DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
Centers for Disease Control
and Prevention (CDC)

Memorandum

Date: March 26, 2001

From: Roy M. Fleming, Sc.D., Director, Research Grants Program RMF
Office of Extramural Programs, NIOSH, D30

Subject: Final Report Submitted for Entry into NTIS for Grant 1 R43 OH003350-01.

To: William D. Bennett
Data Systems Team, Information Resources Branch, EID, NIOSH, P03/C18

The attached final report has been received from the principal investigator on the subject NIOSH grant. If this document is forwarded to the National Technical Information Service, please let us know when a document number is known so that we can inform anyone who inquires about this final report.

Any publications that are included with this report are highlighted on the list below.

Attachment
cc: Sherri Diana, EID, P03/C13

List of Publications - None

Title:	Work Readiness Neurometer
Investigator:	Alan S. Gevins
Affiliation:	One Rincon Center
City & State:	San Francisco, CA
Telephone:	(415) 227-4900
Award Number:	1 R43 OH003350-01
Start & End Date:	9/30/1995–6/30/1996
Total Project Cost:	$74,827
Program Area:	Not NORA
Key Words:	

Abstract:

The overall purpose of the Phase I project was to develop and refine a testing method to assess the work readiness of individuals who work in occupations that require alertness and acute judgment for the operation of high-risk technology. Our approach to this issue was to measure neurophysiological and performance variables recorded from subjects performing attention-demanding cognitive tasks, and to apply neural network pattern recognition analysis to detect subtle multivariate differences between alert and impaired states. During Phase I we sought to test the adequacy of the key signal processing and pattern recognition methods that the device would use, refine a test battery, and define the necessary functionality to design a device suitable for use in work environments. The work completed in Phase I was more than that specified in the original aims. Specifically, we analyzed a larger and more recent database that had more (N=9) subjects and that had alcohol as well as fatigue stressors, rather than the older one described in the proposal that had fewer (N=4) subjects and only fatigue as a stressor. After completing descriptive statistics and individual subject pattern recognition studies, we focused on testing the feasibility of the key underlying principle of the Work Readiness Neurometer; namely, that it is possible to distinguish between alert and impaired states in individuals for whom there is no prior sample of the impaired state, and on other key ideas such as use of task-related EEG rather than resting EEG, and of differentiating different sources of impairment.

Due to the limited scope of a Phase I project, only a small group of subjects were analyzed. Thus, these results must be treated as preliminary and limited in their generalizability. Nonetheless, they are remarkable in that they suggest that impairment-related changes in the EEG are highly reproducible and similar across subjects. They are the first demonstration that a generic (group) EEG pattern recognition network can successfully be applied to a new subject to determine whether he or she is in an Intoxicated or Fatigued state. These results have served to clarify several important issues with respect to the feasibility of developing a work readiness test based on neurophysiological measurements. First, we found that task related EEG signals were more sensitive to states of impairment than were eyes-open resting EEG signals, indicating that the test should require that subjects perform some attention demanding task. Second, we found that both EEG signals and test performance measures during a simple working memory task were more sensitive to states of impairment than were either behavioral measures or EEG signals during a perceptuomotor tracking task,

suggesting that a simple test based on the WM task might alone be adequate for work readiness testing. Third, we found that EEG features provided sensitive indicators of fatigue even under conditions where task performance variables were unaffected. Fourth, we found that the EEG signature of impairment from alcohol was dramatically different from that associated with Fatigue. Fifth, we found that we could dissociate theta band EEG signals related to task difficulty from those related to fatigue using topographic criteria. Finally, we found that it was possible to classify states of impairment in subjects without prior knowledge of what their individual EEG signals look like during impaired states. These findings establish the basic feasibility of creating a sensitive neurophysiological measure of work readiness that would be suitable for use in conventional work environments.

Publications

No publications to date.

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WORK READINESS NEUROMETER

SBIR AWARD No. R43 OH03350
Phase I Final Report

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Project Period. September, 30, 1995- June 30, 1996.

Key Personnel. Alan Gevins, Principal Investigator, 84 hours; Michael Smith, Neuroscientist, 154; Sue Whitfield, Data Analyst, 444; Daphne Yu, Biomedical Engineer, 281; Emiliana Pellouchoud, Technical Associate, 320; Georgia Rush, Research Associate, 234.

Summary of Specific Aims. The overall purpose of the Phase I project was to develop and refine a testing method to assess the work readiness of individuals who work in occupations that require alertness and acute judgment for the operation of high-risk technology. Our approach to this issue was to measure neurophysiological and performance variables recorded from subjects performing attention-demanding cognitive tasks, and to apply neural network pattern recognition analysis to detect subtle multivariate differences between alert and impaired states. During Phase I we sought to test the adequacy of the key signal processing and pattern recognition methods that the device would use, refine a test battery, and define the necessary functionality to design a device suitable for use in work environments. The work completed in Phase I was more than that specified in the original aims. Specifically, we analyzed a larger and more recent database that had more (N=9) subjects and that had alcohol as well as fatigue stressors, rather than the older one described in the proposal that had fewer (N=4) subjects and only fatigue as a stressor. After completing descriptive statistics and individual subject pattern recognition studies, we focused on testing the feasibility of the key underlying principle of the Work Readiness Neurometer; namely, that it is possible to distinguish between alert and impaired states in individuals for whom there is no prior sample of the impaired state, and on other key ideas such as use of task-related EEG rather than resting EEG, and of differentiating different sources of impairment.

Results. We intensively analyzed data from 9 healthy normal subjects (22-25 years of age, 4 female) who performed perceptuomotor and cognitive tasks over the course of a 16 hour period extending from mid-afternoon one day until 0700 the next morning. EEG was recorded while subjects were in a quiescent eye-open resting state and while they performed difficult tasks including a Perceptuomotor Tracking (PT) task, and a Working Memory (WM) task. The PT task is a primitive videogame-style computer-based test that puts significant demands on perceptuomotor tracking skills. Individual runs of PT lasted 3 minutes each. In the WM task, versions of which we have employed in several studies in our lab to study EEG correlates of mental effort (Gevins et al., submitted, 1996; Gevins et al., in press; Gevins et al., 1996), subjects had to compare the spatial location of the current stimulus (one of twelve uppercase letters that appeared on the computer screen) to the position of one which appeared previously. In a difficult version of the task subjects had to compare the current stimulus with that which occurred two trials previously. Thus in this version subjects needed to update the contents of working memory on each trial and maintain two positions in working memory for the duration of two trials (in this case nine seconds). In an easy version of this task, subjects were required to match the position of the current stimulus with the first one that appeared in a block of trials. In both versions of the task, stimuli were presented in blocks of 50 trials, each with an ISI of 4.5 seconds.

Testing Procedure. On a day prior to the test day subjects participated in a practice session in which they completed background questionnaires and informed consent documents and then performed the tasks to a point at which past studies had indicated that behavior and EEG variables would be stable. This included performing 250 trials at each difficulty level in the WM task, and performing the PT task for a total of 45 minutes. On the day of the testing session they arrived in the laboratory in the afternoon and first performed some warm-up exercises with the tasks. After the warmup run the electrode montage was applied to the subjects and they then engaged in five test sessions interspersed with breaks. During each testing session 3 minutes of eye-open resting EEG data were collected prior to task performance, Blood Alcohol Content (BAC) was measured with a breathalyzer, and EEG was collected simultaneously with each run of the tasks. Subjective fatigue ratings were obtained for each testing session using a 7 point scale with end points of "Extremely Alert" and "Extremely Tired". The first formal test session established Baseline levels of performance and EEG variables during an alert mental state. This session involved a total of 6 runs of the PT task and 4 blocks of trials from each of the two WM tasks. This same task protocol was followed in subsequent test sessions. Prior to the next recording session subjects received a small dose of alcohol calculated to raise their BAC to .085, and they then participated in an "Intoxicated state" testing session during the peak of their BAC curve. They then participated in three more recording sessions that extended throughout the night for a total of 5 sessions. A "Fatigued" state recording session was defined on an individual subject basis as the session in which subjective ratings indicated highest fatigue and in which overt test performance was at its lowest level. In four of the subjects this was the fourth recording session which occurred on average around 0300-0400, and in the other five subjects this was the fifth recording session that on average began around 0530. BAC levels in all subjects had dropped below .02 before the fourth recording session.

Electrophysiological Recordings and Pre-processing. EEG was recorded from 28 scalp locations (Fp1, Fp2, AFZ, AF3, AF4, FT9, F7, F3, FZ, F4, F8, FT10, T7, C3, CZ, C4, T8, P9, P7, P3, PZ, P4, P8, P10, O1, OZ, O2, I) using an electronically linked-mastoids reference. EOG activity was recorded from electrodes located above each eye, referenced to an electrode at the outer canthus of each eye. Physiological signals were sampled at 256 Hz, using a band-pass of 0.05 to 100 Hz. Artifacts were marked by artifact detection software algorithms, and the results of this process were then reviewed and edited by expert human judges. Prior to further analyses, eye movement artifacts were corrected with a method that uses an adaptive interference canceler signal processing method (Du, Leong & Gevins, 1994).

Analysis. A two-stage analysis process was performed. In the first stage conventional statistical procedures were used to systematically identify the ways in which behavioral and physiological variables were affected by the experimental manipulations. A second stage of analysis was then performed. This second analysis focused on pattern classification studies, using analogous procedures to those we have used in many prior studies. Classification was performed using a neural network algorithm that iteratively generates and evaluates a two-layered feed-forward neural network from the set of signal features, automatically identifying small subsets of features that produce the best classification on the data set aside for training (Gevins & Morgan, 1986; Gevins, 1980; Gevins & Morgan, 1988). In brief, the algorithm first forms all possible combinations of a small number of candidate features out of a larger pool of candidates (up to 15 in the analyses performed here). These combinations are used to construct candidate neural units to use in the first layer, the "input" layer, of the network; each unit representing a different combination of features. Discriminant analysis is used to determine characteristics of the candidate units. Initially, the candidate unit with the best classification performance is selected and its binary output is weighted and fed into the single, binary output unit of the network. The input unit's weighting and the output unit's threshold are adjusted iteratively to minimize classification error. The algorithm continues to add "input" layer neural units one at a time until a pre-specified limit is reached or an additional unit fails to significantly improve classification accuracy. At each iteration, the algorithm picks the candidate neural unit that maximally improves overall classification performance on the training data. The resulting networks are then tested on independent data not used in training the networks.

Blood Alcohol Levels, Subjective Ratings, and Task Performance measures. Average measured BAC level during the Alert Baseline state was .00 and during the Intoxicated session was .087 [range .075-.124; t(8)=18.25, p < .001]. Subjective fatigue ratings were much higher for all subjects during the Fatigued session than during the Baseline session [5.44 vs 2.33; t(8)=7.35, p < .001]. Scores in the PT task were slightly but reliably lower in the Intoxicated state than at the Baseline state [t(8)=2.79, p < .03], but did not differ between the Baseline and Fatigued states. For the WM task, accuracy was higher [F(1,17)=26.42, p < .001] and RT was faster [F(1,17)=44.49; p < .001] in the easy version than in the difficult version. When comparing the initial session with the impaired ability sessions, accuracy was lower in the Intoxicated state [F(1,17)=10.94, p < .005] and in the Fatigued state [F(1,17)=12.9, p < .002] than in the Alert Baseline state. Further, there was a significant interaction between Fatigue and Task Difficulty [F(1,17)=8.42, p < .01], such that Fatigue had a large impact on accuracy in the more difficult WM task, but did not significantly affect accuracy in the easy WM task. RT was also slowed in the Fatigued state relative to the Alert Baseline state [F(1,17)=11.42, p < .005].

EEG Results, Descriptive Statistics. Fast Fourier transforms were calculated for all contaminant-free EEG segments for correctly performed trials for each subject in each task condition and averaged across segments to produce summary power spectra. Preliminary inspection of these spectra indicated that although individual subjects often displayed idiosyncratic task-related modulation at both lower and higher frequencies, the most pronounced and reliable task- and mental state-related modulation of spectral power occurred in the theta and alpha bands (4-12HZ). Analyses focused on four EEG features in this range that past studies have found to be sensitive to cognitive task manipulations and/or variations in mental state. These included a frontal midline theta signal (5-7Hz), a topographically diffuse, posterior-maximal theta signal (4-6Hz), a slow alpha signal (8-10Hz) that is most prominent at parietal electrode sites, and a fast alpha signal (9-12Hz) that is most prominent at occipital electrode sites. During Baseline recordings the requirement to perform the WM task resulted in an increase (relative to eyes-open resting conditions) in frontal theta [F(2,16)=30.61, p < .001]. Further, frontal theta was higher in amplitude in the difficult WM task condition than in the easy WM task condition (Figure 1). During resting conditions the slow alpha signal was smaller in both the PT task [t(8)=-3.50, p < .01] and the WM task [F(2,16]=7.98, p < .005] than in resting EEG, and it was reduced more in the difficult WM task than in the easy WM task. Similarly, the fast alpha signal was also reduced in the PT [t(8)=-3.00, p < .02] and WM tasks [F(2,16)=53.74, p < .001] relative to the resting conditions, mainly in the difficult WM task (Figure 2).

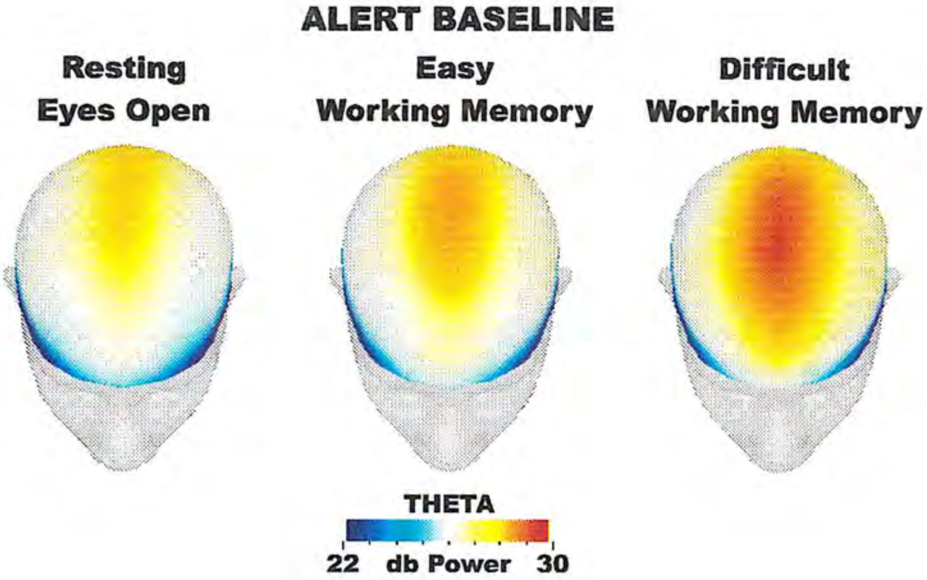

Figure 1. Increasing task difficulty results in increases in EEG theta signals maximal at midline anterior sites.

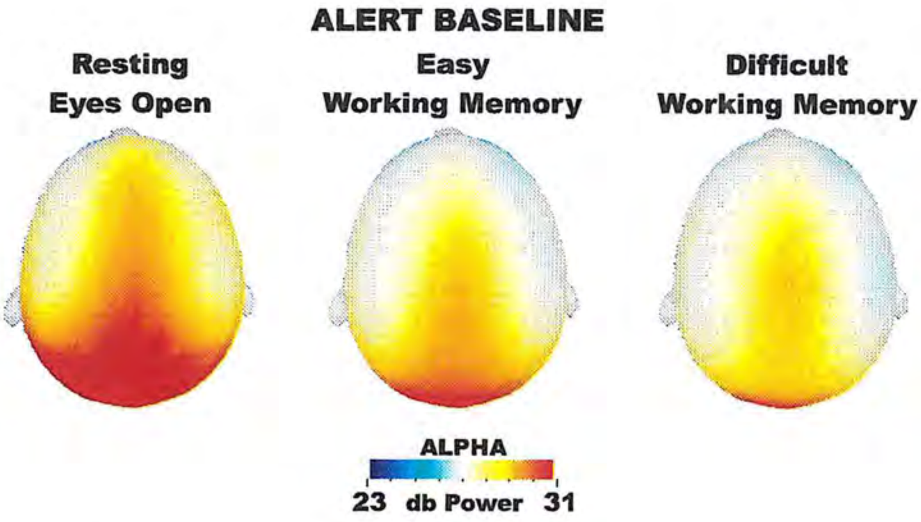

Figure 2. Increasing task difficulty results in decreases in EEG slow and fast alpha signals maximal at posterior sites.

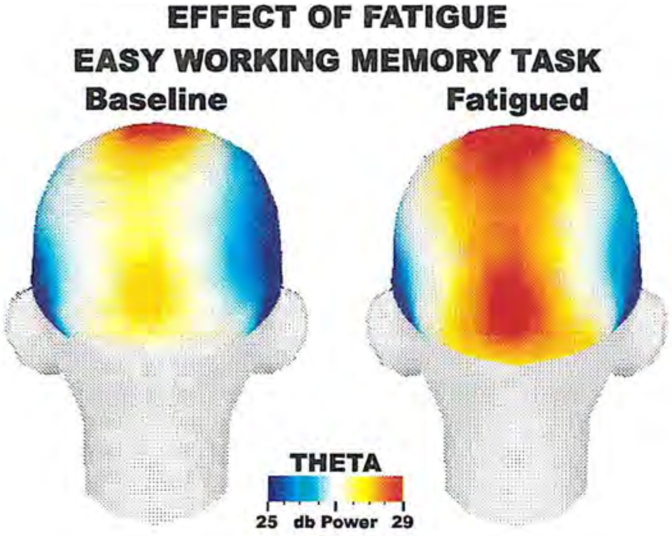

Figure 3. Fatigue results in increases in EEG theta signals, maximal at posterior sites, during the easy working memory task.

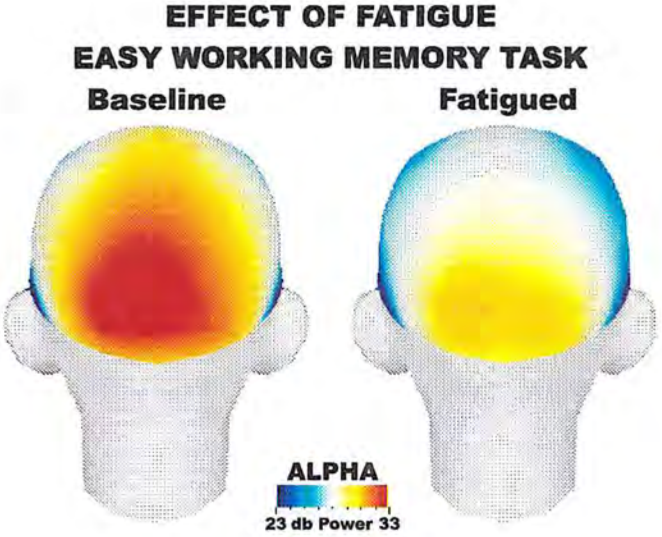

Figure 4. Fatigue results in a decreases in EEG fast alpha signals, maximal at posterior sites, during the easy working memory task.

Changes in neurocognitive state produced by intoxication or fatigue were also associated with changes in the theta and alpha EEGs bands. In general, these changes were less pronounced and often statistically non-significant in the resting EEG data and in the EEG data associated with the PT task, but reliably observed in the EEG recorded during the WM tasks. Frontal theta in the WM task was slightly but significantly elevated in Intoxicated relative to the Alert Baseline [F(1,8)=5.72, $p < .05$]. The Intoxicated state was also observed to reliably increase the strength of the slow alpha signal at parietal sites during the WM task [alcohol: F(1,8)=116.96, $p<.001$] and during the PT task [t(8)= 4.29, $p<.005$], but not during resting states. The diffuse posterior theta and fast alpha signals were relatively insensitive to alcohol.

In contrast, the Fatigued state was associated with a decrease in power in the fast alpha signal relative to the Alert Baseline state (Figure 3) over parietal and occipital sites in the easy version of the WM task [F(1,8)=5.58, $p <.01$], but not in resting data or in data associated with any of the other task conditions. The diffuse theta signal was also sensitive to fatigue, and it displayed distinct task and neurocognitive state correlates from the frontal theta signal. For example, during the Alert Baseline recording, no differences between resting and task conditions were observed for the theta rhythm measured at posterior regions of the scalp. In contrast, the Fatigued state was observed to be associated with an increase in amplitude in the posterior theta signal relative to the Alert Baseline conditions [F(1,8)=19.12, $p<.002$; Figure 4] in the WM task, less so in the PT task (t(8)=2.13, $p < .04$], and not at all in the resting data. Although there is both topographical and frequency domain overlap between the two theta signals, it was possible to systematically dissociate them. For example, when theta measurements from a midline frontal electrode were included in a task difficulty (easy vs. difficult WM) by mental state (Alert vs. Fatigued) ANOVA, main effects of both difficulty [F(1,8)=10.39, $p < .02$] and fatigue [F(1,8)=9.56, $p < .02$] were obtained, but there was no interaction between these factors [$F < 1$]. A derived measurement was then made by subtracting the theta power measured from a posterior midline location from the theta power at the frontal midline location. This would have the effect of removing from the measure any contribution from a topographically diffuse signal, while retaining effects due to a signal that was narrowly distributed around the frontal midline location. When repeating the ANOVA described above on this derived measure, no effect of fatigue was obtained [$F < 1$], but a robust effect of task difficulty was again observed [F(1,8)=11.06, $p < .02$].

Table I) Effects of Changes in Task Difficulty and Mental State on EEG Signals.

	Harder Tasks	**Intoxication**	**Fatigue**
Frontal Theta	Increases	Increases	No effect
Diffuse Theta	No effect	No effect	Increases
Slow Alpha	Decreases	Increases	No effect
Fast Alpha	Decreases	No effect	Decreases

In summary (cf. Table I), changes in task difficulty and neurocognitive state had distinct effects on different EEG signals. These effects are consistent with prior observations from the EEG literature. In the Alert Baseline condition, a frontal midline theta signal (5-7Hz) was found to be larger in more difficult tasks whereas both slow and fast components of the alpha signal were decreased by attention demanding tasks (cf. Berger, 1929; Gevins et al., submitted, 1996; Gevins et al., in press; Gevins, 1995; Gevins et al., 1979a; Gevins et al., 1979c; Gundel &

Wilson, 1992; Ishihari & Yoshii, 1972; Klimesch, Schmike & Pfurtschellar, 1993). Intoxication was found to increase the amplitude of the frontal theta and slow alpha signals (cf. Begleiter & Platz, 1972; Cohen, Porjesz & Begleiter, 1993; Davis, Gibbs, Davis, Jetter & Trowbridge, 1941; Lukas, Mendleson, Benedilt & Jones, 1986). Fatigue was found to increase the amplitude of the diffuse theta signal (cf. Davis, Davis, Loomis, Harvey & Hobart, 1937; Gevins et al., 1977b; Makeig & Jung, 1995) and to decrease the amplitude of posterior alpha (Gevins et al., 1977b).

Individual-Subject Pattern Recognition Results. The descriptive statistics indicate that EEG measures were highly sensitive to variations in mental state, at least in a group-wise statistical sense and especially during the WM task. However they provide little evidence as to whether the effects are robust enough to reliably be used for detecting deviation from an Alert Baseline state in an individual subject. The goal of creating a practical work readiness testing device would be best served by creating an impairment index that utilizes short samples of data collected during a brief simple task battery that could be conveniently obtained from an individual at the start of his or her work shift or at times when circadian or homeostatic cycles were predicted to be lowest. To determine whether the EEG changes observed to accompany intoxication and fatigue could be reliably identified in individual subjects, we first performed a subject-specific neural-network based EEG pattern recognition analyses (cf. Gevins & Morgan, 1988, see description above) on these data to discriminate differences in EEG patterns between the Alert Baseline and Intoxicated and/or Fatigued states. For each subject power spectral features were computed (from the EEG data recorded during the easy version of the WM task across sliding windows of 6-12, 4.5sec trials with an n-1 trial overlap) to serve as inputs to a network. The data were divided into training and testing sets with a 3:1 ratio respectively for both classes. To indicate the significance of testing data set classification accuracy, binomial probabilities were calculated for each test-set classification outcome, with *n* conservatively based on the number of independent (non-overlapping) data samples available for each comparison. Using this criteria, Intoxicated or Fatigued data could be discriminated from Alert data with high statistical significance.

Utilizing alpha and theta features, an average test set classification accuracy of 98% (range 96%-100%) was obtained across subjects for the Baseline vs. Intoxicated comparison, and an accuracy of 92% (range 84%-100%) for the Baseline vs. Fatigued comparison (Table II, Left Side – Individual Networks; average binomial $p < .001$). That is, when trained on examples of a subject's own neurophysiological signals recorded during task performance, it was possible to automatically determine from EEG signals alone whether a new data sample was recorded from the subject when he or she was performing the WM task in an alert or impaired state. These highly significant results were obtained from the EEG data collected during performance of the easy WM task, even though performance accuracy on the test was not significantly affected by fatigue. Finally, to determine whether these methods were adequate to discriminate between two different states of impairment, data from two individual subjects were compared between the Intoxicated and Fatigued states. In both subjects 100% accuracy was obtained ($p < .0001$). Thus, the two different states of impairment produced unique EEG signatures.

Group Network Pattern Recognition Results. While these results are highly encouraging, this type of approach would be difficult to transition into a practical application, because it requires that examples from both alert and impaired states for each subject be used in training the subject-specific neural networks that were utilized (and in most applied contexts only Alert Baseline data would exist for an individual). Hence we subsequently worked on extending this analysis procedure to develop a "group" equation, where a pattern recognition algorithm is trained on data from the alert and impaired states from a group of subjects, and then tested on data samples from subjects who were not part of the training group. A jack-knife procedure was followed, where each subject in turn served as the test case left out of the training (for these analyses, subjects were excluded for whom their datasets contained inadequate numbers of artifact-free trials for the set of common electrodes utilized in the group analysis; this resulted in the elimination of two subjects in each of the group analyses). As shown in Table II (right side- Group Networks), we obtained significant ($p < .05$) classification of Alert Baseline and Intoxicated data samples from each of the test subjects (range 73%-97%; average binomial $p < .001$), utilizing mainly slow parietal alpha and frontal midline theta features. Using this strategy and diffuse theta and fast parieto-occipital alpha EEG features we also obtained significant ($p < .05$) classification (69% to 99%; average $p < .01$) of Alert Baseline and Fatigued data samples from each of the test subjects.

Table II) EEG Pattern Classification Accuracy for Independent Test Data Submitted to Individual and Group Networks; Alert Baseline vs. Intoxicated or Fatigued States

	Individual Networks		**Group Networks**	
Subject	**Intoxicated**	**Fatigued**	**Intoxicated**	**Fatigued**
S1	97%	87%	73%	78%
S2	95%	88%		98%
S3	99%	100%	93%	99%
S4	100%	84%		
S5	100%	96%	97%	73%
S6	100%	94%	94%	
S7	99%	99%	87%	84%
S8	100%	90%	94%	89%
S9	96%	86%	84%	69%

Significance. Due to the limited scope of a Phase I project, only a small group of subjects were analyzed. Thus, these results must be treated as preliminary and limited in their generalizability. Nonetheless, they are remarkable in that they suggest that impairment-related changes in the EEG are highly reproducible and similar across subjects. They are the first demonstration that a generic (group) EEG pattern recognition network can successfully be applied to a new subject to determine whether he or she is in an Intoxicated or Fatigued state. These results have served to clarify several important issues with respect to the feasibility of developing a work readiness test based on neurophysiological measurements. First, we found that task related EEG signals were more sensitive to states of impairment than were eyes-open resting EEG signals, indicating that the test should require that subjects perform some attention demanding task. Second, we found that both EEG signals and test performance measures during a simple working memory task were more sensitive to states of impairment than were either behavioral measures or EEG signals during a perceptuomotor tracking task, suggesting that a simple test based on the WM task might alone be adequate for work readiness testing. Third, we found that EEG features provided sensitive indicators of fatigue even under conditions where task performance variables were unaffected. Fourth, we found that the EEG signature of impairment from alcohol was dramatically different from that associated with Fatigue. Fifth, we found that we could dissociate theta band EEG signals related to task difficulty from those related to fatigue using topographic criteria. Finally, we found that it was possible to classify states of impairment in subjects without prior knowledge of what their individual EEG signals look like during impaired states. These findings establish the basic feasibility of creating a sensitive neurophysiological measure of work readiness that would be suitable for use in conventional work environments.

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