Mount Everest: A Space Analogue for Speech Monitoring of Cognitive Deficits and Stress

PHILIP LIEBERMAN, ANGIE MOREY, JESSE HOCHSTADT, MARA LARSON, AND SANDRA MATHER

LIEBERMAN P, MOREY A, HOCHSTADT J, LARSON M, MATHER S. *Mount Everest: a space analogue for speech monitoring of cognitive deficits and stress.* **Aviat Space Environ Med 2005; 76(6, Suppl.): B198–207.**

In deep-space missions, the basal ganglia and hippocampus, subcortical structures of the brain that play critical roles in motor activity, cognition, and memory, will be vulnerable to damage from cosmic rays. These metabolically active structures are also sensitive to damage arising from the low oxygen content of air at extreme altitudes. We have, therefore, used Mount Everest as an analogue for deep space, where astronauts will be subject to danger and stress as well as neural damage. We can ethically obtain data because our climber-subjects already intend to climb Mt. Everest. We record speech and test cognitive and linguistic performance before, during, and after exposure to hypoxic conditions. From these data we have derived and validated computer-implemented acoustic voice measures that track slight as well as profound cognitive impairment. Vowel duration and speech motor sequencing errors increase as climbers ascend, reflecting degraded basal ganglia activity. These metrics detect deficits in language comprehension and the ability to change plans in changing circumstances. Preliminary analyses also reveal memory deficits reflecting hippocampal damage. Our speech metrics are unobtrusive and do not reveal the content of a verbal message; they could be derived automatically, allowing space crews to detect subtle motor and cognitive deficits and invoke countermeasures before performance is profoundly impaired. In future work we will be validating the voice metrics of stress in collaboration with the Dinges NSBRI laboratory study of task-induced stress. Our procedures can also be applied in general aviation and in the treatment of Parkinson's disease, Alzheimer's dementia, and other neurological disorders.

Keywords: space analogue, cognitive performance, language comprehension, hypoxia, voice analysis.

DEEP-SPACE missions will expose crews to cosmic rays, which can damage structures of the human brain, including the subcortical basal ganglia and hippocampus (37,46). These structures play critical roles in neural circuits regulating motor control, cognition, personality traits, emotion, and contextual learning and memory. Crews will also be subject to stress arising from long voyages in restricted quarters and from external events. Stress, in itself, can adversely affect performance.

As a model for the neurological and stress-induced impairments that may occur in deep space, we have performed cognitive tests on and obtained speech samples from climbers ascending Mount Everest. The metabolically active structures of the basal ganglia and hippocampus are vulnerable to damage from the low oxygen content of air at extreme altitudes (2,5,6,17,19,22–24,41,46). Climbing Mt. Everest is inherently stressful, since it is almost a certainty that some deaths will occur. Our Everest space analogue is unique in allowing us to ethically study subjects at risk for brain damage in a life-threatening situation, since our subject population is restricted to climbers who intend to climb Mount Everest and have traveled there to that end.

Moreover, our Everest space analogue provides a unique control population unavailable in traditional "experiments in nature" such as studies of aphasia. We determine the speech and cognitive performance of individual subjects at Base Camp before exposure to hypoxia and stress and compare these data with performance at higher altitudes where increased hypoxia and greater levels of stress occur. We thus have been able to develop and validate speech measures that can track subtle as well as profound behavioral impairment. The speech measures are inherently unobtrusive; they reflect motor control rather than the content of a message, and no sensors need be attached to the body. The system's output could be made available to crewmembers, who could take appropriate countermeasures before serious deficits occur that compromise performance. An operational system could also be used to monitor cognitive deficits and stress remotely.

BACKGROUND

Recent advances in neurophysiology show that complex behaviors are regulated by neural "circuits" linking activity in different parts of the brain. The basal ganglia and other subcortical structures traditionally associated with motor control are key elements in cortical-striatal-cortical neural circuits that regulate language comprehension and adapting behavior to changing circumstances (1,10,14,15,25,27,28,38,39,43). Neural circuits linking frontal and posterior cortical areas to another subcortical structure, the hippocampus, are involved in forming and retrieving memories and the meanings of words (7,20,47–49).

From the Department of Cognitive and Linguistic Sciences, Brown University, Providence RI (P. Lieberman, J. Hochstadt, M. Larson, S. Mather), and the Department of Psychology, University of California at Berkeley, Berkeley CA (A. Morey).

Address reprint requests to: Philip Lieberman, Ph.D., Department of Cognitive and Linguistic Sciences, Brown University, Providence, RI 02912; Philip_Lieberman@brown.edu.

Although our brains contain many different neuroanatomical structures that carry out distinct operations, these structures usually do not, in themselves, regulate an observable complex behavior. An individual neuroanatomical structure generally contains many anatomically segregated groups, or populations, of neurons that carry out local operations. The neuronal population that carries out a local operation in a given part of the brain projects to anatomically segregated neuronal populations in other structures. Successive links between segregated neuronal populations in different structures form a neural circuit (1,10,14,15,20,25,27,28,38,49). It is the circuit rather than any one of the separate structures that constitutes the brain that is the basis of a complex behavior.

The subcortical structures that constitute the basal ganglia—the striatum (caudate nucleus and putamen) and globus pallidus—support circuits that sequence both motor and cognitive acts. Disruptions in behavior that are seemingly unrelated, such as Parkinson's disease (PD) (18), obsessive-compulsive disorder (16), and schizophrenia (14), derive from the disruption of basal ganglia operations in cortical-striatal-cortical circuits. The basal ganglia serve two basic functions in these circuits. They execute routine sequences of motor commands or mental operations, but they also respond to unusual circumstances to effect a change in the direction of movements and thought processes (13,14, 27,28,38,39). In subjects performing the Wisconsin Card Sorting Test, which involves grouping cards by color, shape, or number of symbols and then changing the sorting criterion, fMRI shows basal ganglia activity when the criterion is shifted (39). In PD (13,38) and at extreme altitudes (6,33,34), basal ganglia function is degraded, resulting in speech motor deficits and in cognitive inflexibility similar to that seen in patients with frontal lobe cortical dysfunction. Mildly and moderately impaired PD patients can exhibit deficits in speech production and the comprehension and production of linguistic syntax similar to those typical of Broca's aphasia (27,28,31,32,42). These syntactic deficits may derive from PD patients not being able to shift among the syntactic "rules" needed to comprehend different grammatical structures (27).

The basal ganglia and hippocampus, as well as the motor cortex, are sensitive to hypoxia, which commonly occurs in mountain climbers at extreme altitudes (2,5,6,17,19,22–24,41,45). The globus pallidus—the principal basal ganglia output structure linking the striatum to the cortex through the thalamus and other subcortical structures—is extremely vulnerable to hypoxic damage (6,19,22–24,41,45). In some circumstances damage may be permanent. Magnetic resonance imaging shows bilateral lesions in the globus pallidus and other basal ganglia structures resulting from exposure to altitude (6,19). Marked behavioral and cognitive disruption, similar to that seen following frontal lobe lesions, was noted for patients with bilateral globus pallidus lesions resulting from extreme hypoxia (23,24). Repeated ascent to altitudes exceeding 8000 m appears to cause permanent cognitive deficits (40) similar to the cognitive inflexibility seen in PD (13) and following surgically induced bilateral lesions to the globus pallidus (43).

GENERAL METHODS AND MEASURES

Speech Production

Studies of compromised basal ganglia activity have shown that one of the primary speech production deficits is a breakdown in sequencing the motor commands necessary to produce stop consonants. The stop consonants of English are produced by obstructing the mouth by closing one's lips (for b or p) or by placing the tongue blade (d and t) or tongue body (g and k) against the roof of the mouth. The obstruction then is abruptly released, permitting the resumption of airflow. The primary acoustic cue that differentiates "voiced" stop consonants such as "b" from "voiceless" stops such as "p" when they occur before a vowel (as in "bat" and "pat") is voice-onset time (VOT). When the speaker's lips abruptly open, a burst of turbulent air results that has distinct acoustic properties. The speaker must also adjust the muscles of the larynx to produce phonation subsequent to the burst. To produce a "b," phonation must occur within 25 ms of lip opening; longer delays will yield the sound "p." **Fig. 1** shows the waveforms of "ba" and "pa" with cursors superimposed that mark the onsets of the bursts and phonation that define VOT. Similar temporal sequences involving the tongue and larynx differentiate "d" from "t" ("do" vs. "to") and "g" from "k" ("god" vs. "cod"). This distinction by VOT appears to hold for all human languages (36). In some languages, phonation preceding the burst defines a third VOT category, "prevoicing."

Thus, speakers must precisely control the sequence of independent motor acts to produce these sounds. VOT sequencing deficits can occur in PD, which primarily affects the basal ganglia "sequencing engine." Computer-implemented analysis revealed significant overlaps between the VOTs of stop consonants such as "t" vs. "d" for some PD subjects (31); that is, VOTs for voiced consonants fell into the voiceless range, and voiceless into the voiced range. While these PD subjects also spoke at a slower rate, they maintained control over the relative durations that differentiate vowels, other durational speech phenomena, and tongue and lip movements.

To obtain measures of speech performance, we tape-recorded subjects as they read aloud, twice, a list of 30 monosyllabic English words starting and ending with stop consonants, such as "bat," "goat," and "dad." We measured VOT and other speech parameters, such as vowel and word duration, by marking the relevant acoustic events with cursors on the waveform display of the BLISS system, developed at Brown University by Dr. John Mertus (29). Subsequent computer programs automatically measured the time intervals, plotted histograms, and calculated means, standard deviations, and ranges for these parameters. The BLISS system also can produce conventional sound spectrograms, perform Fourier analysis of the speech spectrum, estimate the "formant frequency" patterns that distinguish among vowels and consonants, plot the fundamental

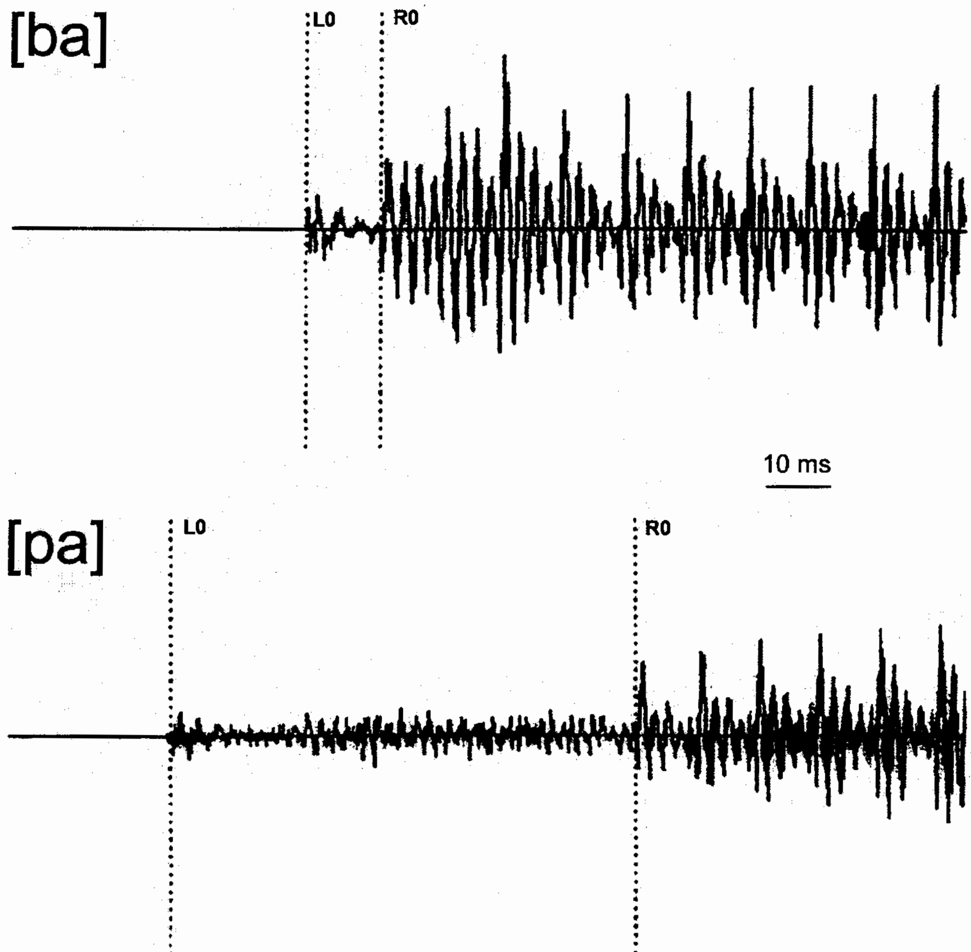

Fig. 1. Speech waveform segments corresponding to the syllables "ba" and "pa" spoken by the same speaker under identical conditions. Cursors have been placed at the onset of the burst caused by opening the lips (L0) and at the onset of periodicity that indicates vocal fold vibration (R0). The marked interval represents voice-onset time (VOT), which differentiates between the two stop consonants in word-initial position.

frequency (F0) contour of an utterance, and calculate "jitter," a measure of period-by-period variation in F0 (26). A number of these measures may provide important indices of emotion and stress.

Cognitive and Linguistic Tests

We administered sentence-picture matching tests similar to those previously used with PD patients and patients with bilateral basal ganglia lesions (31,32,42) to our Everest climber-subjects. These tests include a range of linguistic structures known to place different processing demands on normal adult subjects.

Similarly, we have assessed cognitive set formation and shifting abilities using a test originally designed for use with PD patients: the Odd-Man-Out test (OMO) (13). This sorting test measures two factors: the ability to derive an abstract criterion necessary to solve a problem, and the ability to shift to a new criterion. **Fig. 2** shows two typical OMO test cards. The subject is asked to pick out the "odd" figure. The decision can be based on either shape or size, and either decision is permitted. The subject is then presented with a second card and again asked to pick out the odd image using the same criterion. If the subject uses the alternate "rule" instead

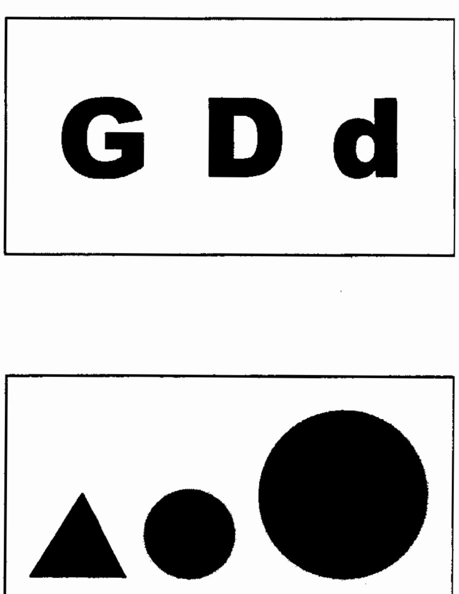

Fig. 2. Two Odd-Man-Out test cards. The figure that "doesn't belong" can be chosen either by shape or by size. For letter stimuli, shape corresponds to the letter's name, while size corresponds to case.

(e.g., shifting to shape after starting with size), s/he is corrected without being explicitly told the criteria. After selecting the odd figure on 10 cards, the subject is asked to use the other criterion to select the odd figure on a set of 10 additional cards. For example, if the subject starts by sorting pictures by their shapes, s/he must then switch to sorting them by size. The subject is then asked to again sort the first 10 cards using the criterion s/he originally used. The sorting criterion is shifted up to 6 times using the same 20 cards.

Neurologically intact control subjects make almost no errors on the OMO. Difficulties on the first and second sorts can reflect deficits in the ability to select a criterion, but subsequent errors are indicative of cognitive shifting deficits. Moderate PD subjects consistently have elevated set-shifting error rates on the OMO (13). Subjects with bilateral basal ganglia damage also have difficulty shifting sorting criteria; they tend to perseverate, holding or shifting back to a previous criterion (42,43). In our most recent Everest study (2004, preliminary report in this paper) we used the Wisconsin Card Sorting Test (39), described earlier, which is more difficult than the OMO and so appears to be more sensitive for determining the effects of hypoxia.

In our 2003 study (reported on in this paper) we included a pilot version of the MiniCog Quick Assessment Battery described by Shephard and Kosslyn (44). After some of the Palm Pilot PDAs on which the MiniCog tests run unexpectedly froze and lost data, the PDA software was modified for 2004 to tolerate low temperatures.

For the 2004 study, Morey adapted a memory test that reflects hippocampal function (7) to run on the Palm PDAs. The subject simply searches for the T in successive arrays of Ls and Ts. Without the subject's awareness, some of the arrays are repeated throughout the task. By comparing response times (RTs) for new vs. repeated arrays, one can measure the amount of implicit contextual learning that has taken place over the task. In a healthy individual, repeated presentation of the same array leads to faster performance: the contextual information contained in the color, orientation, and location of the Ls is implicitly learned and guides the searcher to the T. This facilitation is reflected in a stronger negative trend in RTs over blocks of stimuli for repeated arrays than for new arrays, such that RTs ultimately become significantly faster for repeated arrays (general learning of the task itself can yield a lesser negative trend for new arrays). In amnesic patients, however, no such facilitation is apparent, indicating that implicit contextual learning depends on intact hippocampal function (7).

Test Sites and Schedules

Starting in Kathmandu, Nepal, our Mt. Everest climber-subjects first fly to Lukla at an elevation of 2827 m and then walk for 10 d to Everest Base Camp at 5300 m, where they spend several weeks acclimatizing. This altitude is the highest at which permanent human habitations exist; few people can acclimatize to the lower oxygen content of air at higher altitudes (3). During the acclimatization period Sherpa crews establish a route up the 300-m-high icefall and set up a series of camps—Camp 2 at 6300 m, Camp 3 at 7300 m, and Camp 4 at 8000 m. The Mt. Everest climb entails ascending to Camp 4 and then climbing to the summit. In most years climbers can rarely proceed successively to Camps 2, 3, and 4 and on to the summit without having to return at some point to Base Camp because of high winds, snowstorms, and other adverse conditions. In some instances climbers cumulatively spend weeks at altitudes exceeding 6500 m. Supplementary oxygen generally is not used before reaching Camp 4; most climbers use supplementary oxygen above 8000 m.

Our research team remains at Base Camp throughout the climbing season, which may last up to 2 mo. Pulse oximeter measures and assessments by expedition doctors are used to determine whether individuals have acclimatized at Base Camp. After our volunteer climber-subjects have acclimatized, our team obtains baseline speech samples and administers cognitive tests. For the 2003 and 2004 studies each subject was provided with a Palm Pilot PDA. The subjects familiarize themselves with the Palm Pilot tests at Base Camp, allowing them to eventually reach plateaus reflecting their respective baseline performances after acclimatization. They also practice the sentence comprehension and OMO or Wisconsin Card Sorting tests and reading the word list.

VHF radio links are used to obtain speech samples and administer tests at Camps 2 and 3, and at Camp 4 when possible. The climbers carry the Palm Pilots with them and take the test battery at each location, sometimes repeatedly. The Palm Pilots are also used to record the word-list speech samples, backing up the VHF radio transmissions. Our climber-subjects take the cognitive tests, read the word lists, and converse with our Base Camp research staff when they are hydrated and are in warm, sheltered conditions. The subjects are also tested and recorded on their return to Base Camp after reaching the summit or giving up that goal. Because subjects are generally maximally exhausted on returning to Base Camp but are no longer in acutely hypoxic conditions, the corresponding data offer us a means of factoring out the effects of fatigue from those of hypoxia. Voice recordings from the VHF radio links are recorded on digital tape recorders in both calm and stressful situations throughout these test sessions.

RESULTS

The results discussed below are from experiments run in 1993 (5 subjects), 2001 (11 subjects), 2002 (10 subjects), and 2003 (10 subjects). The findings of these experimental sessions are consistent. We are currently analyzing data from 12 subjects tested in 2004, and report below on preliminary analyses of the implicit contextual learning task.

We first observed suggestive relationships between speech production and cognitive deficits on Everest in our 1993 experiment (33,34). A battery of speech, syntax, and cognitive tests similar to those we had used to assess deficits in PD (32) was administered at Base Camp and when climbers reached Camps 2 and 3. Their VOT sequencing degraded, though to a lesser degree than in PD; VOT values for voiced vs. voiceless stop

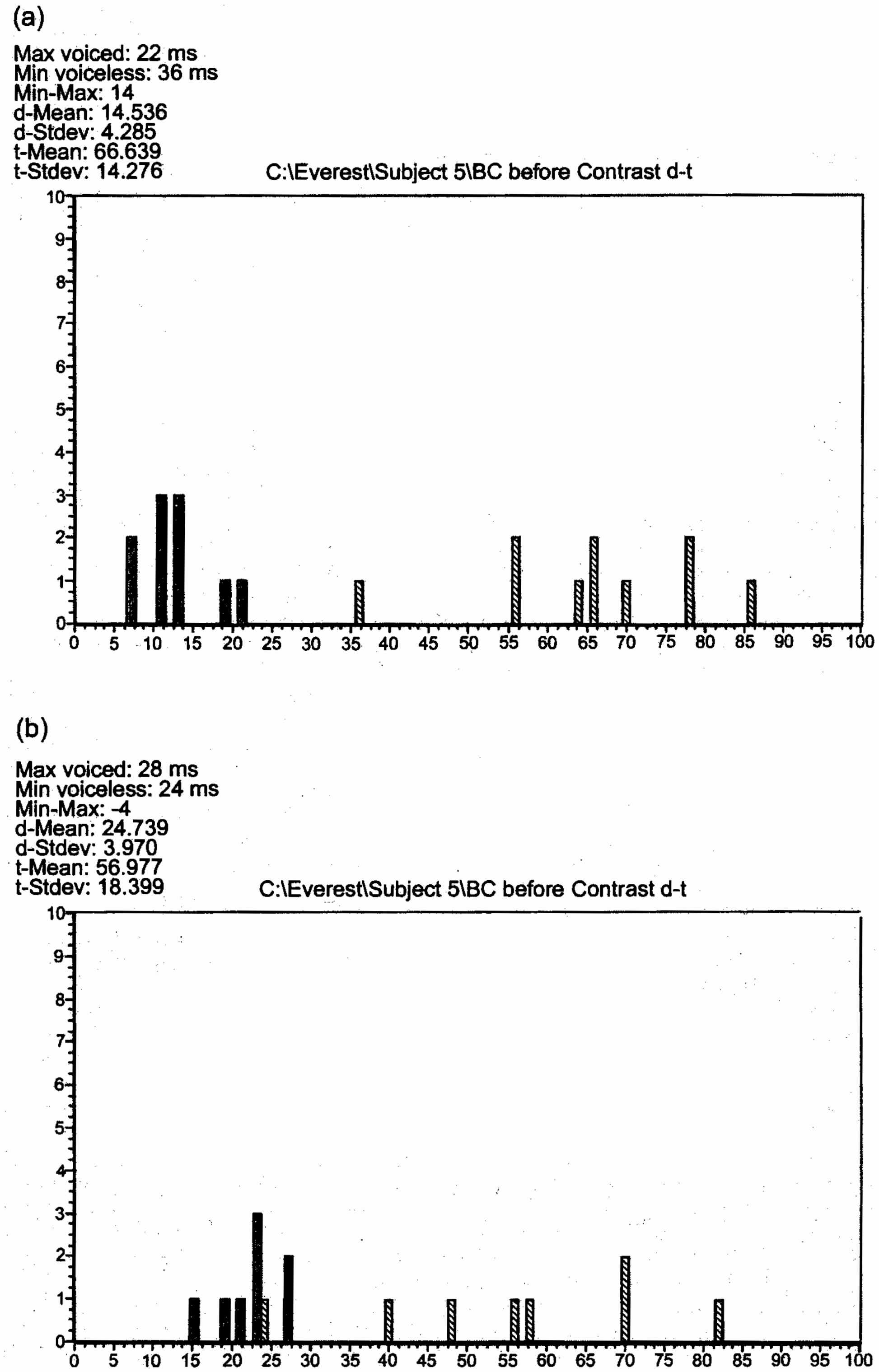

Fig. 3. a) Histogram of VOTs for words beginning with the stop consonants "d" (filled bars) and "t" (cross-hatched bars) produced by a climber at Base Camp before attempting to ascend Mount Everest in 2003. b) VOT histogram for "d" and "t" produced at Camp 2 by the same climber. At this higher altitude the VOTs now overlap, with one "t" word showing an abnormally short VOT within the normal range for "d".

consonants converged but did not overlap. Each subject's minimal VOT separation width was determined by subtracting the longest voiced consonant's VOT from the shortest unvoiced consonant's VOT for each place of articulation (b vs. p, d vs. t, g vs. k). The mean minimal VOT separation width over all five climbers decreased from 24.0 ms at Base Camp to 5.4 ms at Camp 3 ($p < 0.001$). The time needed to comprehend spoken English sentences also increased. RTs were 54% longer at Camp 3 for simple sentences that are readily comprehended by 6-yr-old children. Simple sentence RTs and VOT decrements were highly correlated ($r = -0.77$).

Data from the 31 subjects tested in 2001, 2002, and 2003 have replicated these findings. These studies have allowed us to refine our procedures and develop voice metrics that track slight as well as profound cognitive deficits. Computer-implemented analysis of hypoxic

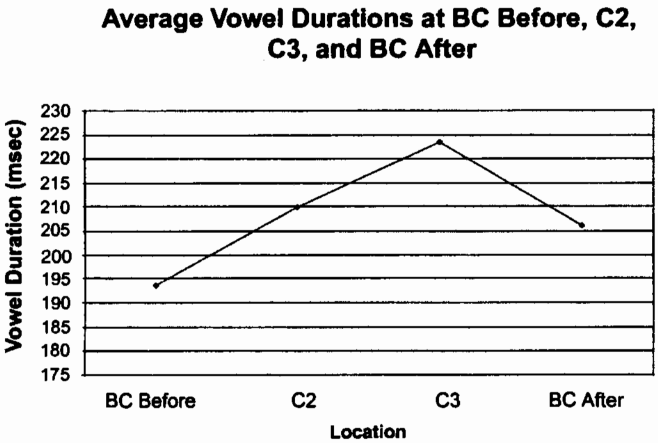

Fig. 4. Change in mean vowel duration with altitude for 10 subjects from the 2002 Mt. Everest expedition. Durations were measured for 60 monosyllabic words produced by each climber at each location.

climbers' speech shows that their VOTs converge compared with their performance at Base Camp; in some instances they even overlap. **Fig. 3a** shows a VOT histogram for "d"s and "t"s produced in word-initial position by one subject of the 2003 study at Base Camp before he attempted to ascend Mt. Everest. Note that the "d" and "t" ranges do not overlap. **Fig. 3b** presents a similar histogram for the same subject at Camp 2. The VOT ranges have converged and now overlap.

Vowel durations also increase at the high camps, reflecting a general slowing down of motor function. Vowel duration increases were an index of hypoxia in a hypobaric chamber experiment that eliminated the effects of fatigue and cold (11). **Fig. 4** shows the general increase of average vowel duration for 10 subjects monitored in 2002. The differences between Base Camp before ascending and Camps 2 and 3 are significant ($p < 0.05$). The difference between vowel duration at Base Camp before starting the climb and on the climbers' return to Base Camp after reaching the summit of Everest is not significant.

As noted above, studies of PD and focal lesions show that VOT convergence and overlap can reflect impaired motor sequencing resulting from degraded basal ganglia function. Like PD patients, hypoxic climber-subjects appear to have difficulty in properly sequencing lip and tongue maneuvers with laryngeal motor control. But as is the case for PD patients, they preserve the intrinsic durational differences that differentiate English vowels and usually can execute the tongue and lip maneuvers needed to produce the correct formant frequency patterns for vowels and consonants (27,28,32). The increase in climbers' vowel duration is consistent with the slowing of motor activity in PD as basal ganglia functions degrade (10,18,38). Hence the speech changes in climbers are suggestive of a specific effect on the basal ganglia.

Fig. 5a shows the typical pattern of decreased VOT separation as a subject sensitive to hypoxia ascends to higher altitudes, followed by a return toward normal ranges when the subject descends. **Fig. 5b** shows the same subject's sentence comprehension error rates at the same locations. Note that as VOT separation width decreases, comprehension errors increase. For the 36 subjects studied in the 4 expeditions from 1993 to 2003, mean RTs on sentence comprehension generally increased at higher altitudes. Errors on the OMO test of cognitive set shifting also tended to increase for many of our subjects as they reached higher altitudes.

We have replicated and refined the general relationship between VOT and sentence comprehension RT noted in our 1993 Everest study (33,34). In our 2002 and 2003 Mt. Everest studies, we tracked VOT range convergence by calculating the mean VOT separation for each subject at each location. For each consonant pair (e.g., b vs. p), we subtracted the mean VOT for the voiced word-initial consonants from the mean voiceless VOT. We then averaged over the three consonant pairs. Mean VOT separation is thus a robust measure of a subject's ability to maintain the temporal sequence of motor commands to lips or tongue so as to produce a stop consonant burst and subsequently position and tension the vocal folds of the larynx to initiate phonation. The median value of comprehension RT increase between higher and lower camps was computed across all subjects and locations. The decrease in the mean VOT separation with altitude was significantly greater

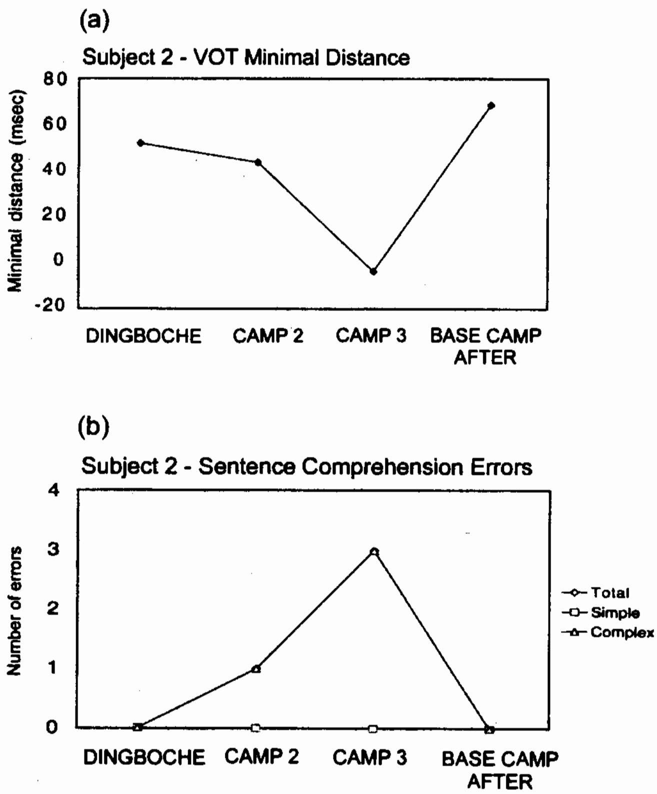

Fig. 5. a) Mean minimal distance between VOTs for the three stop consonant pairs (b-p, d-t, g-k) as produced by a subject in the 2001 Everest expedition at Dingboche, at the high camps on Mt. Everest, and on his return to Base Camp after reaching Everest's summit. Dingboche is a Sherpa settlement at 4200 m, below Base Camp, to which climbers often descend during intervals of inclement weather that preclude climbing. At the highest altitude (Camp 3), the subject exhibits overlap between stop consonant categories, as indicated by a negative minimal distance value. b) Errors on the sentence comprehension task made by the same subject at the same altitudes. The error rate tracks the subject's speech motor control performance, with higher errors accompanying reduced separation between VOTs for stop consonant pairs.

($p < 0.01$) in those instances where RT increases exceeded the median than when they were less than the median.

Detecting Cognitive Impairment in Subjects at Risk

The focus of our Everest space analogue is to develop metrics that will alert space crews at early stages of cognitive dysfunction. It is not surprising that some climbers are more resistant to hypoxia than others and our speech and cognitive measures reflect these differences. We have made use of these individual differences to derive voice measures that identify subjects with greater cognitive deficits.

We determined the degree to which decreased mean VOT separation and increased vowel duration would serve as predictors for increases in sentence comprehension RTs or OMO errors. **Table I** shows the hit, miss, and false alarm rates calculated for these acoustic measures in our 2002 study. A hit was counted whenever a subject whose speech showed effects suggesting hypoxic impairment exhibited evidence of cognitive decline, as measured by increased OMO errors or increased sentence comprehension RTs at a higher camp compared with Base Camp or a lower camp. It was also a hit if a subject with "hypoxia unaffected" speech did not show cognitive impairments at higher camps. A miss occurred when an individual exhibited a decline in cognitive measures but the speech variables did not indicate hypoxic impairment. Finally, a false alarm was tallied if speech variables indicated hypoxic impairment but the cognitive measures did not. Both speech measures were good predictors, with increased vowel duration giving the better hit rate. Vowel duration is also increased in aged people who have difficulty comprehending the meaning of sentences (30).

Our 2003 Everest study piloted the MiniCog cognitive test battery, which allows a more comprehensive assessment of cognitive deficits. A significant positive correlation ($r = 0.61$) was found between increased vowel duration (slower speech) and RT in the verbal working memory task. Verbal working memory involves neural activity in cortical-striatal-cortical circuits involving Broca's area and its right hemisphere homolog, as well as phonetic rehearsal mechanisms in which motor circuits used to produce overt speech apparently covertly maintain words in working memory (21,25,27,28). RTs on the MiniCog spatial working memory and vigilance tasks, which also place loads on the neural substrates of working memory, showed trends toward significant correlations with vowel duration. In contrast, performance on perceptual-motor tasks that do not place demands on striatal circuitry was not affected by altitude. The hit-miss-false alarm procedure described above was applied to the MiniCog working memory and vigilance tasks to determine the degree to which acoustic metrics would identify individuals who were slower at performing these cognitive tasks at altitude; **Table II** shows the results*.

Shifts in personality have been traced to globus pallidus lesions resulting from hypoxia (10,23,24,45). The behavior of one of our climber-subjects, who spent 3 wk at elevations exceeding 6500 m without supplementary oxygen, appeared to reflect disinhibition similar to that noted for basal ganglia lesions (10).

TABLE I. DETECTION OF SENTENCE COMPREHENSION OR SET-SHIFTING DEFICITS VIA SPEECH MEASURES.

Predictive Measure	Hit Rate	Miss Rate	False Alarm Rate
VOT mean separation decrease	0.73	0.20	0.07
Vowel duration increase	0.85	0.00	0.15

TABLE II. DETECTION OF WORKING MEMORY AND VIGILANCE DEFICITS VIA SPEECH MEASURES.

Predictive Measure	Hit Rate	Miss Rate	False Alarm Rate
VOT mean separation decrease	0.71	0.29	0.00
Vowel duration increase	0.43	0.43	0.14

Implicit Contextual Learning

Preliminary analysis of the performance of Mt. Everest climber-subjects on the 2004 memory retrieval task (7) shows deficits that appear to reflect hypoxic insult to the hippocampus. The data were analyzed by performing a statistical regression on the combined results of 24 implicit contextual learning tasks performed at Base Camp before attempting to ascend Mt. Everest, at Camp 2, and at Camp 3. The regression of the Base Camp data revealed a negative trend in RT for both new and repeated arrays. More importantly, the trend was more negative for the repeated arrays than for the new arrays. The regression coefficients were -1.24, $p < 0.001$, and -0.90, $p < 0.001$, respectively. This difference can be attributed to implicit contextual learning for the repeated arrays. In contrast, at Camp 2, while significant negative trends were again found for both new (-1.06, $p < 0.001$) and repeated arrays (-0.90, $p < 0.005$), the benefit of repeated presentation was now absent. At Camp 3, climber-subjects no longer exhibited significant improvement for either new (-0.40, $p = 0.17$) or repeated stimuli (-0.21, $p = 0.48$). Thus the implicit contextual learning effect present at Base Camp is absent when subjects are tested in hypoxic conditions. Based on the work with amnesics implicating the hippocampus in this task (7), these data point to hippocampal function being impaired by hypoxia.

Extreme Speech and Cognitive Deficits

With the exception of one individual, none of our subjects have shown life-threatening cognitive dysfunc-

*The results for vowel duration are less robust than might be expected from the significant correlation with verbal working memory because the criterion for a hit was that RT had increased for at least two of the three tests: verbal working memory, spatial working memory, and vigilance.

tion on Mt. Everest. One young male climber was the unfortunate exception. When tested at Base Camp after acclimatization to altitude, he made no errors whatsoever on the OMO, and his speech was generally within normal bounds. A dramatically different pattern was seen 5 d later, at Camp 2. Acoustic analysis showed aberrant motor control, similar to that of subjects having profound bilateral basal ganglia damage (42), in 32 of 60 words. He also made OMO errors resembling those of subjects with extreme basal ganglia dysfunction (13,42). The subject was able to form a cognitive set: his first set of OMO sorts (done on the basis of size) was error-free. However, when asked to shift the sorting criterion, he had extreme difficulties. After starting to sort the second set of images by shape, he reverted to size. His error rate on each of the second, third, and fourth sorts was 40%. No other subject had such extreme set-shifting difficulties or profound speech production anomalies.

When the subject was advised that he was not functioning normally, he insisted that he was fine. However, it became clear that the cognitive perseveration noted in the OMO had impaired his decision-making ability and altered his personality. The weather took a turn for the worse, but despite the urgings of other climbers at Camp 2 to descend with them to Base Camp, he persisted in following his original schedule. He continued to climb the next day through an intense storm to Camp 3, where he apparently suffered acute mountain sickness. After two nights there, he fell to his death when he attempted to descend to Camp 2 on the fixed ropes that are anchored at intervals to the mountain. Climbers secure themselves to these ropes by attaching a safety harness to them with two carabiners (snap links). To descend safely a climber must execute the proper sequence of motor acts at each anchor point, first unclipping one carabiner and securing it to the next rope, then doing the same with the second carabiner. Basal ganglia dysfunction disrupts the execution of such internally guided, sequential manual motor acts (10,38). Although the subject's death was not witnessed, it was evident that his harness had not been secured. It is probable that the motor and cognitive deficits discerned in our tests at Camp 2 were implicated in his fatal accident. His rejecting the advice of other climbers in so obvious a situation can be viewed as a shift in personality; he had previously acted in a responsible manner.

We are guarding against similar incidents. This event has been related to each new prospective climber-subject. Moreover, our informed consent form now requires that team leaders as well as individual subjects be informed when our procedures suggest cognitive dysfunction.

DISCUSSION AND AIMS OF CURRENT RESEARCH

Our studies demonstrate that cognitive impairments as well as shifts in personality that could compromise deep-space missions can be detected by means of computer-implemented analyses of a person's speech. Our computer-implemented metrics would not impinge on privacy or compromise mission security since they reflect motor control only and do not reveal the content of verbal messages. Moreover, the aspects of speech reflected in these metrics are not under conscious control, so crewmembers will not be able to improve with practice or develop strategies for "fooling" the system. Our goal is to refine and validate these speech metrics as well as ones that reflect both task-induced and life-threatening stress. Stress can severely compromise performance and disrupt interpersonal relationships to the point that a mission must be aborted.

Variations in the fundamental frequency of phonation (F0) can signal emotion and affect, as well as reactions to task-induced or emotional stress (4,8,9,21,35). However, some past studies, including our own (35), relied on speech samples produced by subjects who were asked to read aloud written passages as though they were conveying emotionally charged material. This database may not reflect real-life situations. Fortunately, studies of spontaneous speech in more realistic situations have shown that several acoustic speech measures appear to track stress. For example, jitter, a measure of short-term variations in F0 (26), correlates with both behavioral and physiologic markers (heart and breathing rates, pupil dilation, and cortisol levels) in young children subjected to mild task-induced stress (9).

A recent study demonstrated that the glottal source spectrum – the distribution of energy at the higher harmonics of F0 – may provide a robust measure of extreme positive, extreme negative, or neutral emotional states to human listeners (8). Speech samples were derived from a real-world situation: utterances produced by contestants on American TV quiz shows. The contestants' speech was recorded while they chatted with the host, when they learned that they had "won" $50,000, and when they learned that they had "lost" that sum. Vowel segments that varied in length from 22 to 57 ms (median 30 ms) were then excised. One hundred of these short segments were presented in random order two times each to listeners who were asked to rate whether the signal conveyed a positive, negative, or neutral emotion and the degree to which that emotion was conveyed. There were 3 sets of 10 listeners each that were used: native monolingual American-English, French, and Korean speakers. The listeners consistently associated the short segments with the correct emotional states. The responses of the American, Korean, and French listeners did not substantially differ. The vowel segments were too short to convey either the lexical content or the F0 contours of the utterances from which they were extracted; the acoustic indicator of emotion that was present was the glottal source spectrum.

In our 2004 Everest study, we recorded voice signals from our climber-subjects during routine conversations, while they performed cognitive tests that induce stress, and in life-threatening situations. We will be comparing voice stress metrics for the Everest data with similar metrics for speech collected from subjects exposed to task-induced stress in Dinges's NSBRI-funded laboratory study at the University of Pennsylvania (see 12).

Our techniques have broader potential applications than to space travel alone. In general aviation they could be used to monitor crews for effects of hypoxia resulting from depressurization, which has led to flight disasters in the past. We have applied our speech-analysis methods to the diagnosis and treatment of PD and other degenerative conditions. The MiniCog and implicit memory tasks could be used for the early detection of Alzheimer's dementia. Speech sequencing and cognitive deficits similar to those noted on Mt. Everest are apparent in our ongoing pilot study of children with verbal apraxia deriving from hypoxic basal ganglia damage during birth (2,5).

ACKNOWLEDGMENTS

We would like to thank Lara Vowles for her essential role in testing subjects at Everest Base Camp in 2003 and 2004. Dr. Richard C. Morey graciously guided our statistical analyses. Professor Marvin Chun of the Department of Psychology at Yale University provided the implicit conceptual learning stimuli. Erik Weidemeyer's National Federation for the Blind Everest 2001 expedition and its leader, P.V. Scaturro, were gracious hosts and facilitated our research. Kili Sherpa and his crew provided excellent support during the past 2 yr. Beverly Young is carrying out superb pilot research on children having verbal apraxia. We thank the Palm Corporation for supplying Palm Pilot PDAs. Our research protocol and human subject informed consent form were approved by the Brown University Institutional Review Board and reviewed and approved by the National Space Biomedical Research Institute. Our research has been supported by NASA under grant NCC 9–58 with the National Space Biomedical Research Institute.

REFERENCES

1. Alexander GE, DeLong MR, Strick PL. Parallel organization of functionally segregated circuits linking basal ganglia and cortex. Annu Rev Neurosci 1986; 9:357–81.
2. Azzarelli B, Caldemeyer KS, Phillips JP, DeMeyer WE. Hypoxic-ischemic encephalopathy in areas of primary myelination: a neuroimaging and PET study. Pediatr Neurol 1996; 14:108–16.
3. Bouhuys A. Breathing. New York: Grune and Stratton; 1974.
4. Brenner M, Shipp T, Doherty ET, Morrissey P. Voice measures of psychological stress - laboratory and field data. In: Titze IR, Scherer RC, eds. Vocal fold physiology, biomechanics, acoustics, and phonatory control. Denver: The Denver Center for the Performing Arts; 1985.
5. Burke RE, Franklin SO, Inturrisi CE. Acute persistent suppression of preproenkephaline mRNA expression in the striatum following developmental hypoxic-ischemic injury. J Neurochem 1994; 62:1878–86.
6. Chie U, Y Inoue, Kimura M, et al. Irreversible subcortical dementia following high altitude illness. High Alt Med Biol 2004; 5:77–81.
7. Chun MM, Phelps EA. Memory deficits for implicit contextual information in amnesic subjects with hippocampal damage. Nat Neurosci 1999; 2:844–7.
8. Chung S-J. L'expression et la perception de l'émotion extraite de la parole spontanée: évidences du coréen et de l'anglais [Dissertation in French]. Paris: Université de la Sorbonne Nouvelle, Paris III; 2000.
9. Coster WJ. Aspects of voice and conversation in behaviorally inhibited and uninhibited children [Dissertation]. Cambridge, MA: Harvard University; 1986.
10. Cummings JL. Frontal-subcortical circuits and human behavior. Arch Neurol 1993; 50:873–80.
11. Cymerman A, Lieberman P, Hochstadt J, et al. Speech motor control and acute mountain sickness. Aviat Space Environ Med 2002; 73:766–72.
12. Dinges DF, Rider RL, Dorrian J, et al. Optical computer recognition of facial expressions associated with stress induced by performance demands. Aviat Space Environ Med 2005; 76(6, Suppl.):B172–82.
13. Flowers KA, Robertson C. The effect of Parkinson's disease on the ability to maintain a mental set. J Neurol Neurosurg Psychiatry 1985; 48:517–29.
14. Graybiel AM. The basal ganglia and cognitive pattern generators. Schizophr Bull 1997; 23:459–69.
15. Graybiel AM, Aosaki T, Flaherty AW, Kimura M. The basal ganglia and adaptive motor control. Science 1994; 265:1826–31.
16. Greenberg BD, Murphy DL, Rasmussen SA. Neuroanatomically based approaches to obsessive-compulsive disorder: neurosurgery and transcranial magnetic stimulation. Psychiatr Clin North Am 2000; 23:671–86.
17. Inoue T, Kato H, Araki T, Kogure K. Emphasised selective vulnerability after repeated nonlethal cerebral ischemic insults in rats. Stroke 1992; 23:739–45.
18. Jellinger K. New developments in the pathology of Parkinson's disease. In: Streifler MB, Korezyn AD, Melamed J, Youdim MBH, eds. Advances in neurology, vol. 53. Parkinson's disease: anatomy, pathology and therapy. New York: Raven Press; 1990:1–15.
19. Jeong JH, Kwon JC, Chin JH, et al. Globus pallidus lesions associated with high mountain climbing. J Korean Med Sci 2002; 17:861–3.
20. Kirchoff BA, Wagner AD, Naril A, Stern CE. Prefrontal-temporal circuitry for episodic encoding and subsequent memory. J Neurosci 2000; 20:6173–80.
21. Kotz SA, Meyer M, Alter K, et al. On the lateralization of emotional prosody: an fMRI investigation. Brain Lang 2003; 86: 366–76.
22. Kuoppamaki M, Bhatia KP, Quinn N. Progressive delayed-onset dystonia after cerebral anoxic insult in adults. Mov Disord 2002; 17:1345–9.
23. Laplane D, Baulac M, Widlocher D, Dubois B. Pure psychic akinesia with bilateral lesions of basal ganglia. J Neurol Neurosurg Psychiatry 1984; 47:377–85.
24. Laplane D, Levasseur M, Pillon B, et al. Obsessive-compulsive and other behavioral changes with bilateral basal ganglia lesions. Brain 1989; 112:699–725.
25. Lehéricy S, Ducros M, Van de Moortele P-F, et al. Diffusion tensor fiber tracking shows distinct corticostriatal circuits in humans. Ann Neurol 2004; 55:522–9.
26. Lieberman P. Perturbations in vocal pitch. J Acoust Soc Am 1961; 33:597–603.
27. Lieberman P. Human language and our reptilian brain: the subcortical bases of speech, syntax, and thought. Cambridge, MA: Harvard University Press; 2000.
28. Lieberman P. On the nature and evolution of the neural bases of human language. Yearbook Phys Anthropol 2002; 45:36–62.
29. Lieberman P, Blumstein SE. Speech physiology, speech perception, and acoustic phonetics. Cambridge, UK: Cambridge University Press; 1988.
30. Lieberman P, Feldman LS, Aronson S, Engen B. Sentence comprehension, syntax and vowel duration in aged people. Clin Linguist Phon 1989; 3:299–311.
31. Lieberman P, Friedman J, Feldman LS. Syntactic deficits in Parkinson's disease. J Nerv Ment Dis 1990; 178:360–5.
32. Lieberman P, Kako ET, Friedman J, et al. Speech production, syntax comprehension, and cognitive deficits in Parkinson's disease. Brain Lang 1992; 43:169–89.
33. Lieberman P, Kanki BG, Protopapas A, et al. Cognitive defects at altitude. Nature 1994; 372:325.
34. Lieberman P, Kanki BG, Protopapas A. Speech production and cognitive decrements on Mount Everest. Aviat Space Environ Med 1995; 66:857–64.
35. Lieberman P, Michaels SB. Some aspects of fundamental frequency, envelope amplitude and the emotional content of speech. J Acoust Soc Am 1962; 34:922–7.
36. Lisker L, Abramson AS. A cross language study of voicing in initial stops: acoustical measurements. Word 1964; 20:384–422.
37. Madsen TM, Kristjansen PEG, Bolwig TG, Wortwein G. Arrested neuronal proliferation and impaired hippocampal function following fractionated brain irradiation in the adult rat. Neuroscience 2003; 19:635–42.
38. Marsden CD, Obeso JA. The functions of the basal ganglia and the paradox of stereotaxic surgery in Parkinson's disease. Brain 1994; 117:877–97.
39. Monchi O, Petrides P, Petre V, et al. Wisconsin Card Sorting revisited: distinct neural circuits participating in different

stages of the task identified by event-related functional magnetic resonance imaging. J Neurosci 2001; 21:7733–41.

40. Oelz O, Regard M, Wichmann W, et al. Cognitive impairment, neurologic performance and MRI after repeat exposure to extreme altitude. In: Sutton JR, Coates A, Remmers JE, eds. Hypoxia: the adaptations. Toronto: Decker; 1990:206–9.
41. Pagani M, Ansjon R, Lind F, et al. Effects of acute hypobaric hypoxia on regional cerebral blood flow: a single photon computed tomography study in humans. Acta Physiol Scand 2000; 168:377–83.
42. Pickett ER, Kuniholm E, Protopapas A, et al. Selective speech motor, syntax and cognitive deficits associated with bilateral damage to the head of the caudate nucleus and the putamen: a single case study. Neuropsychologia 1998; 36:173–88.
43. Scott RB, Harrison J, Boulton C, et al. Global attentional-executive sequelae following surgical lesions to globus pallidus interna. Brain 2002; 125:562–74.
44. Shephard JM, Kosslyn SM. The MiniCog rapid assessment battery: developing a "blood pressure cuff for the mind." Aviat Space Environ Med 2005; 76(6, Suppl.):B192–7.
45. Strub RL. Frontal lobe syndrome in a patient with bilateral globus pallidus lesions. Arch Neurol 1989; 46:1024–7.
46. Vazquez M, Gatley J, Bruneus M, et al. Behavioral effects of 1 GeV/n Fe ions and gamma rays [Abstract]. Bioastronautics Investigators' Workshop; 13–15 Jan 2003; Galveston, TX. Houston, TX: USRA DSLS; 2003:201. Available from: http://www.dsls.usra.edu/meetings/bio2003/pdf/Radiation/2231Vasquez.pdf
47. Velanova K, Jacoby LI, Wheeler ME, et al. Functional-anatomic correlates of sustained and transient processing components engaged during controlled retrieval. J Neurosci 2003; 23:8460–70.
48. Wheeler MF, Buckner RJ. Functional dissociation among components of remembering: control, perceived oldness, and content. J Neurosci 2003; 23:3869–80.
49. Wood ER, Dudchenko PA, Eichenbaum H. The global record of memory in hippocampal neuronal activity. Nature 1999; 397:613–6.