulness study. As noted earlier, 1 of the 8 pilots who agreed to be imaged in the fMRI phase was excluded from this analysis.

**Correlations with average flight performance.** The bivariate correlations conducted on the data from the remaining 7 pilots revealed a statistically significant relationship between average flight-performance score and the global number of activated voxels ( $r = .777$ ,  $p = .040$ ). The average flight performance and the activated voxels in the LDLPFC, the LPPC, and the LVLPFC were not significantly correlated ( $r = .2776$ ,  $.4978$ , and  $.4787$ , respectively). When partial correlations were calculated, the only variable to enter the equation was global activation ( $r = .777$ ,  $p = .0397$ ). The partial correlations for LDLPFC, LPPC, and LVLPFC were  $-.6060$ ,  $.1566$ , and  $-.5078$ , respectively. These simple correlations are shown in Figure 5.

Correlational analyses also were conducted between average deviation in flight performance and the averaged percentage of signal change in LDLPFC, LVLPFC, and LPPC of each of the participants. The simple correlations for LDLPFC, LVLPFC, and LPPC were  $.51$ ,  $.42$ , and  $.41$ , respectively. When stepwise regressions were computed, only LDLPFC entered the equation with a correlation of  $.51$  ( $p < .05$ ). The partial correlations (after removing the effects of LDLPFC) for LVLPFC and LPPC were  $-.03$  and  $-.07$ , respectively.

In general, pilots with the most global brain activation during the SWMT in the non-sleep-deprived state showed the greatest resistance to fatigue-related performance decrements during a pe-

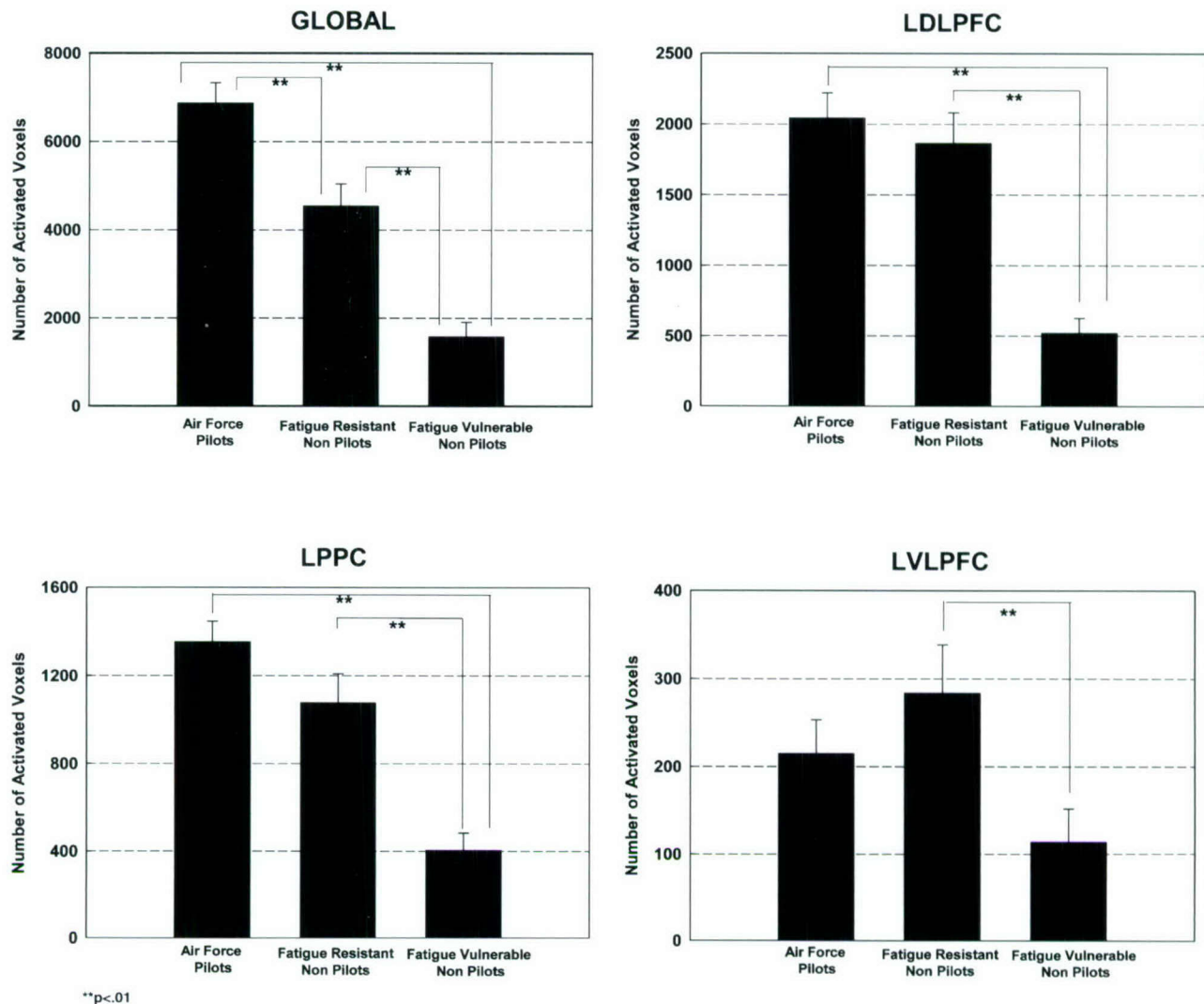


Figure 3. Comparisons of significantly global and regional brain activation in number of activated voxels. Global activation shows that the brain activation in the pilot group was more similar to what was observed in fatigue-resistant nonpilots than in fatigue-vulnerable nonpilots. Similar results are shown in regional activation in the left dorsolateral prefrontal cortex (LDLPFC) and left posterior parietal cortex (LPPC). The cluster threshold used as a cutoff was  $p < .01$ . LVL PFC = left ventrolateral prefrontal cortex.

riod of sleep deprivation. However, it needs to be pointed out that the BOLD fMRI signal is currently interpreted as mainly driven by a regional change in the ratio between deoxyhemoglobin and oxyhemoglobin. A relative decrease in deoxyhemoglobin, compared with oxyhemoglobin, would result in a signal increase due to the different magnetic properties. Thus, the brain activation is inferred from the relative change in blood oxygenation. This measure, in turn, is thought to mainly reflect local synaptic activity rather than neuronal spiking (Jueptner & Weiller, 1995; Magistretti & Pellerin, 1999).

*Correlations with maximum flight-performance deviations.* The bivariate correlation between maximum flight-performance

deviations and global activation in response to SWMT was similar to that observed between average flight-performance deviation and the global activation data (see Table 2). Note that the correlations between the average flight-performance data and the regional brain activation were weak except for the LPPC, which had a correlation of .690 (see Table 2).

Correlational analyses were also conducted between maximum deviation in flight performance and the averaged percentage of signal change in LDLPFC, LVL PFC, and LPPC of each of the participants. The simple correlations for LDLPFC, LVL PFC, and LPPC were  $-.24$ ,  $-.47$ , and  $-.83$ , respectively. When stepwise correlations were computed, LPPC entered the equation with a

Table 1  
Regions of Significant Activations Induced by the SWMT

| Brain region                       | BA        | MNI coordinates (mm) |     |     | Cluster size  |       |
|------------------------------------|-----------|----------------------|-----|-----|---------------|-------|
|                                    |           | X                    | Y   | Z   | No. of voxels | T     |
| Pilot group                        |           |                      |     |     |               |       |
| Left DLPFC                         | 9, 45, 46 | -40                  | 58  | 12  | 3,224         | 15.07 |
| Left VLPFC                         | 44        | -48                  | 20  | 0   | 524           | 19.46 |
| Left SMA involved in the right SMA | 6         | -2                   | 18  | 40  | 2,144         | 21.63 |
| Left posterior parietal cortex     | 7, 40     | -38                  | -66 | 38  | 2,072         | 13.20 |
| Left thalamus                      |           | -18                  | 0   | 10  | 388           | 6.46  |
| Left cerebellum                    |           | -42                  | -64 | -46 | 130           | 5.29  |
| Right DLPFC                        | 46        | 42                   | 0   | 28  | 196           | 6.64  |
| Right VLPFC                        | 44        | 24                   | 62  | -10 | 147           | 6.71  |
| Right premotor area                | 6         | 28                   | 8   | 64  | 89            | 5.77  |
| Right posterior parietal cortex    | 7, 40     | 28                   | -72 | 52  | 827           | 10.00 |
| Right thalamus                     |           | 12                   | 6   | 4   | 216           | 6.44  |
| Fatigue-resistant group            |           |                      |     |     |               |       |
| Left DLPFC                         | 9, 45, 46 | -56                  | 14  | 30  | 5,004         | 11.72 |
| Left VLPFC                         | 44        | -52                  | -4  | 28  | 712           | 8.74  |
| Left SMA involved the right SMA    | 6         | -12                  | -10 | 60  | 1,646         | 7.60  |
| Left posterior parietal cortex     | 7, 40     | -20                  | -74 | 24  | 2,357         | 8.72  |
| Left thalamus                      |           | -30                  | -34 | -20 | 262           | 7.24  |
| Right DLPFC                        | 9, 45, 46 | 34                   | 36  | 24  | 403           | 6.39  |
| Right VLPFC                        | 44        | 32                   | 28  | 4   | 735           | 6.41  |
| Right posterior parietal cortex    | 7, 40     | 28                   | -78 | 24  | 1,372         | 11.50 |
| Right thalamus                     |           | 16                   | -20 | 10  | 92            | 4.86  |
| Fatigue-vulnerable group           |           |                      |     |     |               |       |
| Left DLPFC                         | 9, 45, 46 | -42                  | -14 | 44  | 1,524         | 6.94  |
| Left VLPFC                         | 44        | -44                  | 34  | 0   | 336           | 6.22  |
| Left SMA involved the right SMA    | 6         | -8                   | 10  | 42  | 148           | 6.29  |
| Left posterior parietal cortex     | 7, 40     | -28                  | -82 | 26  | 1,178         | 9.98  |
| Left thalamus                      |           | -28                  | -16 | -24 | 149           | 6.71  |
| Right DLPFC                        | 46        | 48                   | 24  | 20  | 121           | 5.01  |
| Right VLPFC                        | 44        | 36                   | 6   | -20 | 443           | 5.03  |
| Right posterior parietal cortex    | 7, 40     | 34                   | -76 | 26  | 700           | 6.97  |
| Right thalamus                     |           | 20                   | -8  | -4  | 226           | 6.97  |

Note. Thresholds used in the clusters analyses were  $p < .01$  across the three groups. Voxel size =  $2 \times 2 \times 2$  mm<sup>3</sup>. SWMT = Sternberg Working Memory Task; BA = Brodmann area; DLPFC = dorsolateral prefrontal cortex; VLPFC = ventrolateral prefrontal cortex; SMA = supplementary motor area.

correlation of  $-.83$ . The partial correlations (after removing the effects of LPPC) for LDLPFC and LVLPFC were  $.32$  and  $-.04$ , respectively.

#### Relationship Between Flight Performance and Other Variables

To eliminate the possibility that the apparent relationship between the fMRI findings and the flight data was attributable to some confounding factor, an additional analysis was conducted on a variety of other potentially important data. In this stepwise correlational analysis, age, flight experience, amount of sleep prior to performance testing (recorded via actigraphy), amount of self-reported sleep prior to fMRI scanning, and self-reported habitual sleep were examined for the possibility of significant correlations, both with the average flight-performance decrement and the maximum flight-performance deviation. As shown in Table 3, although there were moderate correlations between some of the variables and either the average flight-performance deviation (i.e., sleep before the fMRI) or the maximum flight-performance deviation

(i.e., F117 flight hours, sleep before the fatigue study, and sleep before the fMRI), none of these correlations were statistically significant.

#### SWMT Performance

Although our primary focus in the current article was to explore whether different characteristics of brain activation appeared related to individual differences in fatigue vulnerability on a real-world task (flying an aircraft or aircraft simulator), several analyses were conducted on the results of the SWMT because it was an integral part of the fMRI scanning protocol. The results of the SWMT performance for each group are listed in Table 4. Using an ANOVA, our comparisons between the SWMT performance among the groups revealed statistically significant differences in the groups for correct RTs,  $F(2, 23) = 6.52$ ,  $p = .0057$ , and the RT slopes,  $F(2, 23) = 7.12$ ,  $p = .0039$ . Further analysis indicated the pilots had longer RTs and greater RT slopes than both the fatigue-vulnerable group and the fatigue-resistant group. This difference is probably meaningless because the pilots, unlike the nonpilots,

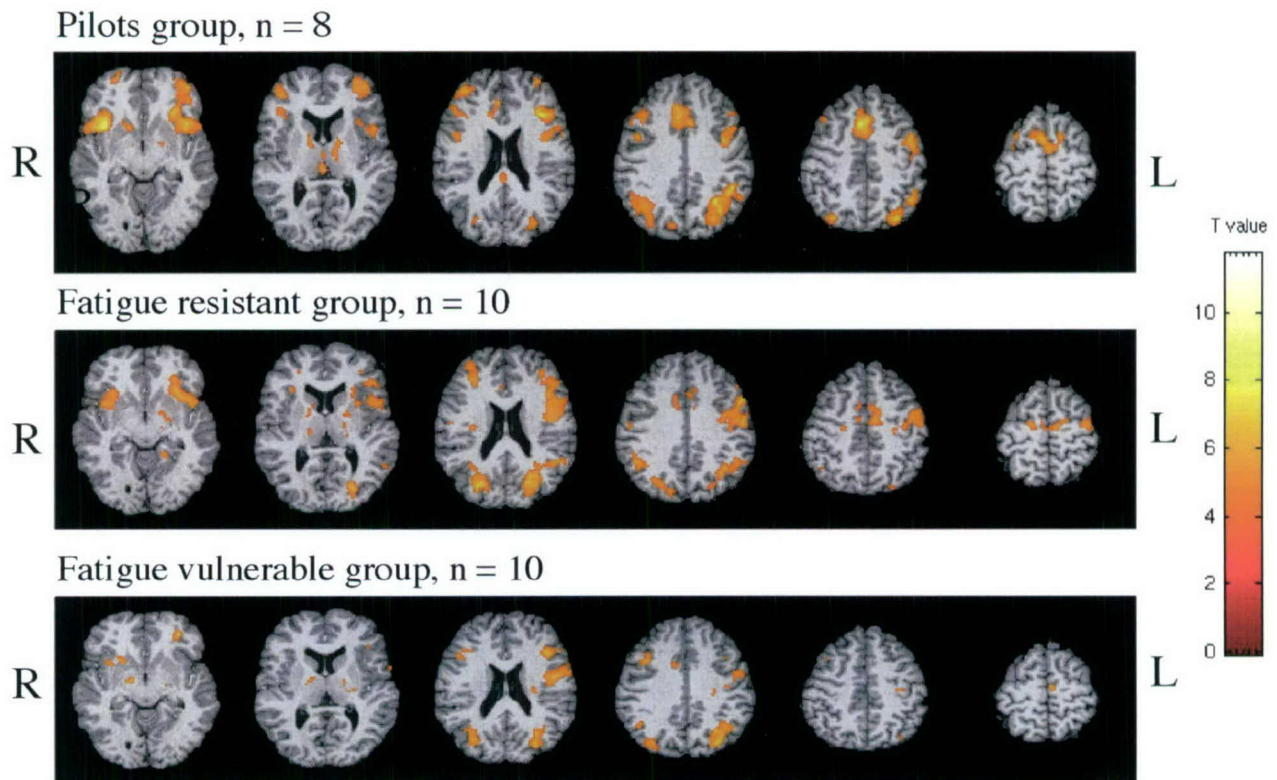


Figure 4. Maps of significantly activated brain regions during the Sternberg task within each group. Maps reached threshold at the identical  $p < .001$  and displayed at six different axial brain levels (from 16 mm below to 64 mm above the bicommissural plane). R = right hemisphere; L = left hemisphere.

were not trained to asymptote on this task because performance on the SWMT was not considered important in this particular phase of the investigation (during which the only purpose of the SWMT was to produce cognitive activation vs. sham for the purpose of fMRI imaging and, subsequently, for correlating activation data with flight-performance data). The two nonpilot groups did not differ significantly from each other. None of the groups differed in response accuracy on the SWMT.

These data were also examined to determine whether performance on the SWMT could be used to predict flight performance, because this would be a less-invasive, simpler test to use than a fMRI. However, results from this analysis indicated there were no significant relationships between performance on the SWMT and either the average flight-performance scores or the maximum flight deviation scores. Table 5 shows the correlations between flight performance and SWMT performance.

Finally, we performed stepwise correlational analyses to determine the relationship between SWMT performance and regional activation using both the number of activated voxels as well as the percent-signal-change data. All three groups were combined for this analysis to strengthen the power with the larger number of participants. Activation at the LDLPFC significantly correlated with RT for correct responses ( $r = .51, p = .0028$ ) and RT slope ( $r = .56, p = .0074$ ). The correlations for all variables are listed in Table 6.

## Discussion

In the current investigation, we reiterated the earlier findings of Caldwell et al. (2004) that there are significant fatigue-related decrements in the simulator-flight performance of experienced pilots who were kept awake for 37 continuous hr. Noticeable accuracy losses became especially apparent after 26–27 hr without sleep and continued throughout the remainder of the sleep-deprivation period. At these times, average group performance declined approximately 45% below well-rested levels. Such findings are consistent with previous reports demonstrating that fatigue impairs a variety of skilled performance as well as vigilance, alertness, and mood (Dinges, 1995).

In addition, the current research confirmed the existence of marked individual differences in fatigue vulnerability similar to those reported by Morgan et al. (1980); Van Dongen, Rogers, and Dinges (2003); and Wilkinson (1974). One of the 10 pilots described in the current research was virtually unaffected by sleep deprivation, whereas others suffered average performance decrements ranging from 11% to 60% and peak performance degradations ranging from 25% to 135%.

However, despite this level of individual variability in fighter-pilot performance, there was evidence from the fMRI scans that as a group, the current sample of F-117 pilots tended to be more physiologically fatigue resistant than another recently evaluated

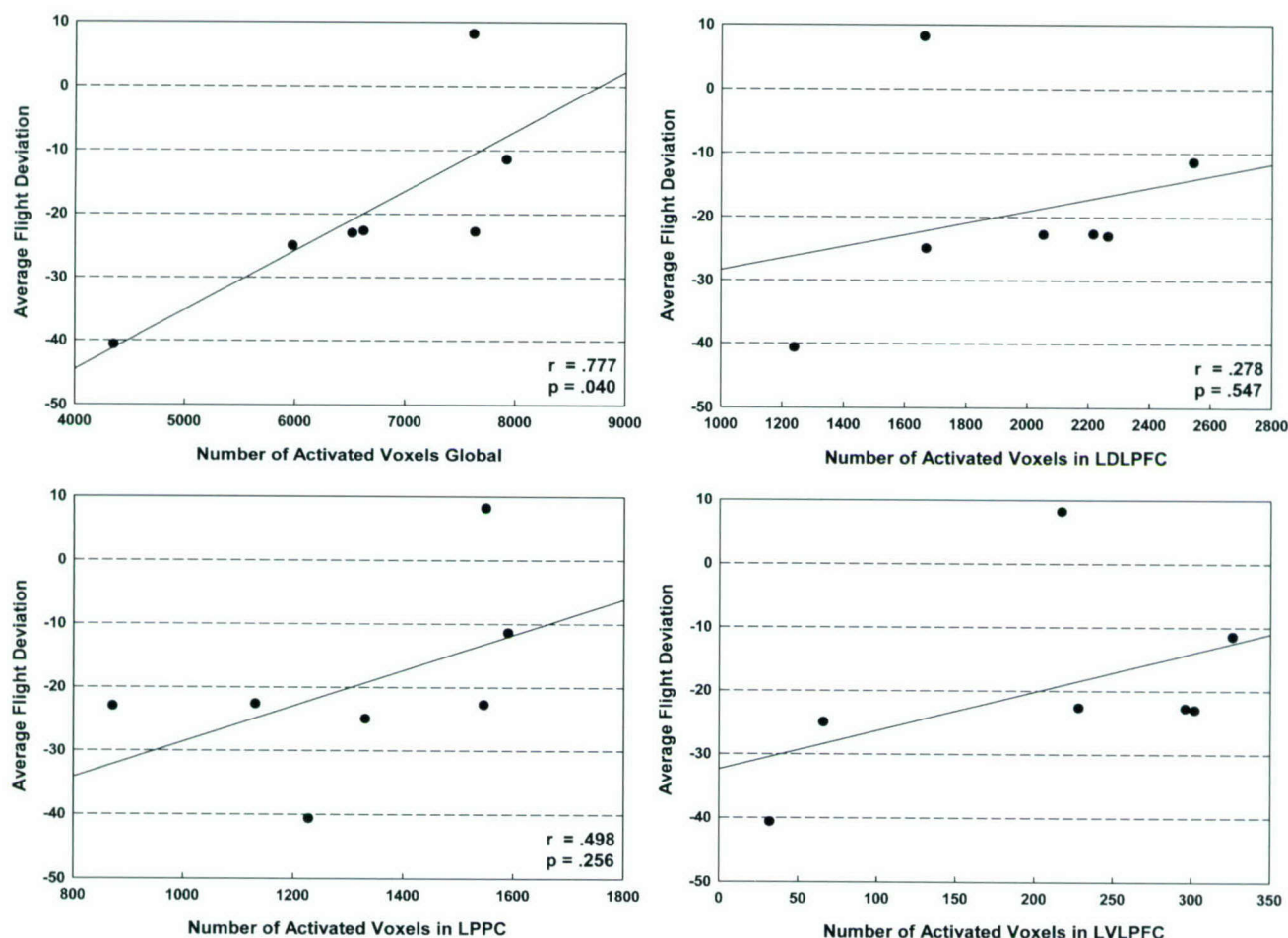


Figure 5. The correlation between the number of activated voxels, global as well as brain regions, and the average flight-performance accuracy of the pilots during sleep deprivation. LDLPFC = left dorsolateral prefrontal cortex; LPPC = left posterior parietal cortex; LVLPPC = left ventrolateral prefrontal cortex.

sample of nonpilot volunteers. The pilot fMRI data revealed baseline patterns of cortical activation that were more similar to those of the fatigue-resistant nonpilots tested earlier by Mu et al. (in press-a) than to those of the fatigue-vulnerable nonpilots tested in this earlier study. In fact, baseline scans indicated that the pilots and the fatigue-resistant nonpilots were characterized by an average of 6,870 activated voxels and 4,545 activated voxels respec-

tively, whereas the fatigue-vulnerable nonpilots had only 1,584 activated voxels during performance of the SWMT. In addition, there were similarities in areas of regional activation (associated with SWMT performance) between the pilot group and the fatigue-

Table 2  
Correlations Between Flight Performance and Brain Activation

| No. of activated voxels | Average flight performance | Maximum flight performance deviation |
|-------------------------|----------------------------|--------------------------------------|
| Global                  | .777                       | .670                                 |
| LDLPFC                  | .278                       | .093                                 |
| LVLPPC                  | .479                       | .271                                 |
| LPPC                    | .498                       | .690                                 |

Note. LDLPFC = left dorsolateral prefrontal cortex; LVLPPC = left ventrolateral prefrontal cortex; LPPC = left posterior parietal cortex.

Table 3  
Correlations Between Flight Performance and Potentially Confounding Variables

| Variable                        | Average flight performance | Maximum flight performance deviation |
|---------------------------------|----------------------------|--------------------------------------|
| Age                             | -.144                      | -.114                                |
| Total flight experience         | -.248                      | -.341                                |
| Flight experience in F-117      | -.125                      | -.501                                |
| Sleep before fatigue study      | .393                       | .538                                 |
| Self-reported sleep before fMRI | -.516                      | -.553                                |
| Self-reported habitual sleep    | .082                       | .204                                 |

Note. fMRI = functional magnetic resonance imaging.

Table 4  
Means (Standard Errors) From the SWMT

| Variable                     | RT for correct responses | Response accuracy | RT slope       |
|------------------------------|--------------------------|-------------------|----------------|
| Fatigue-vulnerable nonpilots | 736.93 (53.60)           | 0.95 (0.01)       | 200.26 (15.88) |
| Fatigue-resistant nonpilots  | 663.88 (65.42)           | 0.97 (0.01)       | 174.33 (21.34) |
| Pilots                       | 982.38 (66.53)           | 0.95 (0.02)       | 282.10 (23.34) |

Note. SWMT = Sternberg Working Memory Task; RT = reaction time.

resistant nonpilot group. This was the case for activation in both the LDLPFC, which is reportedly involved in working memory maintenance and information processes, and in the LPPC, which mediates the short-term storage and retrieval of phonologically coded verbal material (Jonides et al., 1998; E. E. Smith et al., 1998; E. E. Smith & Jonides, 1998) and may have a role in visual and spatial working memory processes. Thus, it is reasonable to expect that the functioning of these brain regions would have an impact on real-world tasks that rely on sustained information processing, continuous comparisons between current performance parameters in mentally stored reference parameters, and awareness of spatial orientation (such as flying an aircraft mission).

Taking both the global and regional data together, it appeared that the pilots as a group were quite fatigue resistant, assuming that an increase in baseline cortical activation is related to an increase in fatigue tolerance as postulated by Mu et al. (in press-a).<sup>1</sup> Further evidence that fMRI characteristics are related to fatigue resistance was offered by the series of within-group analyses used to correlate the pilots' flight data with their fMRI measures of global and regional activation. These analyses revealed statistically significant positive relationships between fatigue resistance (in terms of flight performance) and primarily the amount of global (rather than regional) cortical activation in response to SWMT. Thus, it appears that the greater the amount of general baseline cortical activation, the less performance will be affected by fatigue during a period of sleep deprivation—further confirming the earlier hypothesis set forth by Mu et al. (in press-a). This relationship does not appear to be confounded by participant characteristics such as age, experience, pretest sleep amounts, or habitual sleep needs, although the current small study does not obviate the need to examine these factors in a more systematic manner. In addition, because the pilot group was not trained to asymptote on the SWMT as were the other groups, a different task or a different level of performance on the SWMT may have yielded different

Table 5  
Correlations Between Flight Performance and SWMT Performance

| Variable                 | Average flight deviation | Maximum flight deviation |
|--------------------------|--------------------------|--------------------------|
| RT for correct responses | .44                      | .41                      |
| Response accuracy        | -.10                     | -.35                     |
| RT slope                 | .37                      | .26                      |

Note. SWMT = Sternberg Working Memory Task; RT = reaction time.

Table 6  
Correlations Between Performance on the SWMT and Results of the fMRI

| Variable             | No. of voxels |       |        | % signal change |                   |                   |
|----------------------|---------------|-------|--------|-----------------|-------------------|-------------------|
|                      | LDLPFC        | LPPC  | LVLPPC | LDLPFC          | LPPC              | LVLPPC            |
| RT correct responses | .20           | .18   | -.04   | .51             | -.07 <sup>a</sup> | -.03 <sup>a</sup> |
| Response accuracy    | .11           | -.003 | -.09   | .19             | .05               | .06               |
| RT slope             | .21           | .16   | .04    | .56             | -.13 <sup>a</sup> | .06 <sup>a</sup>  |

Note. SWMT = Sternberg Working Memory Task; fMRI = functional magnetic resonance imaging; LDLPFC = left dorsolateral prefrontal cortex; LVLPPC = left ventrolateral prefrontal cortex; LPPC = left posterior parietal cortex; RT = reaction time.

<sup>a</sup> Partial correlations after removing the effects of LDLPFC.

findings. This possibility also should be addressed in future studies.

The current study—in which active-duty military pilots were tested under conditions of sleep deprivation before later completing non-sleep-deprived fMRI scans—indicated (a) that as a group, even well-trained aviators suffer serious degradations in basic piloting skills, (b) that some pilots are clearly more affected by sleep loss than others, (c) that despite the observed decrements in group performance, the pilots appeared to be less fatigue vulnerable than two previously tested groups of nonpilots (based on the performance of a verbal memory task), and (d) that non-sleep-deprived fMRI evaluations possess use for predicting the degree to which specific individuals will be able to tolerate the fatigue from sleep deprivation (based on correlations between fMRI data and simulator-flight performance).

Further research is recommended to validate these findings in a larger sample of participants, to systematically explore the potentially confounding effects of individual sleep needs, and to determine whether increased fatigue resistance can be learned or otherwise developed. Also, it would be worthwhile to explore whether the use of different types of cognitive tasks during the fMRI scanning procedure affects the predictive use of these scans.

<sup>1</sup> Unfortunately, it is currently not possible to compare behavioral-cognitive fatigue vulnerability across the three groups (pilots, fatigue-vulnerable nonpilots, and fatigue-resistant nonpilots) because although the pilots completed the SWMT while at the imaging facility, they did so only under non-sleep-deprived conditions, and they were not trained to asymptote on the task. A future study hopefully will address this limitation by subjecting both the pilots and the nonpilots to comparable test conditions (sleep-deprived vs. non-sleep-deprived) and requiring comparable behavioral-cognitive testing procedures.

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