

To the Graduate Council:

I am submitting herewith a dissertation written by Efthymios Angelakis entitled "Peak Alpha Frequency: an Electroencephalographic Measure of Cognitive Preparedness." I have examined the final electronic copy of this dissertation for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, with a major in Psychology.

Joel F. Lubar

Major Professor

We have read this dissertation
and recommend its acceptance:

Eric Sundstrom

John Lounsbury

Teresa Hutchens

Accepted for the Council:

Anne Mayhew

Vice Provost and

Dean of Graduate Studies

(Original signatures are on file with official student records.)

**Peak Alpha Frequency: an Electroencephalographic Measure of Cognitive
Preparedness.**

A Dissertation

Presented for the

Doctor of Philosophy

Degree

The University of Tennessee, Knoxville

Efthymios Angelakis

December 2002

ACKNOWLEDGMENTS

I wish to thank all of those who helped to complete my doctoral dissertation: my advisor and mentor, Dr. Joel F. Lubar, for being there whenever I needed him making available his invaluable knowledge and wisdom; my doctoral committee members, Dr. Eric Sundstrom, Dr. John Lounsbury, and Dr. Teresa Hutchens for their fruitful criticisms and suggestions; Mr. Robert Muenchen for his excellent statistical advice; and my lab colleagues Sheryl Brim, Jon Frederick, Noland White, Kerry Towler, Jared Blackburn, Marco Congedo, Leslie Sherlin, Anthony Zoffuto, and Tina Stathopoulou, for their suggestions, teachings, and fellowship during my work at the Brain Research and Quantitative EEG Analysis Laboratory; especially I thank Marco and Les for giving me their Workstation EEG analysis software, and Tina for giving me her TBI data.

Moreover, I like to thank all of those who helped me be in the position of pursuing a doctorate: my parents, Theofanis and Maria, for all of their support; my wife, Tina, for being next to me; my undergraduate professors for preparing me well enough, and especially Dr. Michael Nikoletseas, Dr. Lilly Katsaiti, Dr. Lena Pateraki, & Mrs. Anastasia Logotheti, who believed in me and made me believe in myself.

Finally, I want to thank all of those in the department of Psychology, here, at the University of Tennessee, Knoxville, who accepted me in the doctoral program and supported my graduate studies one way or another: Dr. James Lawler, Dr. Richard Saudargas, Mrs. Connie Ogle, and all the faculty and staff who I worked with since 1998.

ABSTRACT

Background. Electroencephalographic (EEG) peak alpha frequency (PAF) has been shown to correlate with a variety of phenomena, including age, memory performance in healthy and demented individuals, different emotional states, schizophrenia, anxiety, recovery from stroke, cerebral blood flow (CBF) velocity, brain oxygenation, as well as acute administration of stimulant and nootropic substances. These studies have shown that PAF varies between healthy and clinical individuals, with the latter consistently having lower PAF. Moreover, PAF varies between healthy individuals, reflecting cognitive performance, with better performance being associated with increased PAF. Finally, PAF varies within individuals both between developmental stages and between different cognitive tasks, or physiological states induced by administration of various substances.

The present study suggests that among other phenomena PAF reflects a trait or state of *cognitive preparedness*, using three independent datasets from healthy and brain injured individuals. Based on the preceding literature, the following hypotheses were generated. First, that PAF is an index of optimal brain function, being suppressed under traumatic brain injury (TBI). Second, that PAF is negatively correlated with time since TBI, and that it is increased after cognitive rehabilitation of individuals with TBI. Third, that PAF shows cognitive preparedness within individuals, reflecting task performance differences at different days. Fourth, that PAF is increased after tasks more in those individuals who had it lower at initial baseline, being affected by the task that forces them to correct their initial unpreparedness.

Method. Dataset A involved EEG recordings from 15 healthy young adults before, during, and after a set of reading tasks (task duration 5-20 minutes) . Dataset B involved EEG recordings from 10 individuals with TBI and 12 healthy age and sex matched controls, before, during, and after tasks of visual and auditory attention (task duration 20 minutes) (Captain's Log, Braintrain). Dataset C involved EEG recordings from 19 healthy young adults before and after a 3-minute working memory task (WAIS-R Digit Span). In this dataset, the procedure has been repeated in two different days, so within individual differences in PAF and performance could be measured. EEG was recorded at 19 scalp electrodes using the 10/20 international electrode placement system. Average PAF for each recording was reported using the EEG Workstation 2.0 software (NovatechEEG, inc.).

Results. PAF showed significantly lower values in individuals with TBI as compared to matched healthy controls during a post-task eyes-open baseline. PAF recorded at day 1 was significantly correlated with Digit Span performance of the same day but not with Digit Span performance of day 2. Likewise, PAF recorded at day 2 was significantly correlated with Digit Span performance of the same day but not with Digit Span performance of day 1. Moreover, PAF was significantly increased after Digit Span for those participants who had it below the sample median before the task, whereas it did not increase significantly for those who had it above the sample median. However, this was not replicated with PAF before and after reading tasks. Finally, PAF was not found to be significantly correlated to time since TBI, and it did not increase significantly after cognitive rehabilitation of individuals with TBI.

Conclusions. As expected, individuals with brain injury had lower PAF from healthy controls, confirming the consistent direction of PAF differences between normal brain function and pathology, as is the case with other neurological or psychiatric syndromes, including stroke, dementia, and schizophrenia. Interestingly, these differences between individuals with TBI and non-clinical controls were mostly prominent during a baseline that followed a set of cognitive tasks, resembling other physiological indices that require stressing the organ to be assessed (e.g. electrocardiogram).

In addition to its sensitivity to gross brain pathology, PAF was found to be particularly sensitive to brain states within individuals during different days. PAF significantly predicted cognitive performance on a working memory task that was performed immediately after EEG recording, whereas it did not predict performance within a few days. In addition to predict performance, PAF was found to be affected by a working memory task, extending previous research and supporting a strong dual relationship between PAF and cognitive performance. The nature and duration of this state of relationship, however, needs further investigation. Although a short working memory task increased PAF in individuals who had it lower immediately before the task, a longer set of reading tasks failed to replicate this phenomenon. It is suggested that EEG normative databases include PAF into their statistical reports and that neurofeedback protocols to increase PAF are attempted to improve cognitive performance in both clinical and non-clinical populations.

TABLE OF CONTENTS

Section	Page
1. INTRODUCTION	1
2. METHOD	11
3. RESULTS	22
4. DISCUSSION	23
5. CONCLUSIONS	27
REFERENCES	28
APPENDIX	36
VITA.....	45

1. INTRODUCTION

1.1. The EEG alpha rhythm.

The human EEG is largely characterized by synchronous oscillating activity, ranging from 0.1 Hz to 100 Hz, when recorded at the scalp, and is restricted to 1- 45 Hz, when clinical significance is considered (Niedermeyer, 1999). One of the most prominent EEG phenomena, and the first to be discovered, is the *alpha* rhythm, a bursting oscillation between 8 – 13 Hz recorded mostly at posterior cortical areas of awake individuals that have their eyes closed. The alpha rhythm has been extensively studied and its *magnitude* (wave amplitude averaged across time, representing the abundance and/or amplitude of the rhythm) has been positively associated with states of relaxation and mental inactivity (Niedermeyer, 1999). Although alpha is a name assigned to a posterior rhythm and, therefore, reflecting activity of the sensory cortex, similar phenomena are observed in the motor cortex.

Rolandic mu rhythm is an oscillatory activity recorded over the primary motor cortex. Its waveform, amplitude, and spectral distribution resemble those of the alpha (i.e., posterior) rhythm but it reacts to motor rather than sensory activity. However, the reactivity of both alpha and mu seems if not similar at least equivalent, since both decrease in magnitude during activity of the underlying cortex (e.g., eye opening and muscle movement, respectively), and increase in magnitude during rest of the underlying cortex (Niedermeyer, 1999). For the remaining of this manuscript all activity between 8 – 13 Hz will be termed “alpha” and, whenever necessary, its topographical distribution over the cortex will be mentioned to differentiate between sensory and motor brain activity.

The spectral distribution of the alpha rhythm usually resembles a bell shaped curve with an average peak of 10-11 Hz in healthy adults (Klimesch, 1997; Posthuma et al., 2001). This peak is lower (in Hz) in children and the elderly, but also varies between individuals.

1.2. Peak alpha frequency (PAF).

Different formulas have been used to quantify the variation of spectral distribution within the alpha range. PAF measures the discrete frequency with the highest magnitude within the alpha range. Individual alpha frequency (IAF) measures the center of gravity, rather than peak, within the alpha frequency, and has been used as a possibly more accurate - rather than different - measure of PAF (Klimesch, 1997). PAF (or IAF) is an EEG measure that shows the frequency distribution of magnitude within the alpha band (8-13 Hz), but it is not a direct measure of magnitude, and therefore should not be compared to EEG alpha magnitude measures. High PAF means that there is more magnitude at the higher part of the alpha spectrum, and vice versa. An alternative way to observe spectral alpha distribution is to divide the alpha spectrum into two frequency bands above and below the average peak of 10-11 Hz, for example 8 – 10 Hz (low alpha) and 10 – 12 Hz (high alpha), and then observe the differential magnitude of these two sub-bands (e.g., Pfurtscheller, 1989; Doppelmayr, Klimesch, Pachinger, & Ripper, 1998). This is based on the assumption that alpha rhythms are generated by at least two independent pacemakers, one oscillating below 10 Hz and another above 10 Hz. Although the production of the scalp-recorded alpha rhythm is obviously cortical, different theories support cortical and/or thalamic origin of the alpha pacemakers. For example, some researchers have suggested a thalamic origin (Andersen & Andersson,

1968), but others have challenged this view and have suggested a cortical origin (Lopes da Silva, Van Lierop, T.H.M.T., Schrijer, et al., 1973a, 1973b; Nunez, Wingeier, & Silberstein, 2001). Still others speculate a combined model, where low alpha generators are thalamo-cortical and react to attention, and high alpha generators are cortico-cortical and react to memory activation (Pigeau & Frame, 1992; Klimesch, 1997).

1.3. PAF & cognitive performance in healthy individuals.

Several studies have shown PAF to reflect cognitive performance in various areas, including attention, arousal, working memory (WM), long-term memory (LTM), and reading. It has been suggested that PAF variations within individuals reflect attentional demands and/or arousal (Klimesch, Schimke, Ladurner, & Pfurtscheller, 1990). Osaka (1984) reported PAF to show lateralized increases according to the type of cognitive task, in 10 healthy young adults. PAF increased more in the right hemisphere during a visuospatial task and more in the left hemisphere during an arithmetic task. In a different study, Osaka, Osaka, Koyama, Okusa, et al. (1999) found PAF to increase during an auditory working memory task as compared to a control task. Klimesch et al. (1990) reported that IAF during a memory task was correlated with performance in the memory task, in a group of healthy young individuals, and suggested that IAF may be an index of memory ability. In another experiment, these researchers found that individuals with lower memory performance decreased their IAF during increasing memory demands, whereas individuals with higher memory performance had their PAF constant (and higher to that of the first group) during the same conditions (Klimesch Schimke, & Pfurtscheller, 1993). In a resting state immediately after reading, high alpha (10-12 Hz) has been found

to increase in magnitude with no changes in low alpha (8-10 Hz) (Angelakis & Lubar, 2002), suggesting a post-task increase in either PAF or IAF.

PAF has been also related to developmental differences in cognitive performance. A recent study found higher PAF in children with higher reading performance as compared to age-matched controls (Suldo, Olson, & Evans, 2001). This study also found that children with higher reading performance had their PAF at the same level with older children of equal reading performance, and thus interpreted PAF as a maturational index of the brain. In a study with 120 individuals between 46-80 years of age, Li, Sun, and Jiao, (1996) found PAF to decrease with increasing age, and to be correlated with speed and performance in a number of cognitive tasks. In a large twins study with 688 participants, Posthuma, Neale, Boomsma, and de Geus (2001) found PAF and intelligence to be highly heritable, although PAF did not correlate with intelligence.

1.4. PAF & CBF in psychiatric and neurological diagnoses.

Patients of Alzheimer's dementia (AD) have been found to have reduced PAF or IAF when compared to age-matched controls. Klimesch et al. (1990) found that a group of 18 AD patients had 1.46 Hz lower IAF to that of an age-reference control group of 20 (mean IAF for the two groups: 7.58 Hz and 9.04 Hz respectively). Moreover, they found a within-group difference in IAF when memory performance was considered. Both AD patients and controls with better memory performance in the Wechsler Memory Scale had higher IAF than those with worse memory performance, within groups. However, while the AD group showed significant correlations of IAF with memory performance, the control group did not. The authors did not clarify whether the IAF was calculated on

an EEG recorded at the same or at a different day to that of the memory test administration.

Passero, Rocchi, Vatti, Buralassi, et al. (1995) also found reduced PAF in AD patients when compared to age-matched controls, mostly in temporal and parietal areas. These investigators measured also CBF and found it to be lower in AD patients as well, again in temporal and parietal areas. However, contrary to Klimesch and colleagues' findings, PAF was not significantly correlated with cognitive impairment, although CBF was. This may have been due to the difference between IAF and PAF, the former being considered as a more sensitive measure.

Other psychiatric syndromes that involve decreased PAF include schizophrenia, chronic fatigue syndrome, and hemispheric stroke. Patients with schizophrenia showed decreased PAF both before and following treatment with aripiprazole (Canive, Lewine, Edgar, Davis, et al., 1998). In the case of chronic fatigue syndrome, PAF was negatively correlated with total fatigue and "today fatigue" reports (Billiot, Budzynski, & Andrasik, 1997). Hemispheric stroke patients showed PAF decreases in their affected hemisphere only within 48 hours of their acute episode, which were normalized during recovery after 2-4 weeks (Juhasz, Kamondi, & Szirmai, 1997). Interestingly, children with mental retardation showed increases in PAF after six months of pineal hormone treatment (Psatta, Goldstein, & Matei, 1991).

1.5. PAF, emotional states, & arousal.

PAF has been shown to reflect emotional and/or autonomic states. Kostyunina and Kulikov (1995; Kostyunina, 1998) found PAF increases during mental reproduction of joy and anger, and PAF decreases during fear and sorrow, when compared to a neutral

baseline. These changes involved right centro-temporal (C4, T4) and left frontal (F3) and occipital (O1) locations. In a different study, Tiffin, Ashton, Marsh, and Kamali (1995) found that people with poorer sleep and higher anxiety had higher PAF than controls.

Single doses of nicotine and caffeine have been shown to increase PAF. A single cigarette was found to increase PAF at the fourth puff (Knott, 1988). Intravenous administration of nicotine in regular smokers who abstained from smoking for 12 hours produced a linear, dose-related increase of PAF due to increase in high alpha power with no changes in low alpha (Lindgren, Molander, Verbaan, Lunell, et al., 1999). Caffeine has also been associated with increases in PAF accompanied by a decrease in alpha power at occipital sites, in both patients with panic disorder and healthy controls (Newman, Stein, Trettau, Coppola, et al., 1992).

1.6. Piracetam, cerebral blood flow (CBF) & PAF.

Piracetam is a drug that belongs to the nootropic class. Nootropics are defined as mind enhancing drugs that “exert the greatest cognition-enhancing effects under conditions of neural impairment, and ... should generally not produce the kinds of behavioral effects associated with classic psychotropic drugs” (Feldman, Meyer, & Quenzer, 1997, p.902). Piracetam appears to alter acetylcholine (Ach) and norepinephrine (NE) levels, and to alter cellular brain metabolism by increasing the levels of brain adenosine triphosphate (ATP) (Conners & Sparrow, 1999). Piracetam has been found to improve reading performance of healthy and dyslexic children and adults (for reviews, see Wilsher, 1994; Conners & Sparrow, 1999), as well as to improve the symptoms of 10-30 % of patients with Alzheimer’s disease (Pierlovisi, Michel, Sebban, Tesolin, et al., 1991; Feldman, Meyer, & Quenzer, 1997, p.903).

A study with 10 healthy elderly volunteers in their 60's found that acute piracetam administration increased PAF (Saletu et al., 1984). Consequent studies with healthy young volunteers and geriatric patients showed single doses of piracetam to increase high alpha (above 9.5 Hz) magnitude (Kinoshita, 1990), and to prevent changes in the EEG caused under hypoxia without piracetam in healthy volunteers (Saletu, Hitztenberger, Gruenberger, Anderer, et al., 1995).

Some studies have shown a positive relationship between PAF, CBF, and cerebral oxygenation. In two studies, after indomethacin administration (a substance that decreases CBF), a decrease in CBF velocity was accompanied by a 0.3-0.5 Hz slowing of PAF and increases in reaction time in a memory test, in healthy young adults (Hemler, Hoogeveen, Kraaier, Van Huffelen, et al., 1990; Kraaier, Van Huffelen, Wieneke, Van der Worp, et al., 1992), whereas in another study PAF decreased after hypoxia with hemoglobin oxygen (Van der Worp, Kraaier, Wieneke, & Van Huffelen, 1991).

1.7. General conclusions on PAF.

Summarizing the above reviewed literature, PAF (or IAF) seems to be an index of cognitive capacity (called hereafter "cognitive preparedness"), affected by either traits or states of the brain. Regarding its capacity to reflect traits, it has been widely shown that PAF varies between healthy and clinical individuals, with the latter consistently having reduced PAF when compared to healthy controls (section 1.4). When tested in cognitive performance, clinical individuals are shown to score lower than matched healthy controls (Passero et al., 1995; Klimesch et al., 1990), which supports their reduced cognitive preparedness. Moreover, PAF has been shown to reflect maturational traits of reading performance in healthy children (Suldo et al., 2001). Although it did not reflect

intelligence in one large study (Posthuma et al., 2001), PAF has been found to be positively correlated with memory and with speed of processing between healthy individuals (sections 1.3 & 1.6).

Regarding its capacity to reflect states within individuals, PAF (or IAF, or high versus low alpha) has been found to be affected by cognitive tasks, (Osaka et al., 1999; Klimesch et al., 1993; Angelakis & Lubar, 2002), mental reproduction of emotional states, and acute administration of various substances (sections 1.5 & 1.6).

The fact that PAF reflects different levels of CBF and/or cerebral oxygenation (section 1.6) may explain both trait and state differences in PAF, between and within individuals. In the case of brain pathology (section 1.4), lower PAF may reflect larger degrees of permanent or long-term deficits in CBF (traits). In the case of within individual changes, PAF has been shown to reflect differences in CBF and/or cerebral oxygenation due to administration of various substances (sections 1.5 & 1.6) (states). Likewise, PAF changes within individuals during cognitive manipulation may fit a CBF model, too, suggesting that performance differences are due to differences in brain metabolism. However, PAF may also be an indirect correlate of brain metabolism, and its correlation with cognitive performance be due to something different. Whatever the case is, PAF shows a stable direction of relationship with cognitive performance and brain metabolism, and therefore is a valid index of cognitive potential.

1.8. Rationale.

Regardless of its physiological substrate (i.e., whether PAF is a direct result or cause of changes in brain metabolism, or just an indirect correlate of it), the present study suggests that PAF measures *cognitive preparedness*. Cognitive preparedness refers to a

brain trait or state that sets the stage for optimal cognitive performance. Based on the preceding literature, the following assumptions were generated. First, that PAF is suppressed under any *trait* of brain pathology, and that PAF normalizes (increases) as brain functions of damaged brains recover. Second, that PAF fluctuates within healthy individuals according to brain *state*, predicting consequent cognitive performance, and being affected by cognitive tasks.

In order to test these assumptions, three independent datasets were analyzed. One dataset involved EEG recordings of 15 healthy young adults before, during, and after reading tasks. A second dataset involved EEG recordings of 10 individuals with traumatic brain injury (TBI) and 12 healthy controls, before, during and after tasks of visual and auditory attention. Five individuals with TBI from this dataset have also been subjected to cognitive rehabilitation, and EEG recordings were made available before and after rehabilitation. The third dataset involved EEG recordings from 19 healthy young adults before and after a working memory (WM) task. In this dataset, the procedure has been repeated in two different days, so within individual differences in PAF and performance could be measured.

1.9. Hypotheses.

First, if PAF is suppressed under any *trait* of brain pathology, it was expected to show lower values in individuals with TBI as compared to matched healthy controls (hypothesis 1). Second, if PAF normalizes after brain recovery, it was expected that it would be negatively correlated with time between injury and EEG recording in TBI patients (hypothesis 2.a), and would increase after cognitive rehabilitation (hypothesis 2.b). Third, if PAF is a measure of a state of cognitive preparedness in healthy

individuals, then it was expected that PAF from initial resting baseline would correlate higher with WM performance of the same day than to performance of a different day (hypothesis 3.a). Moreover, it was expected that PAF would increase after a task more in those individuals who had it lower before the task. This was based on the assumption that their PAF would be affected by the task, which would force them to correct their initial unpreparedness (hypothesis 3.b).

2. METHOD

2.1. Dataset A.

Participants

Fifteen psychology college students were included, 8 male and 7 female, all volunteering for extra credit. These were selected from an initial sample of 19 (12 male, 7 female) from which four participants (two male and two female) were eliminated from further analysis. This decision was based on poor EEG recordings, or significant deviations from either a normative qEEG database or psychometric testing, according to the following screening process. First, it was determined from their self-reports that no participant had any neurological or psychological history that would significantly affect the qEEG. To cross-validate this decision, relative power reports from the Thatcher Lifespan Normative Database (LND) (Thatcher, Walker, Gerson, & Geisler, 1989) were inspected. Two of them showed significant deviations (higher than normal) in alpha (7-13 Hz) activity in ten frontal locations from the LND; another scored more than one standard deviation below norms on six psychometric tests (IVA scores and five out of six Woodcock-Johnson scores, indicating a possible attention deficit with a reading difficulty); and a fourth one had excessive muscle artifact contamination of the EEG. So, because of clear deviations from normative data, these four students were excluded from the study in order to avoid confounding effects, reducing the initial sample to nineteen participants. All participants were right-handed, as per their self-report.

Materials

A self-report form (see appendix) was administered to collect data on neurological and psychological history. Nine psychometric tests were administered in order to control for

possible cognitive deviancies that would exclude participants from a non-clinical sample. These subtests included the Integrated Visual and Auditory Continuous Performance Test (IVA) that measures attention and hyperactivity; the Vocabulary and Block Design subtests of the Weschler Adult Intelligence Scale III (WAIS-III) that measure linguistic and visuospatial skills; six subtests from the Woodcock-Johnson Achievement Battery Revised (WJ-R), specifically the Letter-Word Identification subtest for the assessment of pronunciation and paralexia reading, the Passage Comprehension subtest for the assessment of reading comprehension skills, the Word Attack subtest for the assessment of phonic, structural and auditory processing skills, the Reading Vocabulary subtest for the assessment of word semantic/conceptual skills, the Calculation subtest for assessment of arithmetic operations skills, and the Quantitative Concepts subtest for the assessment of knowledge of mathematical concepts.

Materials for the five reading tasks were developed in our laboratory. Three excerpts from Homer's *Odyssey* translated to English were used to selectively engage participants into visual, phonological, and semantic processing. Participants were asked to identify target words following different rules for each processing modality. Visual reading required the identification of four-letter words that include at least one "a" (e.g. *have*); phonological reading required the identification of words that included the sound "k" (as in *cross* or *peak*); and semantic reading required the identification of nouns that refer to a non-animate material object or entity (e.g. *table* or *ocean*). In addition to the three texts, one list with grammatically spelled and misspelled words and one list with pairs of numbers were administered. The list of words required the identification of misspelled words where misspellings consisted of reversed "b" as a "d" and vice-versa, or reversed

"p" as a "q" and vice-versa (e.g., *ranbom* or *quarty*). The list of pairs of numbers required the identification of pairs where one number was a multiple of the other (e.g., 2-4 or 15-3).

Texts were selected so that they were narrative, easy to read, and with a minimum number of proper names. Moreover, all three texts contained 20 (+/-1) target words for all three reading requirements, but in different positions randomly. The two lists also contained 20 targets.

Apparatus

EEG was recorded with a Lexicor Neurosearch 24 analog to digital system, and all data were stored and visually artifact rejected using a Pentium 120 MHz computer, and Lexicor's v41e software. Nineteen-channel electrode caps using the 10/20 international electrode placement system by Electro Cap Inc. were used, with linked ear lobe references. The EEG data were collected with a band-pass filter set at 0.5-32 Hz for 128 samples per second recordings and at 0.5-64 Hz for 256 samples per second recordings. Digital EEG was processed by Fast-Fourier Reading materials were presented on a 17" color screen of a Pentium computer. In order to identify possible distinct EEG abnormalities, the Thatcher-Lifespan Normative Database (LND) was used to compare participants' eyes closed resting EEG recordings to a normative sample of non-clinical individuals of similar sex and age.

Procedure

All data were collected in a quiet windowless laboratory room with fluorescent lighting and no other persons present except for the participant and the experimenter. Participation was completed in two sessions on different days. All EEG recordings were

completed within the first day of participation. On this day, participants were first asked to complete a self-report form concerning personal history on any psychological or neurological diagnosis (including reading difficulties), current prescription medication usage, head injuries, age, sex, and handedness (left or right). Then participants were fitted with the Electro Cap, and impedance at all channels was measured to be below 5 kOhms.

Participants were seated in an armchair with instructions to direct their eyes toward a computer screen at a distance of 60 cm. Nineteen-channel EEG activity was recorded in the following order: first, during an eyes-closed resting condition (ECB); second, during an eyes-open resting condition (EOB), where participants were instructed to focus on the notepad window on the computer screen, while no text was running; then, five reading tasks (the three Odyssey texts, a list of misspelled words and a list of numbers) and a post-task eyes-open resting condition (PTR) were administered in a counterbalanced order across participants, during which EEG was recorded.

All target items were randomly distributed within the texts. The three Odyssey texts were always presented in the same order, but for different reading requirements (i.e. visual, phonological, or semantic), according to the counterbalanced order. In addition, the two reading lists and the PTR were included in the counterbalanced procedure but the PTR was always preceded by at least one reading task. This varied presentation order was employed to avoid confounding of order effects and text related effects.

In order to minimize eye movements and control speed of stimulus presentation, reading materials were computerized and presented in a self-running mode through a 1 x 5 cm Notepad window (Microsoft Windows 95), with the aid of Keyboard Express (Insight Software Solutions), which programmed the DELETE key of the computer to

continuously strike every 100 milliseconds, "pulling" the text into the left side of the notepad window. This ensured that the resulted texts were presented at a pace of two words per second. This presentation mode obliged participants to focus on a limited area to read, while the text was running through the window at a constant speed.

Each recording lasted 3.3 minutes, between which participants had the opportunity to rest, stretch, and relax for 1 minute. Before recording each reading task, a practice portion mimicking each task was administered for 30 seconds, which enabled the participants to become familiar with the task demands. All reading was silent. While reading, participants were responding to target word identification by pressing a key on the computer keyboard with their right hand. This key put a marker on the EEG recording, which was later compared (during data analysis) with a timed key of correct responses. This was done by visually inspecting the raw EEG files for markers at specific times according to the timed keys, with +/- one-second allowance for differential reaction time and synchronization of the EEG and the Keyboard Express. The procedure was completed within 120 minutes. During the second day of participation, within one week after the EEG recording, participants were measured using the psychometric tests.

2.2. Dataset B.

Participants

Ten individuals (5 males and 5 females) with traumatic brain injury (TBI) and acquired attention deficits, and 12 age, sex, and education matched controls provided the data for this dataset. The TBI patients have been referred either by the Association of Brain Injured patients of Knoxville or from the Disability Service of the University of Tennessee (UT), whereas the controls were recruited from UT's undergraduate

population. Ages ranged from 20 to 45. All TBI patients had had their accident occur at least one year before starting the project in order to avoid spontaneous recovery, usually happening the first 6 months after the accident. Their accident had occurred at different time periods, starting from one and a half to twenty years before their coming to the study. Participants were not engaged in any therapy or medication that particular period of the study.

Materials

All participants took the WAIS-R Digit Span and Digit Symbol subtests, the Paced Auditory Serial Addition Test (PASAT), and the Integrated Visual and Auditory (IVA) continuous performance test (Braintrain). Digit Span assesses working memory, short-term memory, sequential processing and learning ability. Digit Symbol assesses perceptual organization, sequential processing, learning ability, visual short-term memory and visual-motor coordination. PASAT assesses information processing skills and the IVA different types of auditory and visual attention. Cognitive rehabilitation involved Captain's Log (Braintrain), a computerized program for the remediation of attention deficits.

From the above tests, in the WAIS-R Digit Span subtest, the orally presented 3-9 digits have to be orally reproduced forward and backwards. In the WAIS-R Digit Symbol there are nine symbols paired with nine digits. The examinee has 1 1/2 minutes to fill in as many symbols as he can, under the numbers on the answer sheet. In the PASAT test, numbers are orally-presented from a tape. The individual had to add each number he/she hears to the immediately previous number and say the resulting number. In the IVA test,

the participant hears or sees on the screen either the number “1” or the number “2” and must click the mouse only when he/she hears or sees number “1”.

The six cognitive tasks during which EEG was recorded were taken from the Captain's Log software program that measures and trains different types of attention. Each one of them lasts for 3 minutes, and all together lasted for approximately 20 minutes. In the first task the participant listened to two patterns of rhythm and had to chose whether they were the same or different by clicking on the respective (“same” or “different”) box. In the second task the person chose between two patterns of melody. In the third task the person had to click the mouse each time two of three boxes (the center one with each of the lateral ones) matched in color. In the fourth task the person clicked the mouse each time the box matched in color with the rectangular border line. In the fifth task the person saw a series of numbers/letters appearing one after another and had to click the mouse each time he/she saw the number or letter designed as target from the beginning. In the sixth task the person clicked the mouse each time he/she saw a box of particular size but not when boxes of other sizes appear.

Training (when applied) involved 25 tasks from the Captain’s Log training software, including the six tasks described above and other of similar nature, for the improvement of visuospatial memory, visual motor skills, visual alternating attention, verbal memory, auditory memory, working memory, memory for figures, choice reaction time, auditory discrimination and perceptual skills.

Apparatus

EEG was recorded with a Lexicor Neurosearch 24 EEG recorder, using a head cap with electrodes set according to the 10/20 international standard. The "attention skills

tasks" of the Captain's Log program were presented in a computer screen 50cm from the participants' eyes. The participants responded using the computer's mouse. Speakers with adjustable volume were also used.

Procedure

During the first day, participants were tested with the psychometric tests. On a following day, EEG was recorded during an eyes-open and an eyes-closed resting baseline, during the six Captain's Log cognitive tasks, and during a second post-task eyes-open resting condition. Five out of the 10 TBI participants were also trained three times per week for the remediation of their attention skills, 50 minutes per session, for 22 sessions with the Captain's Log software. After completion of the 22 training sessions, all the assessment tests and EEG recordings were administered again. EEG capping procedures were identical with those of dataset A. All EEG data were recorded at 128 samples per second and other equipment settings as in dataset A.

2.3. Dataset C.

Participants

Nineteen undergraduate psychology college students were included, 6 male and 13 female, all volunteering for extra credit.

Materials

The Stanford Sleepiness Scale (SSS) was administered to measure self-reported drowsiness, and the Digit Span subtest of the WAIS-R was administered as a working memory task (see dataset B materials for description).

Procedure

Participation involved two sessions at different days, during which identical procedures took place. First, participants were put the electro-cap on (see dataset A for details) and were asked to fill the SSS. Then, EEG was recorded during an eyes-closed and an eyes-open resting baseline. After these recordings the Digit Span test was administered, and immediately after (less than one minute) a final EEG eyes-closed resting baseline was recorded. EEG was recorded at 128 samples per second during the initial eyes-closed baseline, and at 64 samples per second during the following two recordings. All other EEG procedures and settings are identical as in dataset A.

2.4. Data analysis.

All raw EEG data were visually inspected and all epochs including artifacts due to muscle movement or tension were removed from further analysis. Epochs with slow-wave activity seen primarily in FP1 and FP2 were rejected, being interpreted as vertical eye or eyelid movements; and epochs with convergence between F7 and F8 were rejected, being interpreted as lateral eye movements. Moreover, epochs with high-frequency activity primarily in peripheral channels were rejected, being interpreted as muscle tension. Average PAF for each recording was reported using the EEG Workstation 2.0 software (NovatechEEG, inc.). PAF was defined as the discrete frequency that has the highest magnitude in each recording, within the range of 8 to 13 Hz for each of the 19 channels. All EEG recordings of 128 and 256 samples/second were down-sampled to 64 samples per second, to yield frequency resolution of $\frac{1}{4}$ Hz. This was done by averaging every 2 or 4 samples, for the 128 and 256 recordings respectively.

Since most data were found to be not normally distributed, non-parametric procedures were used to test all hypotheses. Hypotheses 1, 2.a, and 2.b were tested using dataset B. Hypothesis 1 was tested with Mann-Whitney U-tests comparing PAF between TBI individuals and healthy controls during initial resting eyes-closed baseline (ECB), during initial eyes-open baseline (EOB1), during the second cognitive task of melody discrimination (TASK), and during post-task eyes-open baseline (EOB2). Moreover, because some conditions were found to violate homoscedasticity between groups in dataset B, t-tests that correct for heteroscedasticity were used for these conditions. Hypothesis 2.a was tested with correlations between time from injury (in months) and PAF, using Spearman's non-parametric test. For this hypothesis, three participants were excluded from the analysis because their clinical history involved multiple days (or even months) of coma after the injury, leaving a sample size of 7. Hypothesis 2.b was tested with Mann-Whitney U-tests comparing pre and post treatment PAF for the 5 trained TBI participants, for ECB, EOB1, and EOB2.

Hypothesis 3.a was tested using dataset C, by correlating PAF from initial resting baseline of each day to Digit Span performance of each day, and then testing for significance using Spearman's non-parametric test. Finally, hypothesis 3.b was tested for two different tasks, Digit Span and reading, using datasets C and A. This was tested by dividing participants into two groups (for each dataset separately), one whose PAF at initial resting baseline was higher to the group's median, and one whose PAF was lower. Then, differences between PAF before and after Digit Span, or reading, were tested, using Mann-Whitney U-tests.

For the statistical analyses Excel 2000 (Microsoft Inc.) and SPSS 10.07 (SPSS Inc.) software were used. Because of the large number of statistical analyses, a-level for statistical significance was adjusted to avoid type-I error (false positives). Since each hypothesis involved more than one conditions (e.g., hypothesis 1.a included four conditions, ECB, EOB1, TASK, and EOB2), a-level was adjusted using a sequential Bonnferroni adjustment for multiple comparisons for the number of conditions involved. This technique increases the power of the standard Bonnferroni adjustment, reducing the probability of type-II error (Rice, 1988; Miller, 1981; Holm, 1979). First, the values of all 19 electrodes were averaged for each condition. Then, the alpha level .05 was divided by the total number of conditions for each hypothesis (e.g., $.05 / 4 = .0125$). All p-values were rank-ordered, and the smallest p-value was compared to the corrected a-level (.0125). If the p-value was smaller, it was considered significant. Then, the corrected a-level was multiplied by 2 ($.0125 * 2 = .025$) to test the second smallest p-value, and if that was found significant, too, the initial a-level was multiplied by 3 ($.0125 * 3 = .0375$), and so on, until the p-value became greater than the adjusted alpha level. If the averaged condition was found significant, then individual electrodes were tested with uncorrected alpha-level (.05), to reveal topographical distribution. In case that averaged electrodes would not yield significant results, then the alpha-level for each condition would be further corrected by 19 electrodes.

3. RESULTS

Because of the large number of statistical analyses, significant results are reported in tables 1, 3, and 4, for hypotheses 1, 3.a, and 3.b respectively. Hypothesis 1 (dataset B) was supported (see table 1 and figure 1). Average PAF across 19 electrodes was significantly lower in individuals with TBI as compared to matched healthy controls in EOB2 (PAF-TBI: 8.83, controls: 9.81; Mann-Whitney z : 2.24, $p=.010$).

Hypothesis 2.a (dataset B) was not supported. There were no significant correlations between PAF and time since TBI. Hypothesis 2.b was not supported either. There were no significant increases of PAF after cognitive rehabilitation of participants with TBI.

Hypothesis 3.a (dataset C) was supported (see table 2 and figure 2). Average PAF across 19 electrodes recorded at day 1 was significantly correlated with Digit Span performance of the same day ($r=.48$, $p=.021$) but not with Digit Span performance of day 2 ($r=.32$, $p=.10$). Likewise, average PAF recorded at day 2 was significantly correlated with Digit Span performance of the same day ($r=.42$, $p=.040$) but not with Digit Span performance of day 1 ($r=.27$, $p=.14$).

Finally, hypothesis 3.b (datasets C & A) was partially supported (see figure 3 and table 3). In dataset B, average PAF across 19 electrodes was significantly increased after Digit Span for those participants who had it below the group median before the task (day 1: 8.47-9.55 Hz, $p=.005$; day 2: 8.85-9.29 Hz, $p=.008$), whereas it did not increase significantly for those who had it above the group median (day 1: 9.95-10.30 Hz, $p=.107$; day 2: 10.33-10.40 Hz, $p=.107$). However, dataset C did not show any significant results with PAF before and after reading tasks.

4. DISCUSSION

The results of this study are consistent with previous research showing a stable direction of PAF difference between normal brain function and pathology. As expected, individuals with TBI had lower PAF from healthy controls, as is the case with other neurological or psychiatric syndromes, including stroke, dementia, and schizophrenia (see section 1.4). Although EOB2 was the only condition to be considered statistically significant in its results, the other three conditions (ECB, EOB1, and TASK) were very close to reach significance (they would all be considered significant at the .10 α -level). Interestingly, these differences between individuals with TBI and non-clinical controls were mostly prominent during a baseline that followed a set of cognitive tasks, resembling other physiological indices that require stressing the organ to be assessed (e.g. electrocardiogram). Therefore, it is suggested that future versions of qEEG normative databases include PAF into their brain maps and statistical comparisons. Furthermore, it is suggested that future versions of normative databases include post-task resting conditions. It has been shown in the results of hypothesis 1 and in other studies (Angelakis & Lubar, 2002) that the alpha frequency band is particularly sensitive to task conditions immediately after the task. Moreover, post-task resting EEG recordings are not only sensitive to brain phenomena, but also clean from muscle artifacts caused by the task.

In addition to its sensitivity to gross brain pathology, PAF was found to be particularly sensitive to brain states within individuals during different days (hypothesis 3.a). PAF significantly predicted cognitive performance on a working memory task that was performed immediately after EEG recording, whereas it did not predict performance

within a few days (although it showed a non-significant trend). This finding is further validated by the similarity of correlations between the two days (same day correlations: $r_{1-1}=.48$, $r_{2-2}=.42$; different day correlations: $r_{1-2}=.32$, $r_{2-1}=.27$). These results show that PAF can be more sensitive to a cognitive state than to a trait, and that it may reflect day-to-day, or even moment-to-moment changes in cognitive preparedness, rather than a stable ability as suggested by Klimesch et al. (1990) whose reported resting state was not an initial resting recording but a non-processing part of a task recording (see section 1.3). This may also be the reason why Klimesch et al. (1990) failed to find a correlation between IAF and memory performance in their control group (see section 1.4). If PAF was not recorded at the same day and shortly before the memory test then random changes in cognitive preparedness would not be able to predict memory performance as was the case with the results of hypothesis 3.a. However, PAF of individuals with AD may reflect a trait of an acquired deficit in varying degrees, due to different stages of the disease among individuals. Therefore, PAF of individuals with AD would be able to reflect memory performance even at a different time or day.

The results of hypothesis 3.a seem to challenge the previous suggestion of using PAF in normative qEEG databases, since it is here shown to vary within individuals according to temporary states and, therefore, lose its validity as a reliable trait measure. However, this finding (of unstable PAF) is based on an initial resting baseline rather than on a post-task resting condition as was the case with the results of hypothesis 1. Still, to overcome any doubts, one can re-test by recording EEG at two or more different days and monitor PAF reliability. If it is found consistently abnormal, then it can be interpreted as a trait difference.

Discussing further the results of hypothesis 3.a, of particular interest is the topography of this preparedness, which in both days is observed mostly at frontal electrodes, a cortical area that is well known to specialize in working memory functions (see figure 2). This observation extends Osaka's (1984) findings of lateralized PAF increases, during different cognitive tasks, according to task type (see section 1.3). Further research may try to test whether PAF at other areas can predict cognitive potential for functions served by these areas, like for example left parietal areas for language comprehension, or centro-coronal areas for motor functions, etc.

Results on hypothesis 3.b showed that not only PAF before a cognitive task affected performance on the task (hypothesis 3.a) but also performing a cognitive task affected PAF. It was shown that individuals who were not prepared for the task, as indicated by their initial PAF, were forced to correct their unpreparedness by increasing their PAF as a result of the task. This observation extends the findings of Osaka (1984) and Osaka et al. (1999) (where PAF increases were observed during performance of a task, see section 1.3), and strengthens the relationship between PAF and cognitive performance, possibly to a direct level. In other words, PAF and cognitive performance may be directly affecting one another.

This finding may explain further the results of hypotheses 1 and 3.a. At initial rest, healthy individuals may show a random distribution of their PAF, due to a particular state of cognitive preparedness and, therefore, not show as a distinct group difference from individuals with TBI. However, when a task forces them to correct their unpreparedness, then healthy individuals show their actual PAF potential, which clinical individuals are not able to reach. Related findings were reported by Klimesch (1997) who showed that

groups of bad and good memory performers had greater PAF differences during a memory task than during an initial resting baseline.

The fact that PAF increases have been noticed after acute administration of stimulants like nicotine and caffeine (see section 1.5), or nootropics like piracetam (see section 1.6) shows that cognitive exercise may be an alternative to drug administration for acute changes of the brain's function. The nature and duration of this state of preparedness, however, needs further investigation. Although a short working memory task increased PAF in individuals who had it lower immediately before the task, a longer set of reading tasks failed to replicate this phenomenon. One way to explain this is by referring once more to Klimesch (1997). He reports similar findings with groups of bad and good memory performers, where increasing task demands differentiate the two groups until the capacity threshold is reached. In this case, both bad and good performers tended to decrease their PAF. We can assume, then, that in the case of the long reading tasks of dataset A, the capacity threshold was reached and PAF declined after a possible initial increase.

One weakness of this study is the small sample sizes of the groups involved, especially for individuals with TBI. Hypothesis 2.b was particularly weak in that sense, since sample size was 5 (the minimum sample size allowed for the statistical test performed). Similarly, hypothesis 2.a had a very small sample size ($n=7$) and this may have caused the lack of significant results in testing these two hypotheses. This assumption is supported by the non-significant trends in hypothesis 2.a that were in the predicted direction (see figure 4). Future research may attempt to re-test these two hypotheses using larger sample sizes.

5. CONCLUSIONS

The present study supported the idea of PAF being an index of cognitive preparedness that not only differentiates between healthy and TBI individuals, but also fluctuates within healthy individuals at different days, and predicts their fluctuations in a cognitive task. The fact that post-task PAF is more powerful to show differences between healthy brains and brain with pathology, suggests that the brain can show more of its condition when it is put under stress, just like other organs of the body. Moreover, it showed that performing a cognitive task has the potential to change the brain's state in the same direction as taking a drug would do. It is suggested that EEG normative databases include post-task PAF into their statistical reports and that neurofeedback protocols to increase PAF are attempted to improve cognitive performance in both clinical and non-clinical populations. Moreover, it is suggested that these neurofeedback protocols include post-task PAF training, based on the observation that individuals with TBI showed their greatest difference from non-clinical controls immediately after a task.

REFERENCES

Andersen, P., & Andersson, S. A. (1968). *Physiological Basis of the Alpha Rhythm*. New York: Appleton-Century-Crofts.

Angelakis, E., & Lubar, J. F. (2002). Quantitative Electroencephalographic Amplitude Measures in Young Adults During Reading Tasks and Rest. *Journal of Neurotherapy* (in press).

Billiot, K. M., Budzynski, T. H., & Andrasik, F. (1997). EEG patterns and chronic fatigue syndrome. *Journal of Neurotherapy*, 2(2): 20-30.

Canive, J. M., Lewine, J. D., Edgar, J. C., Davis, J. T., Miller, G. A., Torres, F., & Tuason, V. B. (1998). Spontaneous brain magnetic activity in schizophrenia patients treated with aripiprazole. *Psychopharmacology Bulletin*, 34 (1): 101-105.

Conners, C. K., & Sparrow, E. P. (1999). Nootropics and foods. In John Scott Werry and Michael G. Aman (Eds.) *Practitioner's Guide to Psychoactive Drugs for Children and Adolescents*, 2nd ed., (pp. 413-432). New York: Plenum Medical Book Company.

Doppelmayr, M. M., Klimesch, W., Pachinger, T., & Ripper, B. (1998). The functional significance of absolute power with respect to event-related desynchronization. *Brain Topography*, 11(2), 133-139.

Feldman, R. S., Meyer, J. S., & Quenzer, L. F. (1997): *Principles of Neuropsychopharmacology*. Sunderland, MA: Sinauer.

Hemler, R. J. B., Hoogeveen, J. H., Kraaier, V., Van Huffelen, A. C., Wieneke, G. H., Hijaman, R., & Glerum, J. H. (1990). A pharmacological model of cerebral ischemia: The effects of indomethacin on cerebral blood flow velocity, quantitative EEG, and cognitive functions. *Methods and Findings in Experimental and Clinical Pharmacology*, 12 (9): 641-644.

Holm, S. (1979). A simple sequentially rejective multiple test procedure. *Scandinavian Journal of Statistics*, 6: 65-70.

Juhasz, C., Kamondi, A., & Szirmai, I. (1997). Spectral EEG analysis following hemispheric stroke: Evidences of transhemispheric diaschisis. *Acta-Neurologica-Scandinavica*, 96 (6): 397-400. Klimesch, W. (1997). EEG-alpha rhythms and memory processes. *International Journal of Psychophysiology*, 26: 319-340.

Kinoshita (1990). Quantitative pharmaco-EEG study of nootropics. *Psychiatria-et-Neurologia-Japonica*, 92 (5): 255-276.

Klimesch, W., Schimke, H., Ladurner, G. & Pfurtscheller, G. (1990). Alpha frequency and memory performance. *Journal of Psychophysiology*, 4: 381-390.

- Klimesch, W., Schimke, H., & Pfurtscheller, G. (1993). Alpha frequency, cognitive load, and memory performance. *Brain Topography*, 5(3): 241-251.
- Knott, V. T. (1988). Dynamic EEG changes during cigarette smoking. *Neuropsychobiology*, 19 (1): 54-60.
- Kostyunina, M. B. (1998). Human EEG during mental reproduction of emotionally significant events. *Zhurnal Vysshei Nervnoi Deyatel'nosti Imeni I P Pavlova*, 48 (2): 213-221.
- Kostyunina, M. B. & Kulikov, M. A. (1995). Frequency characteristics of different emotions: EEG spectral analysis. *Zhurnal Vysshei Nervnoi Deyatel'nosti Imeni I P Pavlova*, 45(3): 453-457.
- Kraaier, V., Van Huffelen, A. C., Wieneke, G. H., Van der Worp, H. B., & Bar, P. R. (1992). Quantitative EEG changes due to cerebral vasoconstriction: Indomethacin versus hyperventilation induced reduction in cerebral blood flow in normal subjects. *Electroencephalography and Clinical Neurophysiology*, 82 (3): 208-212.
- Li, D., Sun, F., & Jiao, Y. (1996). Frontal EEG characters in aging and the correlativity with some cognitive abilities. *Acta Psychologica Sinica*, 28(1): 76-81.

- Lindgren, M., Molander, L., Verbaan, C., Lunell, E., & Rosen, I. (1999).
Electroencephalographic effects of intravenous nicotine: A dose-response study.
Psychopharmacology, 145 (3): 342-350.
- Lopes da Silva, F. Van Lierop, T.H.M.T., Schrijer, C. F., & Storm van Leeuwen, W.
(1973a). Organization of thalamic and cortical alpha rhythm: Spectra and
coherences. *Electroencephalography and Clinical Neurophysiology*, 35: 627-640.
- Lopes da Silva, F. Van Lierop, T.H.M.T., Schrijer, C. F., & Storm van Leeuwen, W.
(1973b). Essential differences between alpha rhythms and barbiturate spindles:
Spectra and thalamocortical coherences. *Electroencephalography and Clinical
Neurophysiology*, 35:641-645.
- Miller, R. G., Jr. (1981). *Simultaneous Statistical Inference*. N.Y.: McGraw Hill
- Newman, F., Stein, M. B., Trettau, J. R., Coppola, R., & Uhde, T. W. (1992).
Quantitative electroencephalographic effects of caffeine in panic disorder.
Psychiatry Research, 45(2): 105-113.
- Niedermeyer, E. (1999). The normal EEG of the waking adult. In Niedermeyer, E., &
DaSilva, E. L. (Eds.) *Electroencephalography: Basic principles, chemical
applications, and related fields* (4th ed., pp.131-152). Baltimore: Williams &
Wilkins.

- Nunez, P. L., Wingeier, B. M., & Silberstein, R. B. (2001). Spatial-temporal structures of human alpha rhythms: Theory, microcurrent sources, multiscale measurements, and global binding of local networks. *Human Brain Mapping, 13*: 125-164.
- Osaka, M. (1984). Peak alpha frequency of EEG during a mental task: Task difficulty and hemispheric differences. *Psychophysiology, 21(1)*: 101-105.
- Osaka, M., Osaka, N., Koyama, S., Okusa, T., & Kakigi, R. (1999). *Cognitive-Brain-Research, 8(3)*: 365-368.
- Passero, S., Rocchi, R., Vatti, G., Burgalassi, L., & Battistini, N. (1995). Quantitative EEG mapping, regional cerebral blood flow and neuropsychological function in Alzheimer's disease. *Dementia, 6(3)*: 148-156.
- Pfurtscheller, G. (1989). Spatiotemporal analysis of alpha frequency components with the ERD technique. *Brain Topography, 2*, 3-8.
- Pierlovisi, L. M., Michel, B., Sebban, C., Tesolin, B., Chave, B., Sambuc, R., Melac, M., Gastaut, J. L., Poitrenaud, J., & Millet, Y. (1991). Spectral analysis of the EEG in Alzheimer's disease changes induced by piracetam. *Neurophysiologie Clinique, 21(5-6)*: 411-424.

Pigeau, R. A., & Frame, A. M. (1992). Steady-state visual evoked responses in high and low alpha Subjects. *Electroencephalography and Clinical Neurophysiology*, 84(2): 101-109.

Posthuma, D., Neale, M. C., Boomsma, D. I., & de Geus, E. J. C. (2001). Are smarter brains running faster? Heritability of alpha peak frequency, IQ, and their interrelation. *Behavior-Genetics* 31 (6): 567-579.

Psatta, D. M., Goldstein, R., & Matei, M. (1991). EEG mapping in mentally retarded children by synthetic arginine vasotocin administration. *Revue Roumaine de Neurologie et Psychiatrie*, 29 (1-2): 9-16.

Rice, W. R. (1988). Analyzing tables of statistical tests. *Evolution*, 43 (1): 223-225.

Saletu, B., Hitzenberger, G., Gruenberger, J., Anderer, P., Zyhlarz, G., Linzmayer, L., & Rameis, H. (1995). Double-blind, placebo-controlled, pharmacokinetic and -dynamic studies with 2 new formulations of piracetam (infusion and syrup) under hypoxia in man. *International Journal of Clinical Pharmacology and Therapeutics*, 33(5): 249-262.

- Suldo, S. M., Olson, L. A., & Evans, J. R. (2001). Quantitative EEG evidence of increased alpha peak frequency in children with precociously reading ability. *Journal of Neurotherapy*, 5(3): 39-50.
- Thatcher, R. W., Walker, R. A., Gerson, I. & Geisler, F. (1989). EEG discriminant analyses of mild head trauma. *EEG and Clinical Neurophysiology*, 73: 93-106.
- Tiffin, P., Ashton, H., Marsh, R., & Kamali, F. (1995). Pharmacokinetic and pharmacodynamic responses to caffeine in poor and normal sleepers. *Psychopharmacology*, 121 (4): 494-502.
- Van der Worp, H. B., Kraaier, V., Wieneke, G. H., & Van Huffelen, A. C. (1991). Quantitative EEG during progressive hypocarbia and hypoxia: Hyperventilation-induced EEG changes reconsidered. *Electroencephalography-and-Clinical-Neurophysiology*, 79(5): 335-341.
- Wilsher, C. R. (1994). Pharmacological treatment of dyslexia. In K. P. Van Den Boss, L. S. Siegel, D. J. Bakker, & D. L. Share's (eds.) *Current Directions in Dyslexia Research*. Lisse: Swets & Zeitlinger.

APPENDIX

TABLE 1. Hypothesis 1: TBI vs. controls.

HYPOTHESIS 1										
	ECB		EOB1		TASK			EOB2		
	M-W z	p-value	M-W z	p-value	M-W z	p-value	p-het.	M-W z	p-value	p-het.
FP1	-0.96	ns	-1.53	ns	-1.20	ns	0.046	-1.57	ns	ns
FP2	-2.29	0.010	-1.81	0.040	-0.10	ns	ns	-1.51	ns	ns
F7	-0.46	ns	-1.29	ns	-0.57	ns	ns	-2.49	0.006	0.005
F3	-1.59	ns	-1.28	ns	-1.04	ns	ns	-1.93	0.030	0.014
FZ	-2.20	0.015	-1.33	ns	-1.66	ns	0.013	-1.81	0.040	0.017
F4	-1.83	0.035	-0.67	ns	-0.80	ns	ns	-1.32	ns	ns
F8	-2.40	0.008	-0.53	ns	-0.27	ns	ns	-1.24	ns	ns
T3	-1.23	ns	-1.09	ns	-0.13	ns	ns	-1.86	0.035	0.039
C3	-1.65	ns	-1.53	ns	-1.87	0.035	0.019	-2.66	0.004	0.002
CZ	-1.69	0.047	-0.27	ns	-1.73	0.047	0.013	-3.07	0.001	0.001
C4	-1.69	0.047	-0.47	ns	-1.75	0.040	0.017	-2.80	0.002	0.002
T4	-0.66	ns	-0.10	ns	-0.46	ns	ns	-1.07	ns	ns
T5	-1.50	ns	-2.19	0.015	-2.52	0.006	0.003	-1.33	ns	ns
P3	-1.93	0.030	-2.32	0.010	-1.29	ns	0.036	-2.36	0.008	0.011
PZ	-2.75	0.002	-2.49	0.006	-2.55	0.004	0.002	-2.92	0.001	0.002
P4	-1.73	0.047	-2.00	0.025	-2.08	0.018	0.013	-2.43	0.007	0.015
T6	-1.39	ns	-0.13	ns	-0.40	ns	ns	-1.56	ns	ns
O1	-0.80	ns	-0.93	ns	-0.87	ns	ns	-0.93	ns	ns
O2	-1.33	ns	-1.52	ns	-2.18	0.015	0.014	-2.19	0.015	0.021
MEAN	-1.58	0.061	-1.52	0.070	-1.35	0.09	0.051	-2.24	0.010	0.010

Z-scores (Mann-Whitney) and p-values (1-tailed) for the differences in PAF between TBI (n=10) and non-clinical control (n=12) participants during eyes-closed baseline (ECB), eyes-open baseline (EOB1), cognitive task (TASK), and post-task eyes-open baseline (EOB2). In all significant differences TBI had lower PAF than controls.

TASK and EOB2 did not meet equality of variance between the two groups for some electrodes, so p-values from t-tests corrected for heteroscedasticity are also reported (p-het.) Bold typed p-values are corrected for multiple comparisons. Notice that post-task eyes-open baseline (EOB2) shows the greatest effect. For a graphical display, see figure 1.

TABLE 2. Hypothesis 3.a. Correlations between PAF & DS.

HYPOTHESIS 3a									
	PAF1					PAF2			
	DS1		DS2			DS1		DS2	
	corr	p-value	corr	p-value		corr	p-value	corr	p-value
FP1	0,31	ns	0,10	ns		0,22	ns	0,43	0,036
FP2	0,43	0,038	0,23	ns		0,28	ns	0,65	0,002
F7	0,48	0,023	0,15	ns		0,36	ns	0,28	ns
F3	0,46	0,028	0,15	ns		0,35	ns	0,49	0,020
FZ	0,41	0,047	0,21	ns		0,32	ns	0,44	0,035
F4	0,42	0,040	0,20	ns		0,21	ns	0,43	0,038
F8	0,33	ns	0,30	ns		0,20	ns	0,28	ns
T3	0,58	0,006	0,42	0,041		0,24	ns	0,28	ns
C3	0,36	ns	0,12	ns		0,28	ns	0,37	ns
CZ	0,22	ns	0,08	ns		0,27	ns	0,37	ns
C4	0,23	ns	0,02	ns		0,34	ns	0,31	ns
T4	0,42	0,043	0,51	0,015		0,21	ns	0,34	ns
T5	0,33	ns	0,31	ns		0,32	ns	0,31	ns
P3	0,25	ns	0,26	ns		0,30	ns	0,43	0,038
PZ	0,13	ns	0,00	ns		0,32	ns	0,39	ns
P4	0,36	ns	0,14	ns		0,20	ns	0,52	0,014
T6	0,37	ns	0,15	ns		0,33	ns	0,44	0,034
O1	0,12	ns	0,13	ns		0,31	ns	0,29	ns
O2	0,22	ns	0,15	ns		0,27	ns	0,26	ns
MEAN	0,48	0,021	0,32	0,096		0,27	0,136	0,42	0,041

Correlations (corr) and p-values for Spearman's non-parametric test for the association between PAF at day 1 (PAF1) and day 2 (PAF2) with Digit Span at day 1 (DS1) and day 2 (DS2). Bold typed p-values are corrected for multiple comparisons. Notice that significant correlations are those between PAF and Digit Span during the same day.

TABLE 3. Hypothesis 3.b. Low vs. high PAF before & after DS.

HYPOTHESIS 3b									
	day1_high-PAF		day1_low-PAF		day2_high-PAF		day2_low-PAF		
	M-W z	p-value	M-W z	p-value	M-W z	p-value	M-W z	p-value	
FP1	-0,42	ns	-2,39	0,009	-0,42	ns	-2,21	0,014	
FP2	-0,35	ns	-2,16	0,016	-1,47	ns	-2,21	0,014	
F7	-0,85	ns	-2,24	0,012	-0,83	ns	-2,39	0,008	
F3	-0,84	ns	-1,72	0,043	-0,74	ns	-1,60	ns	
FZ	-0,56	ns	-2,44	0,007	-0,74	ns	-1,60	ns	
F4	-0,42	ns	-2,21	0,014	-1,19	ns	-1,83	0,034	
F8	-0,56	ns	-2,32	0,010	-0,76	ns	-2,21	0,014	
T3	-0,56	ns	-1,96	0,025	-0,41	ns	-1,20	ns	
C3	-0,21	ns	-1,84	0,033	-1,13	ns	-1,29	ns	
CZ	-0,77	ns	-2,25	0,012	-0,65	ns	-1,58	ns	
C4	-0,59	ns	-1,60	ns	-1,38	ns	-0,74	ns	
T4	-0,17	ns	-1,84	0,033	-1,37	ns	-0,74	ns	
T5	-2,31	0,010	-2,67	0,004	-0,37	ns	-1,24	ns	
P3	-2,50	0,006	-2,37	0,009	-0,27	ns	-1,84	0,033	
PZ	-1,84	0,033	-2,26	0,012	-0,56	ns	-2,03	0,021	
P4	-1,90	0,029	-2,20	0,014	-1,63	ns	-0,96	ns	
T6	-1,84	0,033	-2,43	0,008	-0,96	ns	-0,32	ns	
O1	-2,67	0,004	-2,27	0,012	-0,60	ns	-2,12	0,017	
O2	-1,98	0,024	-2,55	0,005	-1,16	ns	-2,20	0,014	
MEAN	-1,24	0,107	-2,55	0,005	-1,24	0,107	-2,43	0,008	

Mann-Whitney z scores (M-W z) and p-values for PAF increases after Digit Span (ECB - PTR), for participants with PAF higher to the group's median (high-PAF) and with lower to the group's median (low-PAF), for day 1 and day 2. Bold typed p-values are corrected for multiple comparisons. Notice that participants with lower initial PAF show the greatest effect.

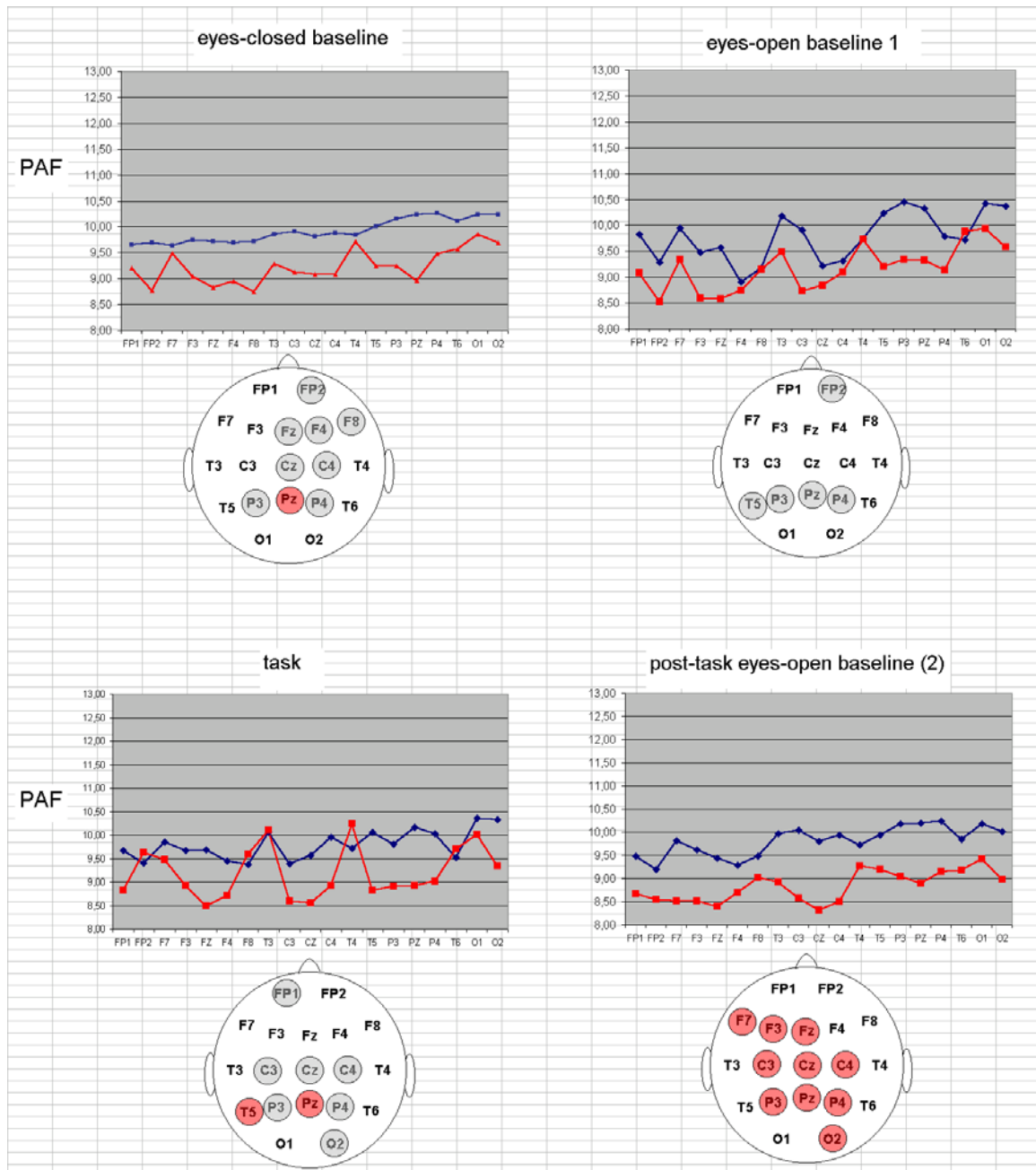


FIGURE 1. Hypothesis 1. TBI vs. controls.

PAF differences between individuals with TBI and non-clinical controls.

Red line: TBI, blue line: controls. Red circles: significance corrected for multiple comparisons. Grey circles: significance NOT corrected.

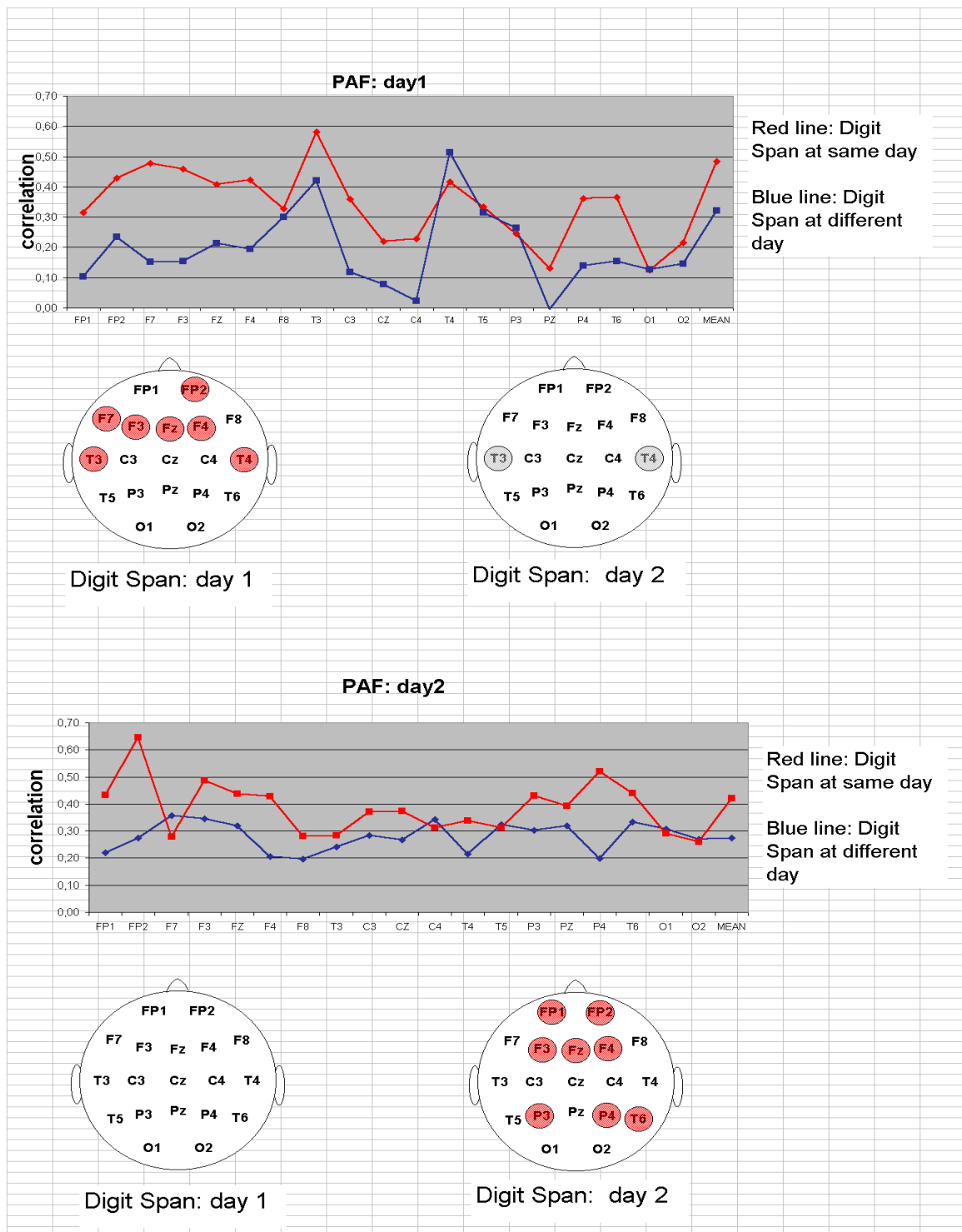


FIGURE 2. Hypothesis 3a. Correlations between PAF & DS.

Correlation coefficients between WAIS-Digit Span and PAF at two different days. Red circles: significance corrected for multiple comparisons. Grey circles: significance NOT corrected.

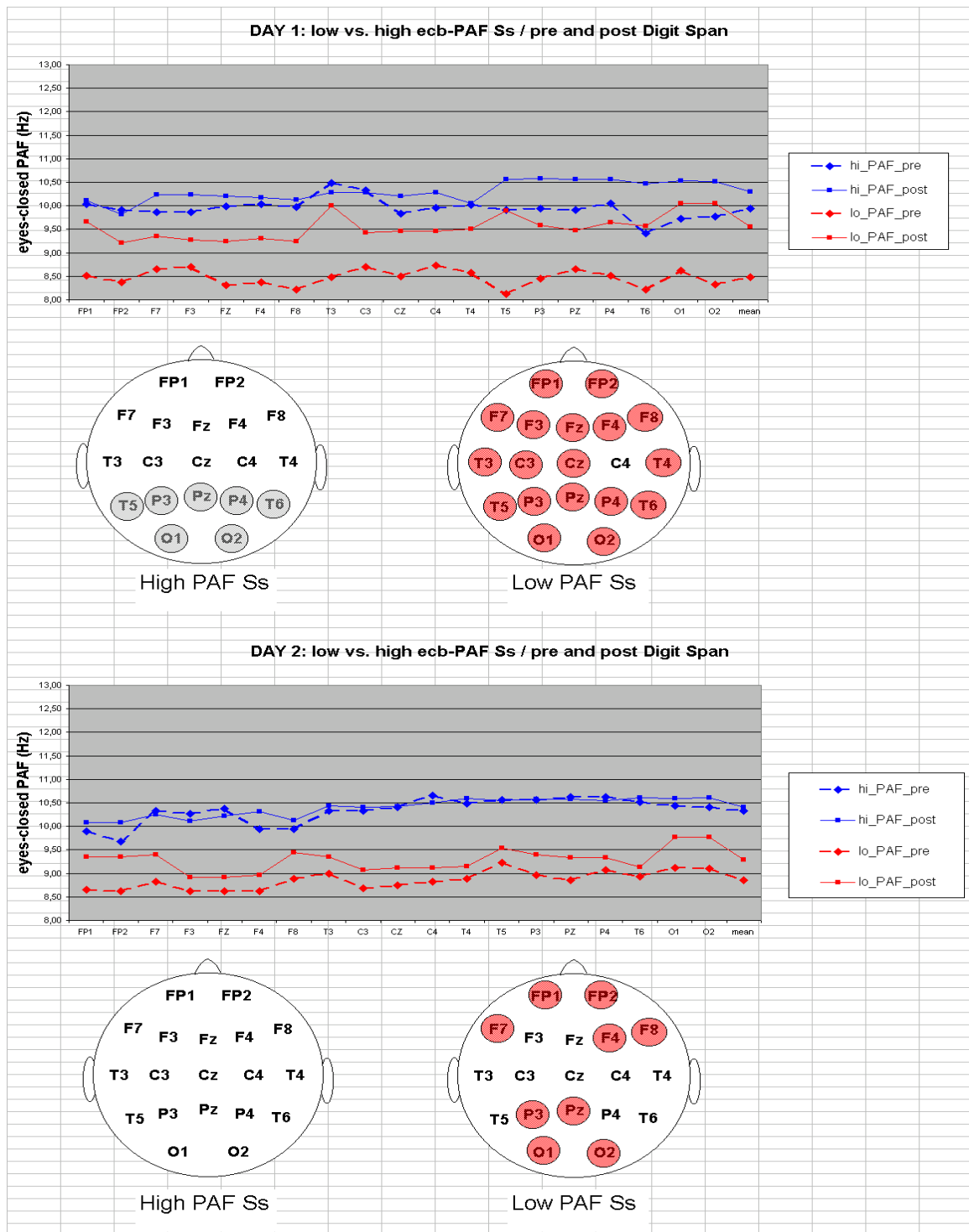


FIGURE 3. Hypothesis 3b. Low vs. high PAF before & after DS.

Participants with higher PAF (blue lines) and lower PAF (red lines) to the group's median: PAF before and after Digit Span. Red circles: PAF significant increases corrected for multiple comparisons. Grey circles: PAF increases NOT corrected.

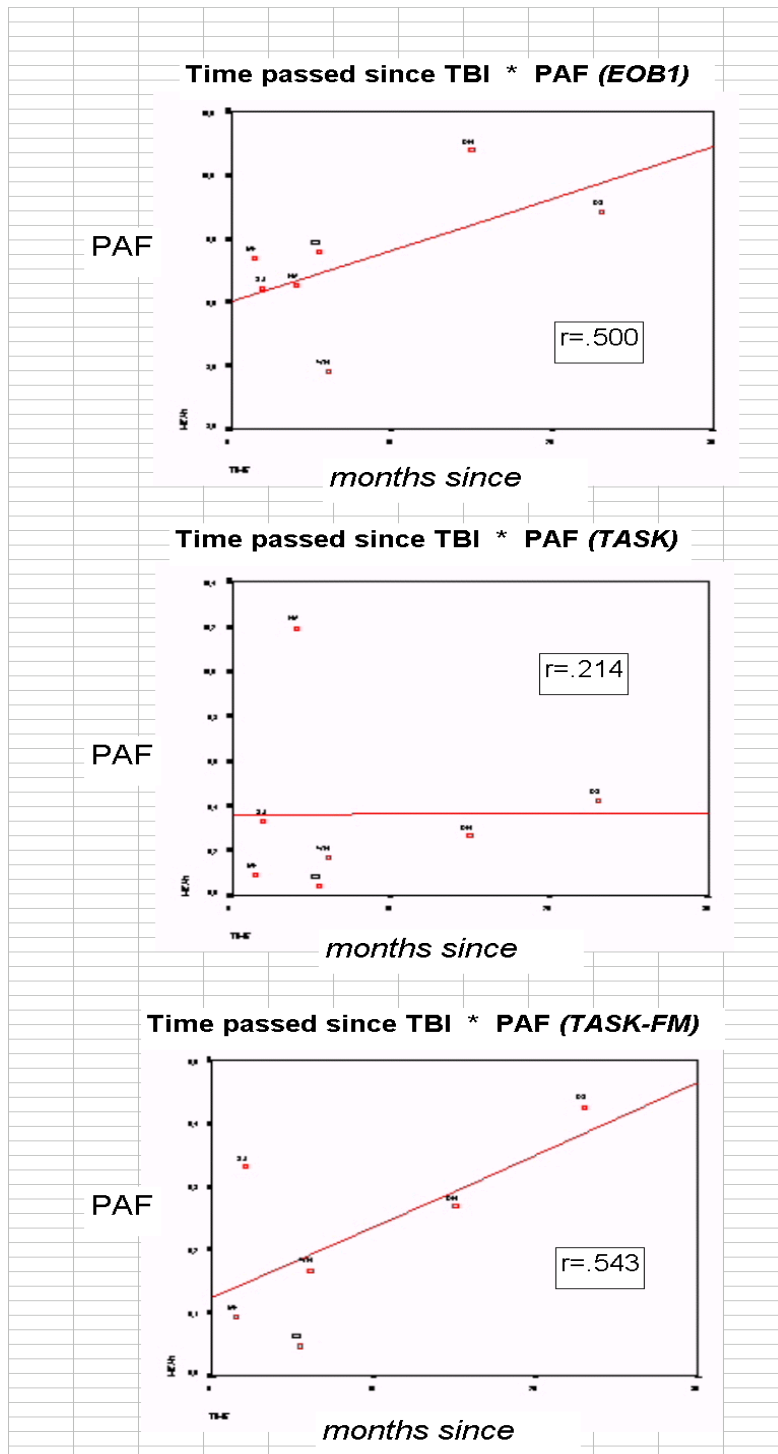


FIGURE 4. Hypothesis 2a. Correlations between between time since TBI and PAF. Scatterplots and correlation coefficients for the relationship between time since TBI and PAF at eyes-open baseline (EOB1), and cognitive task (TASK) ($n=7$). The third scatterplot and correlation coefficient are for TASK if one participant (FM) is excluded ($n=6$).

QUESTIONNAIRE FOR PARTICIPATION IN THE STUDY:

**"EEG DIFFERENCES BETWEEN VISUAL, PHONOLOGICAL, AND
SEMANTIC READING, IN COLLEGE STUDENTS"**

Principal investigator: Efthymios Angelakis, M.A.

Co-principal investigator: Joel F. Lubar, Ph.D.

I am going to ask you some personal information needed for this study. The use of this information is strictly limited to the purposes of this study and it will be available only to the above investigators. This information is confidential, if however you feel not comfortable to answer any of the following questions, ask for the next question.

1. Which hand do you write with? Right ___ Left ___ Both ___
2. Have you ever been diagnosed as learning disabled? ___ Dyslexic? ___
If yes, give more specific details _____.
If no, have you ever experienced difficulties with reading? (e.g. too slow reading, too tiring, too many misperceived words, etc.) _____.
3. Have you ever been diagnosed with an attention deficit disorder (ADD/ADHD)? _____
If no, have you ever experienced systematic difficulties to concentrate and/or focus attention on a task? _____.
4. Have you ever had any head injury? _____.
Surgical operation on the head? _____.
Lost consciousness for more than one minute? _____.
5. Have you ever had epileptic seizures? _____.
6. Have you ever had any neurological diagnosis? _____.
7. Do you need correcting lenses for vision ? (specify) _____.
8. Are you currently using any prescription medication? _____.
9. What is your gender? Male ___ Female ___
10. What is your date of birth? (MM/DD/YY) _____.

I.V.A. scores _____.
WAIS Voc. score _____ W-J scores 22 _____ 23 _____ 31 _____ 32 _____.
Notepad scores _____.
Name _____ Date _____ Time _____.
Participant No. _____ Counterbalancing order _____.
Task scores: T-visual _____ T-phonological _____ T-semantic _____.
Words: _____.

Vita

Efthymios Angelakis was born and raised in Athens, Greece, on April 1, 1965. He graduated high school in 1982, and since then he worked as a commercial agent until 1996. In 1990 he got a diploma in cinema directing from the School of Theatre and Cinematography Eugenia Hatzikou, in Athens. In August 1998 he graduated his B.A. with a major in Psychology from Deree College, The American College of Greece, Athens, and in May 2000 he graduated his M.A. with a major in Psychology from the University of Tennessee, Knoxville, TN.

Efthymios is currently in the process of completing his doctorate in psychology at the University of Tennessee, Knoxville, and has accepted a postdoctoral research fellowship at the department of Psychology, University of Pennsylvania, Philadelphia.