Neurosensory Optimization of Information Transfer (NOIT, 56469-LS), Final Report for US Army Research Office Contract No. W911NF-11-C-0081

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Contents

Neurosensory Optimization of Information Transfer

Statement of the problem studied

The overall goal of this research is three-fold: a) to improve scientific understanding of human cognition and performance concerning the structure and function of brain networks that control attention to external stimuli, including single modalities such as vision or hearing, and multimodal integration, and their associated behavioral and physiological manifestations, b) to improve the quantitative measurement and analysis of the electrical activity of the brain, or EEG, using state-of-the art electronics, computers, signal processing and computational methods, c) to develop methods and systems capable of aiding, improving or optimizing cognitive performance, particularly on tasks requiring selective spatial attention and responses to events signaled by visual stimuli. The relevance of these goals is obvious when we consider the high perceptual and cognitive demands that modern command, control and communications systems place on their human operators. Examples of such systems, in which sustained, error-free human performance is critical for safety and mission effectiveness, include air traffic control, land or sea vehicle control, and especially the control of manned or unmanned aircraft.

Improved Understanding of Cognition and Performance

The Classic LANT Paradigm

Our approach to improved understanding of cognition focuses on the processes that route information from the eyes to centers for decision making and action in the brain. Using a Lateralized Attention Network Test or LANT, developed by Eran Zaidel at UCLA, we influence the flow of information through the brain of a human observer whose task is to detect, recognize, and classify a brief visual target stimulus presented in the near periphery of the visual field.

In the basic original LANT paradigm (Figure 1), a trial begins with the observer holding his gaze on a *fixation* cross in a computer-controlled display. After a delay of 400 ms, a brief *spatial cue* appears for 100 ms to the left or right of the cross, which triggers an automatic shift of spatial attention to this point. Since this shift of attention is handled automatically by attention networks in the brain it requires no special efforts by the observer. The shift of attention triggered by the cue serves to prime that region of the visual field for priority processing of new information. When the cue disappears, there is a delay of 250 ms, after which a target appears at the same location. The target is a central arrow flanked by two arrows above and two more below, forming an array of five arrows. The observer's task is to classify the central or target arrow as pointing either upward or downward using a keyboard to press one key for up or another key for down. The sequence of cue and target happens too fast for the observer to direct his gaze to the cue location, forcing him to respond to events perceived in the periphery.

In fact we require subjects to keep their gaze fixed on the central fixation point. In this way we effectively lateralize the cue and target to one visual hemifield.

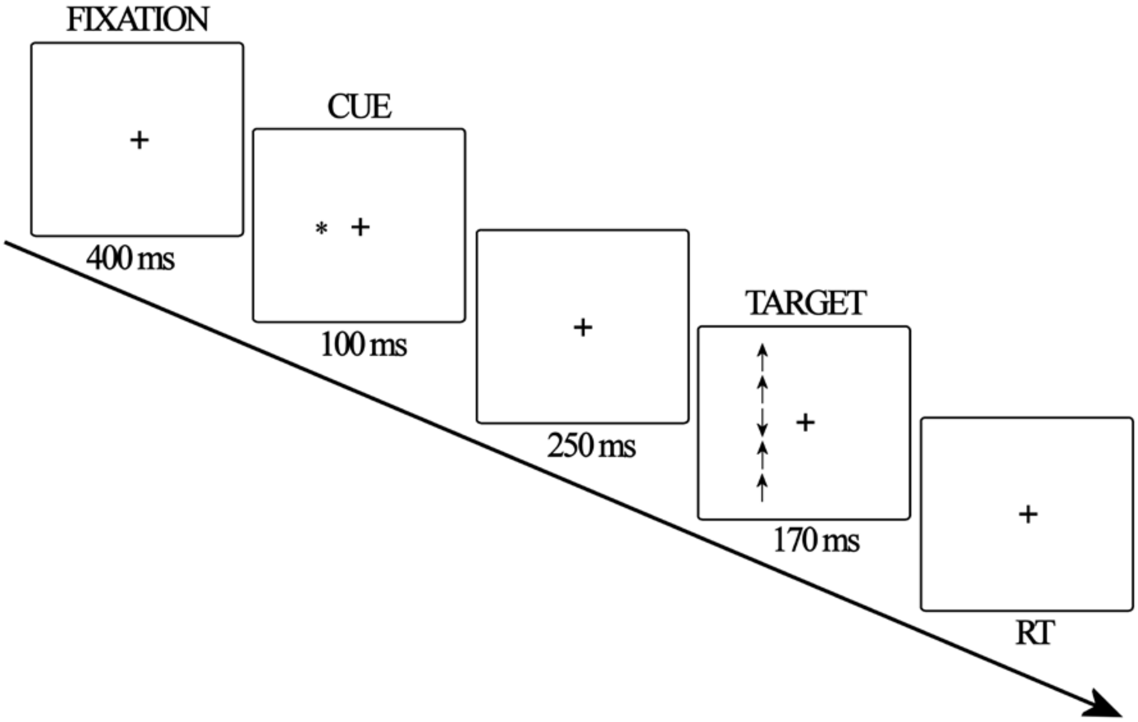

Figure 1. Schematic diagram of the basic Lateralized Attention Network Test (LANT).

We gauge the observer's performance by measuring the reaction time, or how long it takes the observer to press a key, and the accuracy of the response. Because the brain splits the representation of the visual field down the middle, with the left hemifield projected onto the visual cortex of the right hemisphere and the right hemifield projected onto visual cortex of the left hemisphere, one hemisphere dominates the processes of detecting and classifying the target (Figure 2). Although the hemisphere that "views" the target dominates perceptual processes, the motor cortex in that hemisphere will eventually share a copy of the selected response information with the other hemisphere by sending impulses across the anterior mid-body of the corpus callosum, the main bridge of nerve fibers that connects the two sides of the brain and allows them to cooperate. Ultimately, either or both hemispheres can participate in orchestrating a response to the target. Decisions concerning response selection will also involve several other networks of attentional and executive control, which draw upon distributed processing resources across many brain areas. A simplified model of these networks was developed by Michael Posner and his colleagues, allocating functions of alerting, orienting, and executive control to three distinct anatomical networks. Functional neuroimaging studies have shown that the three networks show distinct patterns of regional activations: thalamic, parietal, and anterior cingulate, respectively (Table 1).[1]

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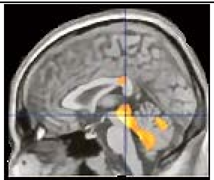
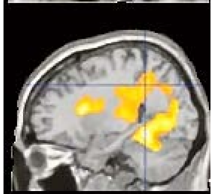
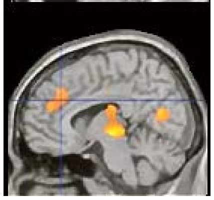
[1] For a review, see Raz, A. & Buhle, J. (2006). Typologies of attentional networks. Nature Reviews Neuroscience 7, 367-379.

Table 1. Anatomical distribution of attention networks.

Network	Region of Activation	Anatomical Pattern
Alerting	Thalamic	
Orienting	Parietal cortex	
Conflict	Anterior cingulate cortex	

What makes the LANT interesting is that there are several ways to “trick” the observer into responding slowly or inaccurately. First, the cue may be intentionally misleading. For example, we may present an *invalid cue,* e.g., a cue that appears in the right hemifield followed by a target in the left hemifield. This spatial misdirection primes the wrong hemisphere of the brain by shifting attention to the side opposite from which the target will appear. When the target appears on the side opposite the cue, attention networks in the brain must shift attention all the way across from one side to the other. The shift is necessary to enable the observer to attend to the target quickly enough to classify it correctly. But this shift takes extra time compared to when targets appear at the same spot primed by the cue, leading to longer reaction times for the *invalid cues* than those for *valid cues.* This extra time arises from processes in the superior colliculus that plan eye movements, which also serve as the mechanism for the movement of attention from one hemifield to the other, i.e., attentions shifts are like virtual eye movements. Manipulating cue validity allows us to engage the orienting networks of the left and right hemispheres somewhat independently and measure their operation in terms of reaction time and accuracy for valid or invalid cues.

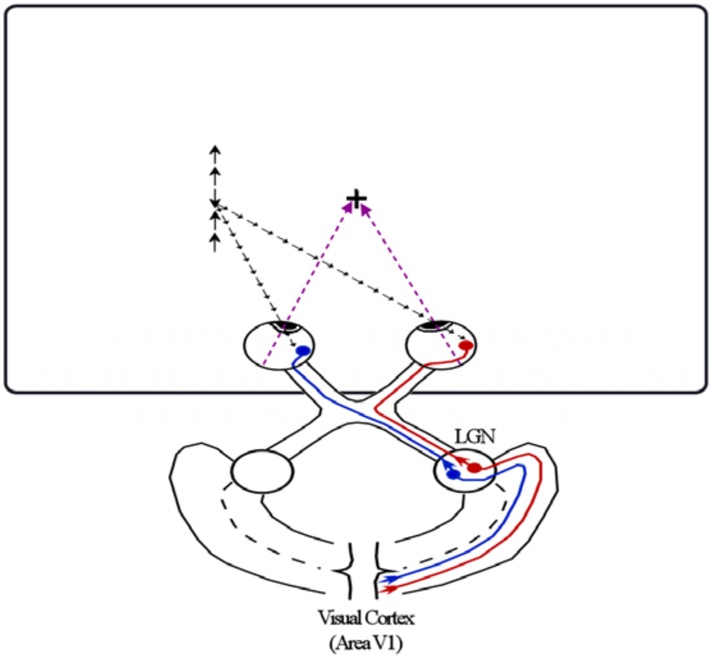


Figure 2.When an observer gazes at a central fixation cross targets appearing in the left visual field are directly represented in the primary visual cortex in the right hemisphere of the brain.

We may also present a cue that tells the observer when a target is about to appear but not where. These *neutral cues* may appear in the middle of the display or at both of the possible target locations. In this case nothing reliably biases attention to one side or the other so the cue provides no specific benefit to either side and attention remains focused in the middle of the display at the fixation cross. Many experiments have shown that observers respond faster to valid cues than to neutral cues because priming the correct location gives attention a head start in the right direction. We call the increased speed of response of valid vs. neutral cues the *orienting benefit,* because it results from the proper orienting of attention to the target location. On the other hand, observers respond more slowly to targets after invalid cues than they do with neutral cues. This is because the invalid cue gives attention a head start in the wrong direction, and when the target appears attention must make a U-turn and head back to the other side. We call the decreased speed of response to invalid vs. neutral trials the *orienting cost,* because it results from the improper orienting of attention to the wrong location for the target. The difference between benefits and costs of orienting is about 20 to 40 ms, but this depends on other factors of the experiment and on individual differences in observers.

Another twist that makes the LANT interesting is the orientation of the extra arrows flanking the central target arrow. When all the arrows point in the same direction, observers respond faster than when the flankers point in the opposite direction, as pictures in Figure. 2. When the flankers are incongruent with the target observers respond more slowly than when they are congruent. It is possible to use neutral flankers as well. We refer to the effects of flanker congruity as *conflict effects*, and these produce benefits when flankers are congruent or costs when they are incongruent, much like the orienting costs and benefits. However, conflict costs and benefits are typically larger than orienting costs and benefits, about a 100 ms difference between congruent and incongruent flankers. Manipulating congruency of flankers in left or right hemifields allows us to differentially engage the executive networks of the left and right hemispheres and measure their operation in terms of reaction time and accuracy for congruent or incongruent flankers.

Similarly, the alerting network may be engaged and measured by comparing reaction time and accuracy for a neutral cue versus no cue. We call the increased speed or accuracy of a response following a neutral cue as compared to no cue an *alerting benefit.*

Increasing Ecological Validity of the LANT

Besides manipulating the validity of spatial cues and flanker congruity, we can manipulate other properties of cues and targets, the context in which they appear and the pace of the test. Previous work by Andrew Hill and Eran Zaidel during the first year of this project found that speeding up the LANT preserves all of these effects, but also introduces effects on the accuracy of responding that mirror the costs and benefits of orienting and conflict. Other work by Caroline Crump and Eran Zaidel during the first year, showed that varying the emotional quality of the cues, even when emotion was irrelevant to the task produced patterns of costs and benefits that shed light on individual differences in anxiety. Caroline's experiment used happy or angry faces for cues instead of abstract symbols. Observers who rated themselves as having high anxiety using the State-Trait Anxiety Scales had more difficulty resolving conflict for targets following angry-face cues than happy-face cues, but only when those cues were directly processed by the right hemisphere of the brain. Appendices A and B provide detailed descriptions of the experimental results in Year 1.

In the second year of this project we examined this effect again but with the added manipulation of the context in which cues and targets appeared. In Experiment 2, described separately, we used either a happy or scary background image for presentation of the stimuli. Again we found that the happy and angry faces were processed differently by high- or low-anxiety types, and this effect was amplified by the negatively charged background. We explicitly tell participants that the backgrounds have positive or negative emotional content; this is not the case for the cues. We do not require participants to attend to the emotional qualities of the cues or identify them in any way. The emotional quality of the cues is strictly implicit and automatic, and that can indirectly inform us about elements of the participants' true personality and mood. In addition we used this design to assess the effects of mental fatigue on LANT performance, brain electrophysiology, and to test for interactions of fatigue with personality and attention network functions.

Experiment 2: Using the eLANT to Assess the Impact of Mental Fatigue on Attention Networks and Brain Electrophysiology

During the second and third year of the project, we designed and executed Experiment 2, a complete study of behavioral performance, brain electrophysiology and personality effects using the eLANT version designed by Caroline Crump. We now report on the effects of self-rated fatigue on hemispheric attention networks and on EEG-based models for assessing the development of mental fatigue over time during eLANT performance. Here we provide a high-level summary of the results.

Impact of Mental Fatigue on Attention Networks

The specific design of the eLANT for Experiment 2 used happy or sad faces as cues and up or down-facing arrows as targets with flanking arrows of congruent or incongruent directions (Figure 3).

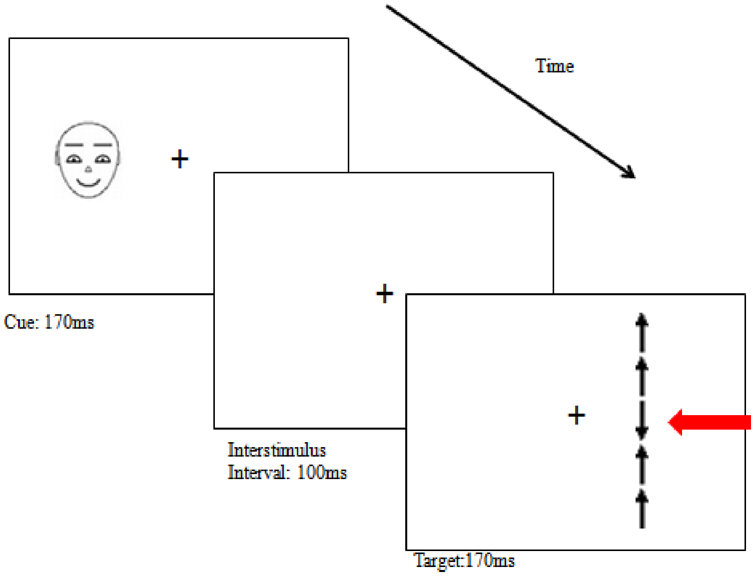


Figure 3. Sample eLANT trial. Red arrow points to target stimulus. Target stimulus may be in same direction as flanker arrows (congruent) or in the opposite direction (incongruent). In this trial the cue was *invalid* because it appeared in the left hemifield followed by a target in the right. It was also an incongruent target because the target arrow pointed down and flankers pointed up.

Results

- Fatigue had a pervasive effect on performance on the eLANT and showed significant interaction with all three components: attention networks, emotional condition, and laterality.
- There were significant effects of mean fatigue scores (derived using factor analysis) involving response hand, others involving visual field, and yet others involving both. However, pre-testing fatigue scores were associated with significant interactions involving the input visual field, while post-testing fatigue scores were associated with significant interactions involving response hand. Thus, fatigue appear to exert effects both on early temporal stages of the trial (involving differences in visual hemifield) and on later stages of the trial (involving differences in response hand).
- The data suggest that fatigue has selectively detrimental effects in the right hemisphere. Participants who reported high levels of fatigue showed relatively low performance for happy face cues in the left visual field as compared to the right visual field.
- As may be expected from prior mental fatigue research, fatigue was also detrimental to the function of the executive network. High fatigue participants had greater Conflict than low fatigue participants.
- The data also suggest a possibly novel effect of relatively higher impact of mental fatigue on Orienting than Alerting. There were subtle (higher-order) effects of the subjective fatigue factor, which were stronger for Alerting than for Orienting.

Conclusion

Our design of the eLANT for Experiment 2 was superbly sensitive to the effects of fatigue. This has two implications for optimizing behavior: (1) It suggests combinations of factors that lead to particularly high or low levels of fatigue, allowing for targeted manipulation of target types to enhance performance during fatigue. (2) The conditions that characterize optimal performance can be analyzed by PARAFAC Atoms and used as targets for EEG Biofeedback.

Experiment 3: Development of EEG Biofeedback Training to Enhance Attention Network Function and Counteract Mental Fatigue

The component of the NOIT program that begins with Experiment 3 focuses on using EEG biofeedback to enhance human performance through training the attention networks of the brain. The idea is that reinforcing certain EEG patterns with operant conditioning may promote optimal physiological processes and lead to enhanced attention network performance. For many years, therapists have used EEG biofeedback to treat Attention Deficit Disorders or ADD /ADHD. Although skepticism has been strong, recent controlled studies have led the American Academy of Pediatrics to conclude that EEG biofeedback is highly effective for treating ADD[2],[3],[4] and the FDA recently approved the first clinical device for applying EEG biofeedback therapy in ADD/ADHD[5]. Other basic research has shown that various forms of EEG biofeedback may alter or enhance human performance of attention, memory, and other cognitive tasks. In a recent review of 23 relevant studies, Gruzelier[6] concludes that EEG biofeedback training may enhance a wide range of cognitive functions, including sustained attention, orienting and executive attention network functions, spatial rotation, complex psychomotor skills, implicit procedural memory, recognition memory, perceptual binding. Other, more general, enhancements were found for intelligence, mood, and well-being.

Our interest in EEG biofeedback is two-fold: 1) to solve the mystery of EEG biofeedback by inducing changes in brain function and behavior then modeling the changes in terms of network functions, 2) to apply EEG biofeedback to human performance optimization, especially to attention network enhancement and to counteract the effects of mental fatigue under conditions of sustained performance.

Accordingly, the high level goals for Experiment 3 were:

- To develop and apply effective EEG biofeedback strategies for enhancing attention network performance.
- To assess the effects of EEG biofeedback on lateralized attention network performance and mental fatigue.

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[2] Arns M, de Ridder S, Strehl U, Breteler M and Coenen A (2009). Efficacy of Neurofeedback Treatment in ADHD: the Effects on Inattention, Impulsivity and Hyperactivity: a Meta-Analysis. Journal of Clinical EEG & Neuroscience 40: 180-189.

[3] Gevensleben, H., Holl, B., Albrecht, B., Vogel, C., Schlamp, D., et al. (2009). Is neurofeedback an efficacious treatment for ADHD?: A randomized controlled clinical trial. Journal of Child Psychology and Psychiatry, 50, 780-789.

[4] Appendix S2: Evidence-Based Child and Adolescent Psychosocial Interventions (2010). Pediatrics 125: S128.

[5] FDA Affirms Brainwave Diagnostics for ADHD. https://www.theneurocore.com/neurocores-eeg-biofeedback/

[6] Gruzelier, J. H. (2013). EEG-neurofeedback for optimising performance. I: A review of cognitive and affective outcome in healthy participants. Neuroscience & Biobehavioral Reviews 44, 124–141.

- To develop automated procedures for recognizing states of mental fatigue from EEG measures.

The longer term goal of these experiments, and which we aim to pursue further in Experiment 4, is to develop task design and feedback training strategies which maximize cognitive performance and minimize the effects of fatigue in sustained performance situations, such as in military or civilian command, control and communications.

Design of the eLANT for Experiment 3

The design of Experiment 3 allows us to explore orienting and conflict, as in other LANT designs, with the addition of control over cueing within or between visual hemifields. Also, by running for a period of time long enough to develop mental fatigue effects we may examine the rate at which networks for control of attention in each hemisphere fatigue, or generally, how fatigue interacts with eLANT performance. We may also assess individual differences in mood and anxiety, controlling for these factors and testing the effects of individual differences. This design allows us to “personalize” the LANT for assessment as well as for optimizing performance of the task in specific individuals.

This design follows the principle that the hemispheres of the brain are two separate information processors, which can work independently or cooperatively to perform tasks. Accordingly, we designed our research system to emphasize lateralized (hemispheric) presentations and responses, measure left and right hemispheric activation and connectivity, and estimate the degree of independence/limitation of resources within and between the hemispheres.

The final version of the LANT for Experiment 3 allows us to address several important theoretical issues. First, the experimental paradigm permits varying loci for targets in the four quadrants of the visual field. Specifically there are four possible target locations for each of the (Figure 4). This makes it possible to separately assess the effects of spatial cue validity within and between hemispheres. Third, the experimental design incorporates simultaneous presentation of both peripheral automatic spatial cues and centrally presented control cues, at arbitrary rates of validity. Fourth, we changed the stimuli we use to measure Conflict Resolution because identification of the targets in the Eriksen flanker task deteriorates with peripheral targets off the horizontal meridian due to the steep and asymmetric loss of acuity. Instead, the new stimuli consist of two small shapes that occupy more or less the same physical space. Our data show that these embedded shapes in the four target positions two degrees off fixation exhibit “standard and expected” Orienting and Conflict effects in response time.

There are good reasons for each of these design changes. In general, “movements of attention” are believed to consist of plans for fixating eye movements in the corresponding direction. These plans are sensitive to acquired visual scanning habits, for example left-to-right reading in English and right-to-left reading in Hebrew. We must consider such individual and cultural differences in modeling attention networks.

Including both central and peripheral cues is also important because tactical information display systems combine multiple sources of information, both strategic/top-down as well as automatic/bottom-up. This can be well modeled by using central symbolic spatial cues, which are believed to be sensitive to the rate of validity, vs. peripheral automatic spatial cues, which are believed to be insensitive to the rate of validity. We believe that he two types of cues engage two independent attentional systems with different time courses and their interactions are still largely unknown. Priming by automatic cues builds up quickly and reverses after 300 ms, which is known as inhibition of return. By contrast, priming by controlled cues builds up more slowly and remains stable for several seconds.

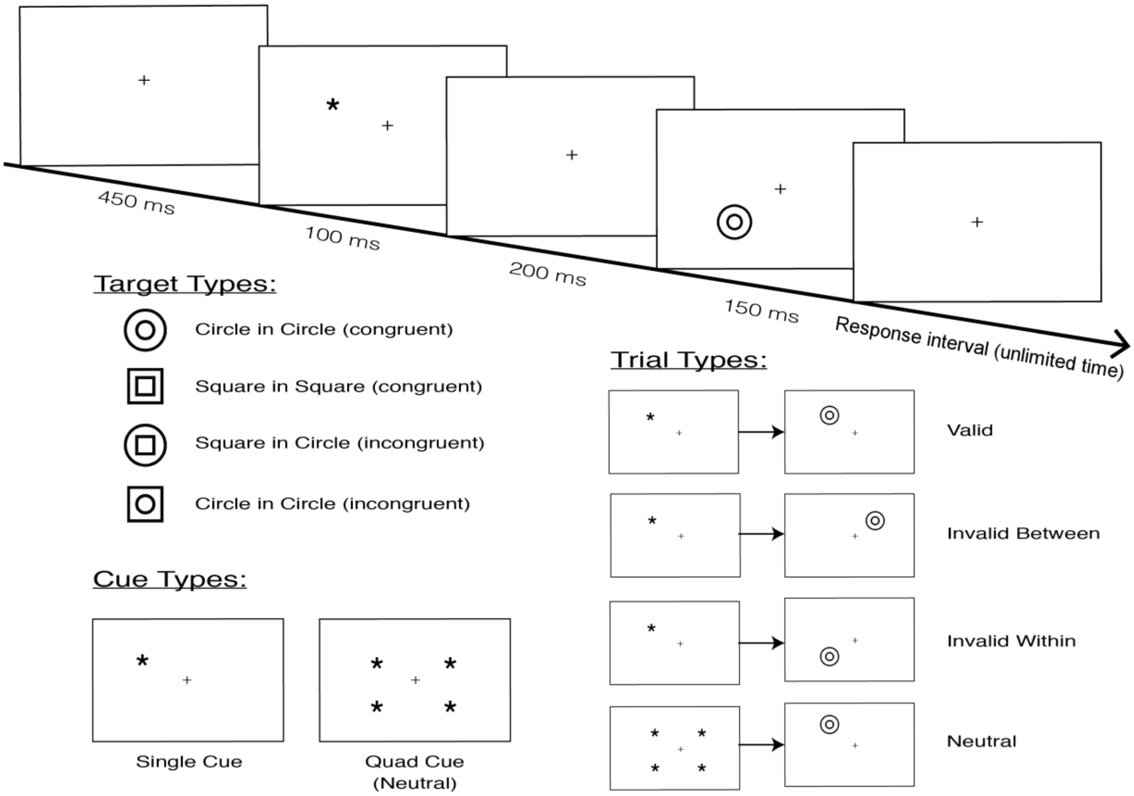

Figure 4. Display design for Experiment 3. Cues include single or quad (neutral). Trial types may be valid, neutral, invalid within-hemisphere or invalid between-hemisphere. Targets are the inner squares or circles and distractors are outer squares or circles; congruent = square-in square or circle-in-circle; incongruent = circle –in-square or square-in-circle. Demo sequence: during the inter-trial interval of 450 ms, and throughout each trial, a fixation cross appears in the center of the display. With the aid of a head and chin read, subjects keep their gaze fixed on this cross. After the intertrial interval, a trial begins with the appearance of a cue with a duration of 100 ms. Then the cue disappears followed by a cue-target interval of 200 ms. Then a target appears for 150 ms. When the target disappears and an unlimited response interval begins during which subjects must indicate circle or square target type with a key press. The response ends the trial and a new 450 ms intertribal interval follows. The self-paced nature of the trials allows for the detection of unusually long response times, which may indicate lapses of attention or alertness characteristic of mental fatigue. [7]

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[7] Our prior design for Experiment 3 included using an eye-tracker interface for the LANT using our EEtrac software. However, during initial tests, we found unexpected timing reliability issues. To solve these issues would have required hardware upgrades and software development costs well beyond the scope of our funding. To stay in scope and meet our main design objectives, we decided to use our existing e-Prime system with a chin rest to ensure stable fixation. This system is reliable for timing and gaze control but does not allow the eyes to move to various fixation points on the display. The eye-tracker based system will allow this and can be deployed for future experiments but will require additional development costs.

Improving the Quantitative Measurement and Analysis of the Electrical Activity of the Brain

We have spent considerable efforts to extend and improve our methods as needed to analyze EEG recorded during LANT tasks as well as for other data analyses. First we added capabilities for input and output of several EEG formats including EDF, EDF+, BDF, Biosemi, Neuroscan and others. We also improved the general function and reliability of the APECSgui interface. We acquired a license for Brain Vision Analyzer 2 (BVA2), a leading software for general EEG signal processing and successfully linked this to APECSgui for data processing workflows. With the aid of BVA2 we have increased efficiency for preprocessing large volumes of EEG data. In addition we wrote custom C and MATLAB functions to import data files produced by BVA2 directly into APECSgui. These workflows are now standardized and efficient and have been applied to the data sets we report here.

More importantly, we added new brain imaging functions to our toolbox, allowing us to compute spherical and 3D-mesh type Laplacian transformations of surface EEG potentials and export of EEG segments for analyses with sLORETA. The Laplacian transforms allow us to measure high-resolution surface potentials from the outer cortex while the sLORETA method allows us to infer deeper EEG sources with somewhat lower spatial resolution.

Using these methods we have confirmed the value of multiway analyses of EEG for assessment of functional brain networks. The approach is to use EEG atoms estimated with parallel factor analyses or PARAFAC to identify periods of EEG recordings or epochs that have a high activation level of these atoms. Then we take the raw EEG signals from these epochs and compute Laplacian or sLORETA source localizations. We are presented results of this approach at a meeting on machine learning methods in September 2013. A copy of the paper is enclosed with this report as Appendix C.

In addition, we have been applying these methods to the elucidation of mechanisms underlying change with EEG biofeedback. Our approach is two-pronged. First we have used data from Andrew Hill‘s controlled study of normal subjects trained to increase C3SMR, C4SMR or C3Beta bands. Second we are using data from wounded warriors and ADD/DHD patients being treated by Don Durousseau at the Peak NT clinic in Herndon, VA. The results were presented at the ISNR society in Dallas during September 2013. A copy of the abstract for the presentation is also enclosed with this report as Appendix D.

Developing Methods and Systems for Aiding, Improving or Optimizing Cognitive Performance

Our primary approach is to allocate different components of the task to the two hemispheres of the brain in such a way that behavior is optimized, given estimates of an individual’s current mental state. Adverse mental states, such as cognitive fatigue or cognitive overload, are of great concern for human performance, especially for soldiers exposed to sleep deprivation, stress, or excessive mental and physical demands. We can assess such states operationally using PDT’s APECS system. APECS is a software toolbox for developing and testing EEG-based mental state estimation algorithms, which was developed in part under prior ARO-funded R&D programs.

Another approach is to control specific components of attention by modulating the activity of functional brain networks using EEG biofeedback. We may accomplish this by discovering which EEG signals reflect the activation of specific brain networks then rewarding increases or decreases in these signals. For example, if certain EEG signals reflect positive or negative aspects of visual spatial attention (i.e., increasing Alerting and Orienting Benefit and decreasing Conflict and Orienting Cost) we may reward increases or decreases in those signals such that network activations move toward levels at which performance is optimal. Rewards may be explicit feedback signals such as visual or auditory stimuli, or changes in tasks or contexts that promote desired changes in the EEG signals. We hypothesize that four key networks are relevant here: default mode, salience, switching and dorsal attention. During periods of rest the brain's default mode network or DMN dominates cortical activation, consuming vast amounts of the brain's energy reserves. When the DMN is highly active, attention to sensory stimulation is attenuated and reaction times to events in the environment are slowed. During these periods we allocate attention to ourselves and engage in "internal" tasks, such as mind wandering, or autobiographical memory.

Fur future research we may implement this by directing task-relevant visual stimuli to a specific visual hemifield with the aid of a real-time system that a) continuously tracks gaze, and b) continuously estimates mental states. Our EEtrac system can present stimuli that are contingent on instantaneous gaze and EEG-based mental state estimates. The programming support to enable this is in place and has been tested, and will support the implementation of Experiment 4. Additional support for software to ensure adequate event timing control will be required for this implementation. We think that cost will be justified by producing an essentially open-source system that may be of value to a much wider range of users than our group.

Summary of the Most Important Results

APECS Algorithm Development and Applications

During this contract, we made continuous advances in extending and refining the APECS algorithms that we use to estimate mental states. We further expanded and refined our MATLAB toolbox called APECSgui. APECSgui allows non-experts to perform all of the necessary steps to create powerful models for mental state estimation and to export them to the EEtrac system for real-time applications. The GUI provides for data file importing, preprocessing, segmentation, feature extraction, modeling, and classifier construction. In addition APECSgui now exports EEG segments selected by PARAFAC or NPLS atoms to codes for EEG source localizations with the aid of spline and 3-D mesh Laplacians and sLORETA.

We have also interfaced APECSgui with BVA2 through a variety of software interfaces. At the simples level we can export EEGs from BVA2 the MATLAB transformation tool then apply our APECSgui transformations, and return the results to BVA2 for visualization. We found the transform mechanism in BVA2 for MATLAB to be exceedingly slow for large EEG files. So we focused instead on writing new codes that speed the import of EEGs exported from BVA2. This approach has proven to be highly efficient. We now do all preprocessing steps in BVA2 including filtering, re-referencing, channel re-naming, ocular artifact reduction, interpolation of bad channels, and semi-automatic detection and marking of EMG and other uncorrectable artifacts. The results are exported as "generic data" including headers and markers. We wrote MATLAB codes *bva2raw.m* and *bva2epoch.m,* which allow us to directly create continuous or epoched EEG data files for immediate use in APECSgui. These routines also keep track of event types and artifacts as needed for inclusion in, or exclusion, from APECS models and classifiers.

We have applied the APCESgui software extensively to EEG data from the UCLA studies of lateralized attention and analysis of resting state networks. Initial findings show that EEG atoms (multiway components) with stable scalp topography and spectral envelopes can be reliably measured over many days in single subjects.

Analyses Completed in FY2014-2015

Analyses of EEG Atom Metrics in EO/EC, BFB, LANT, and CPT Tasks from Experiments 1-3

We analyzed EEG atoms in 30 participants from Experiment 1, which included resting, biofeedback and LANT conditions. The APECSgui software allowed us to measure "standard" EEG atoms across conditions in individual participants. We also observed that the frequency spectra of these atoms resembled classic EEG frequency bands, including theta, alpha 1, alpha 2, SMR, beta 1 and beta 2 (Figure 5). We used these data to validate the entire chain of BVA2-APECS processing steps and found that the quality and reliability of the results has improved substantially. We found remarkably similar average atoms patterns for 17 subjects of Experiment 2 (Figure 6) and four subjects of Experiment 3 (Figure 7).

We conclude that using PARAFAC to decompose EEG into meaningful atoms can be highly consistent across completely different groups of individuals and under varying conditions. This approach to quantitative EEG is novel and powerful and may also serve as a basis for practical applications. For example, both research and clinical assessments of EEG currently lack global integrative measures such as those afforded by PARAFAC atoms. Other approaches, such as independent components analysis or principal components lack the means to provide unique representations of spatial and spectral aspects of EEG rhythms while preserving a time history of their contributions to the overall EEG observed under various conditions. We expect that further research and development of the atom approach to EEG decomposition will lead to powerful research and clinical metrics

Studies of Lateralized Attention Networks and their Interactions with Mood or State/Trait Anxiety using the eLANT

The UCLA team completed work to further describe the specializations of left and right hemispheres in visual attention tasks. A detailed report on the results is included in Appendix E. This work primarily consisted of behavior and mood analyses of Experiment 2 – the ecologically valid LANT or eLANT. This work has shown that the eLANT is highly sensitive to the emotional valence of cues and contexts. More interestingly, it shows that these effects interact with individual differences, particularly for levels of anxiety. Briefly, the results of Experiment 2 show that we can identify sensitive behavioral measures of fatigue which are associated with differential contributions both of attention networks and of the emotionality of the backgrounds/cues when performing the LANT. **In particular, we found that participants with low levels of weariness were more flexible in demonstrating and switching hemispheric asymmetry across test conditions.** This result suggests that selection of individuals based on the degree of weariness induced by hemispheric attention tasks could serve to select those who are candidates for tasks demanding such flexibility or for training designed to increase such flexibility. Additional assessment using EEG metrics of fatigue could enhance such selections or serve as dynamic criteria for training.

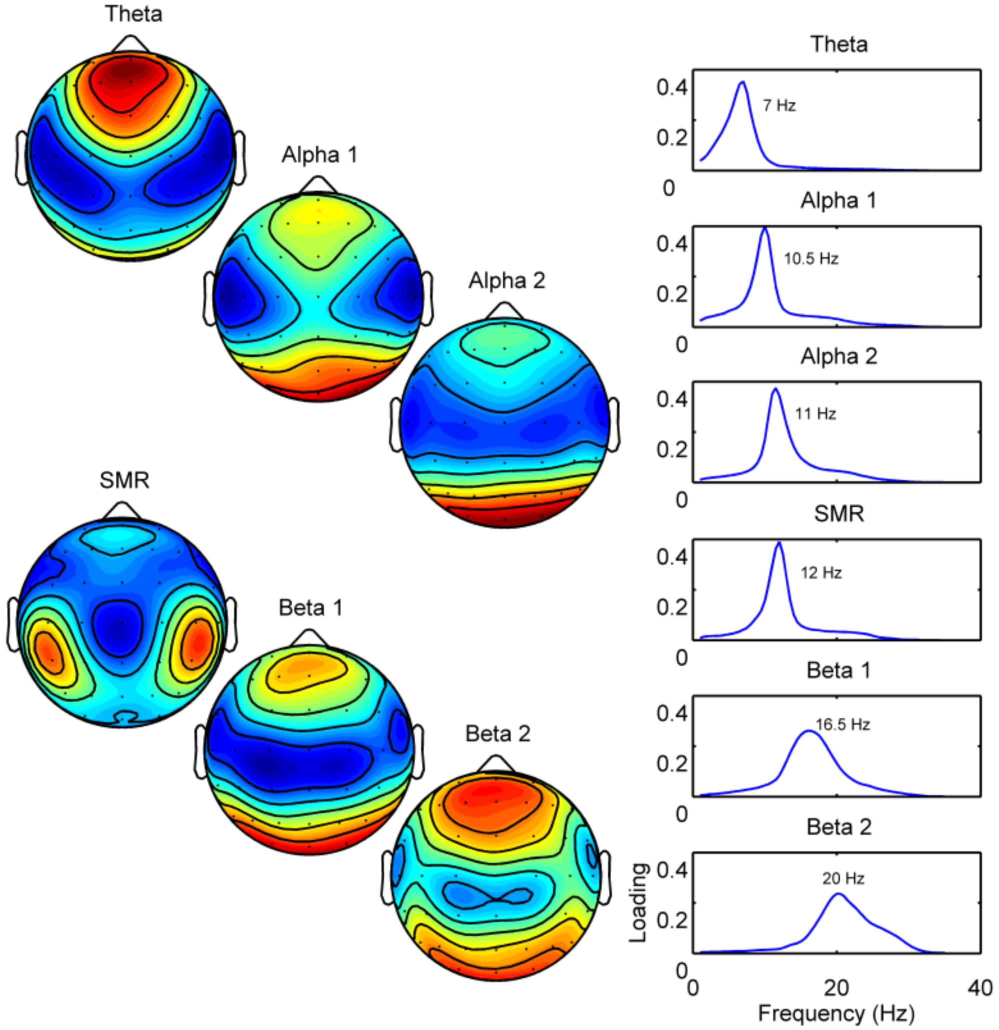

Figure 5. Grand average EEG atoms from 30 subjects' eyes-open and eyes-closed resting state in Experiment 1 including theta, alpha 1, alpha 2, SMR, beta 1 and beta 2. Each subject's EEG atoms were separately estimated, then the spectral and spatial loadings of the atoms were averaged and plotted.

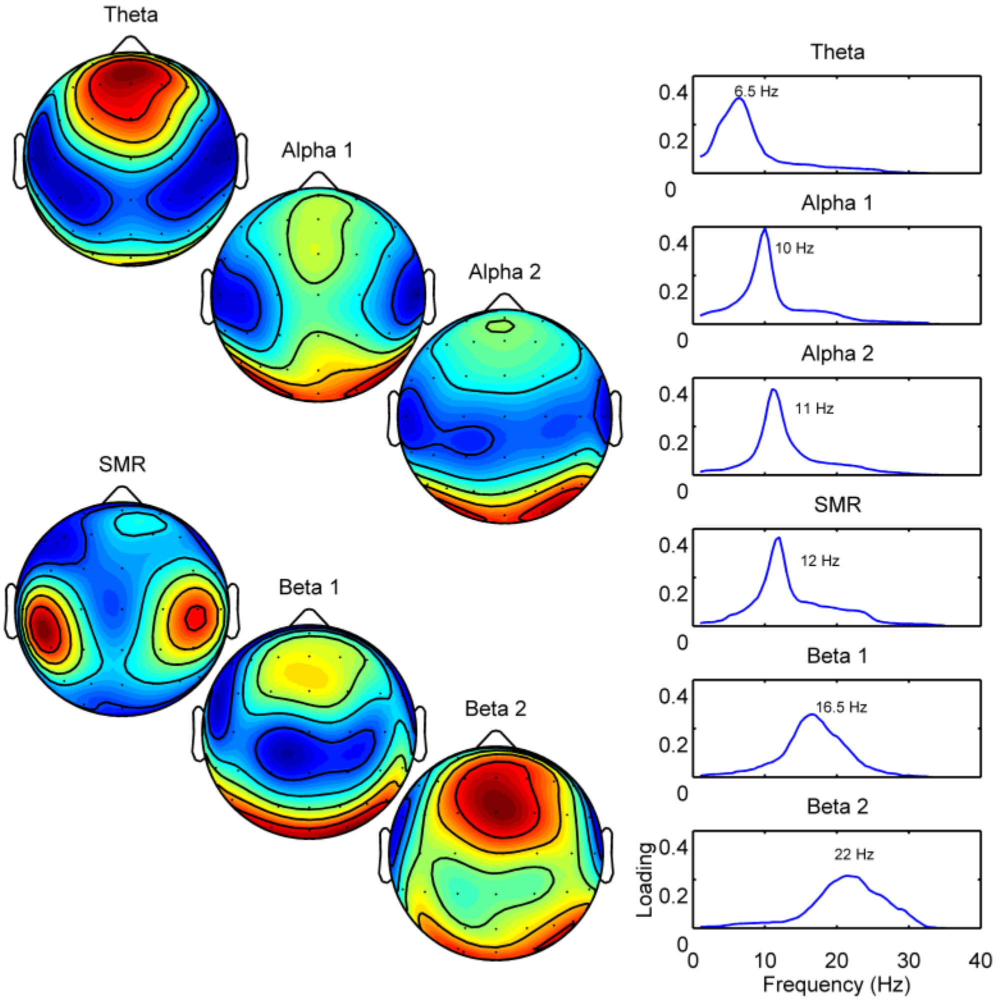

Figure 6. Grand average EEG atoms from 17 subjects' eyes-open and eyes-closed resting state in Experiment 2 including theta, alpha 1, alpha 2, SMR, beta 1 and beta 2. Each subject's EEG atoms were separately estimated, then the spectral and spatial loadings of the atoms were averaged and plotted.

Analyses of EEG Correlates of Mental Fatigue during Mental Arithmetic Performance

In a related effort supported in part by this contract, we also applied APECSgui to analyses of mental fatigue during performance of a mental arithmetic task, and this resulted in a recent peer-reviewed article published in 2015 (Appendix F). This analysis showed that a related APECSgui algorithm, KPLS Atomic Decomposition, was able to track the development of mental fatigue over a three hour period of performing mental arithmetic (data were collected in a prior NASA study and re-analyzed using APECSgui). The key atoms represented frontal theta band activity and parietal alpha band activity (Figure 8). By combining the time-scores of these atoms in a classifier, good separation of alert and fatigue states was possible using single 13-s segments of EEG (Figure 9). The development of fatigue over time was traceable and highly consistent across participants, showing that most people experienced an increase in fatigue in 15-30 minutes and were continuously fatigued after 30-75 minutes (Figure 10). Interestingly some individuals were fatigue-resistant and maintained alertness for as long as 90-120 minutes.

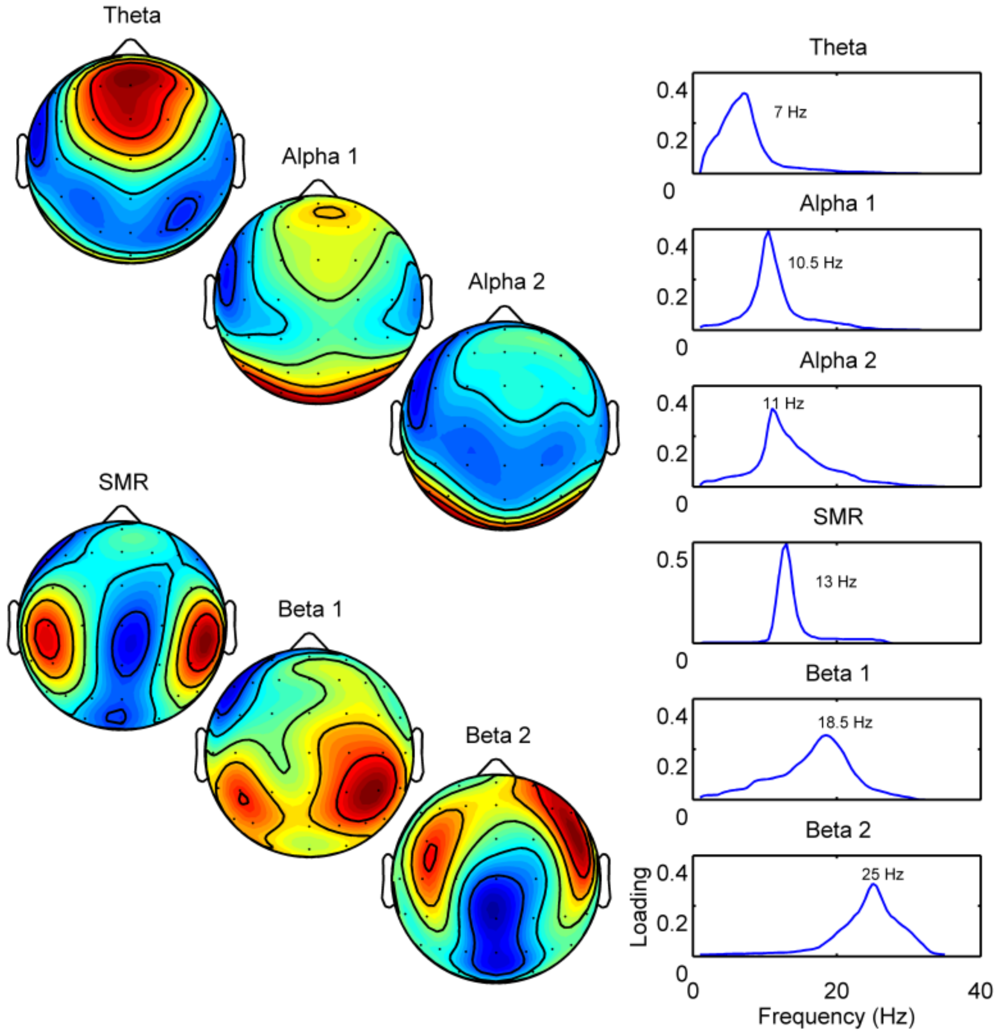

Figure 7. Grand average EEG atoms from four subjects' eyes-open and eyes-closed resting state in Experiment 3 including theta, alpha 1, alpha 2, SMR, beta 1 and beta 2. Each subject's EEG atoms were separately estimated, then the spectral and spatial loadings of the atoms were averaged and plotted.

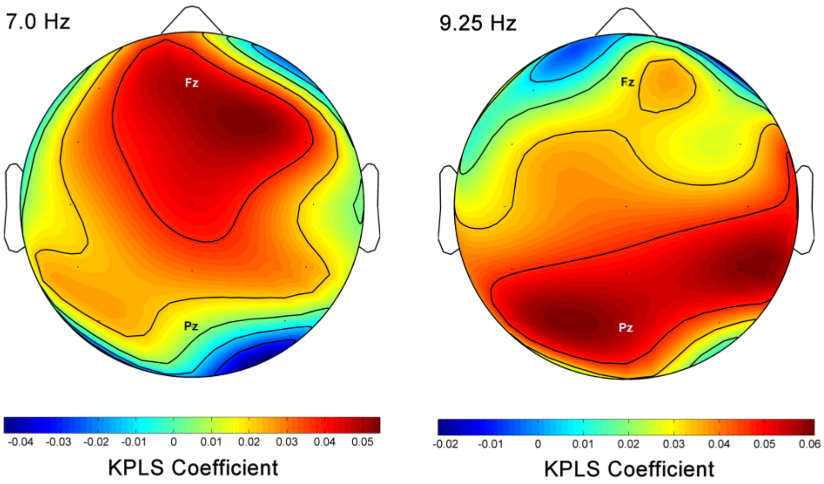

Figure 8. Topographical maps of the coefficients for the first KPLS components that discriminated alert and fatigue states at the peak frequencies in theta band (left, 7.0 Hz) and alpha band (right, 9.25 Hz) for one subject (S7) during mental arithmetic performance. The colored areas are spherical spline interpolated values, with the largest values in red and the smallest in blue. Electrodes nearest the maxima were Fz for the theta band and Pz for the alpha band.

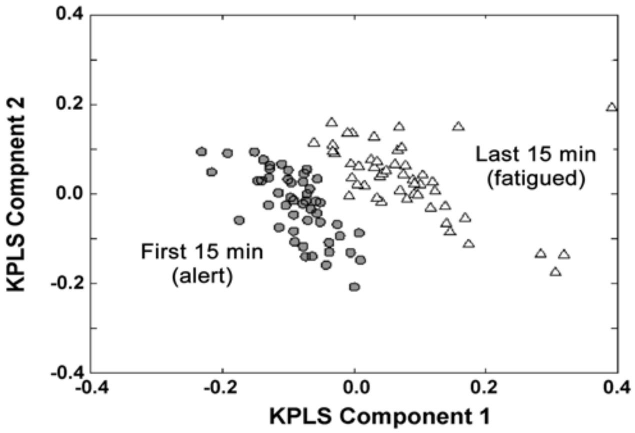

Figure 9. Example of KPLS scores predicted for single-trial EEG spectra for early (dark circles) and late (light triangles) blocks of the mental arithmetic task in one subject (S3).

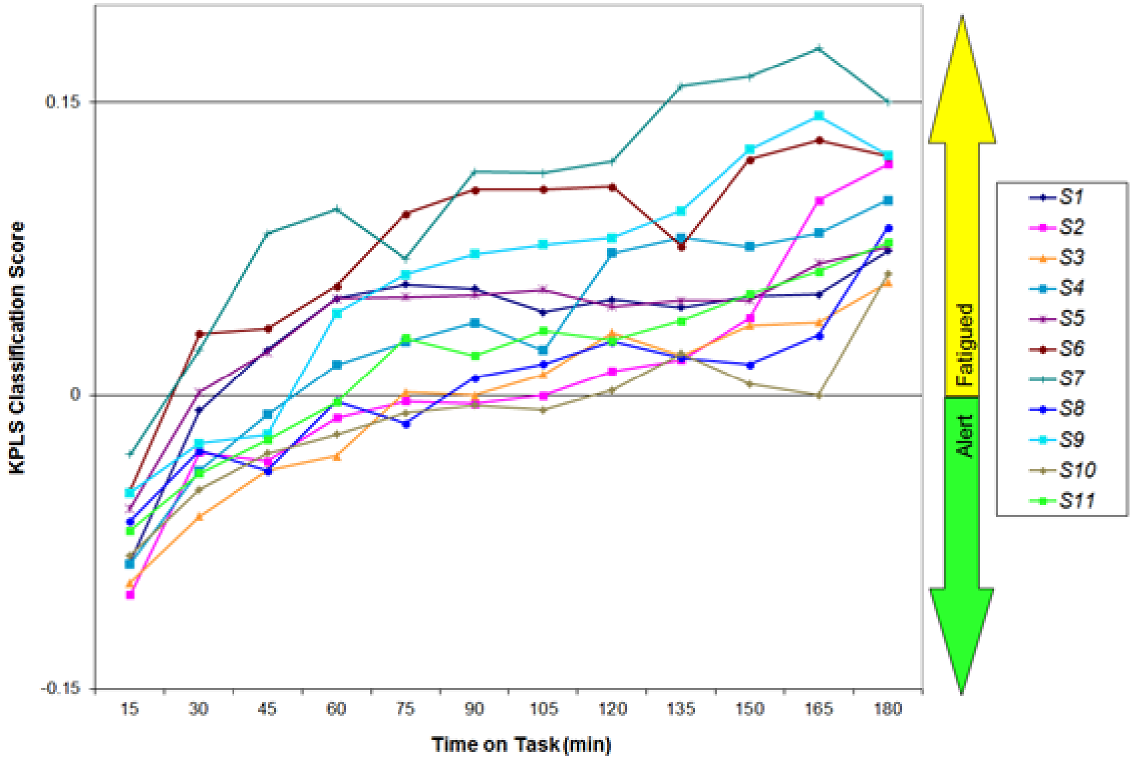

Figure 10. Means of the KPLS classification scores for each 15-minute block in 11 subjects who completed 12 blocks or 180 minutes of continuous mental arithmetic performance. For subject S3 the points in the range 30 to 150 min (Blocks 2-10) correspond to the centers of the clouds of points shown moving from the alert region to the fatigue region in Figure 8. Negative scores represent alert states and positive scores represent fatigue states.

Analyses of Fatigue Effects and EEG Correlates in Experiment 2

We have also analyzed the extensive EEG data collected during Experiment 2. We tested a total of 25 participants, of which a subset of 10 participants repeated the test session on a second day. A session consisted of five segments, 1) rest with eyes closed one minute, 2) rest with eyes open one minute, 3) a one-hour performance of the eLANT using two emotional spatial cues (happy or angry faces) and two emotional backgrounds (happy couple or a fierce shark), 4) rest for one minute with eyes closed, 5) rest for one minute with eyes open. We continuously recorded 64 channels of EEG and four channels of EOG using a Biosemi Active Two system during each of the five segments. A separate report on these analyses is included in Appendix G.

The analyses show that using the APECS NPLS algorithm to develop EEG-based classifiers can lead to useful EEG-based models of fatigue that develops over time in the eLANT task. The results generally agree with our findings in mental arithmetic, that most subjects begin to experience fatigue in as few as 15 minutes on task. In addition, atoms with loadings focused in the alpha and theta bands were important.

As we may expect, we observe that training with same-day data in single subjects leads to the most successful models. However, interestingly, models derived from on day’s data can successfully predict EEG-based estimates of fatigue on another day.

Perhaps most surprisingly, a model that used several subject’s combined data was successful in predicting fatigue in the individual subjects whose data entered the model.

And using four subjects' data to predict fatigue in a fifth subject was also moderately successful.

Considerably more analysis, which is beyond the scope of this contract, will be needed to understand the physiological significance of the atoms entering these models. Also we need to survey more subjects and tasks systematically. Nevertheless we may conclude that single-subject and normative models of mental fatigue for attention tasks can be developed successfully and applied generally across time and subjects.

Analyses of LANT Behavioral Effects and EEG Correlates in Experiment 3

Solving the Mystery of EEG Biofeedback

Theoretical Development

We further developed our theoretical model for the brain networks and processes underlying changes resulting from EEG biofeedback treatments.

EEG patterns recorded from the human scalp tend to show systematic patterns in relationship to behavior in three or four frequency bands recorded at specific sites: Theta (6-8 Hz), Alpha (8-12 Hz), SMR (12-15 Hz), low beta (15-18 Hz) and High Beta (18+ Hz). There is now substantial evidence that these systematic patterns can be changed by direct conditioning of a person's own EEG. Using this technique, it is possible to ameliorate developmental deficits, such as ADHD, or even to improve native skills, such as athletic or artistic talent. Yet, little is known about the process that mediates such changes. In fact, the process seems to present some perplexing challenges as follows:

- Changes seem to occur too quickly to be explained by classical or operant conditioning. Most often, training seems to change long-term behavior without long-term changes to the trained band.
- Effective training requires little conscious attention and can occur in normal adults just as well as in young children and even autistic patients.
- Reward and training seem to occur in the absence of a specific goal behavior.
- There are large individual differences in susceptibility to EEG Biofeedback training.

Few experiments on the effects of EEG Biofeedback demonstrated systematically and successfully that the following all occur: (1) conditioning/learning actually occurred; (2) the experimental protocols differ systematically from a placebo control group, (3) the effects of training are protocol-specific, (4) the effects of training are site-specific. In a prior ARO-funded experiment, we assessed two different common clinical protocols at the same training site (C3-Beta and C3-SMR) and we contrasted the same protocol at two different sites (C3-SMR vs. C4-SMR). We also assessed a double-blind sham group whose EEG Biofeedback protocol consisted of segments of EEG Biofeedback sessions of other participants, corrected for the participant's motor artifacts. We measured the electrophysiological effects of EEG Biofeedback by comparing the resting state EEG before and after training. We measured the behavioral effects of EEG Biofeedback by comparing performance on the LANT before and after several sessions of training. We also analyzed associated changes in the electrophysiology (ERP) of the behavioral trial. Moreover, our paradigm allowed us to address site-of-action specificity by comparing the performance of the LANT in each hemisphere separately following training to only one of them.

We found selective behavioral decrease in Conflict (resulting from flanker arrows pointing in directions opposite to target arrows) in the right hemisphere following C3-Beta training. There was also a systematic change in the P3 components of the ERP following C4-SMR training. Thus, we demonstrated site-of-training specificity (C4-SMR had significant effects on the electrophysiology that did not occur following C3-SMR training), we demonstrated training-protocol specificity (C3-Beta had significant effects on the behavior that did not occur following C3-SMR), and we demonstrated site-of-action specificity (C3-Beta resulted in changes in the right hemisphere, but not in the left). However, there was no evidence for conditioning/learning in any of the trained bands following any of the training sessions. How could this have happened? We suggest the following information processing model:

- Effective EEG Biofeedback training occurs during activation-deactivation sequences of the Resting State Default Mode Network and the Dorsal Attention Network.
- The Default Mode Network is activated during tasks involving autobiographical memory, envisioning the future, theory of mind, and moral decision-making. The common element is self-introspection in a social emotional context.
- Activation of the Default Mode Network is associated with deactivation of externally directed networks (visual, auditory, somatosensory, executive), which are engaged during problem-solving, attention-demanding tasks.
- The activation of the Default Mode Network is preceded by switching attention from the “outside” to the “inside,” i.e., following the deactivation of the Dorsal Attention Network, if no other network activates, then the DMN automatically activates. This is the result of its being the default mode network.
- During EEG Biofeedback training, the Default Mode Network is oriented to self, but alternates in activation with networks that are sensitive to outside feedback.
- EEG Biofeedback training rewards specific EEG patterns. The most common approach is to reward specific EEG bands (e.g., alpha, SMR) at specific electrodes or electrode combinations.[8] We consider that all EEG patterns, whether simple or complex by the experimenter’s or therapist’s definition are actually highly complex phenomena at macroscales of the EEG.[9]

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[8] EEG feedback may also be contingent on inhibiting other patterns such as rewarding SMR while inhibiting theta and high beta bands. More esoteric feedback involves rewarding coherences of frequencies between electrode pairs, specific temporal components of EEG derived with methods such as Independent Components Analysis or ICA, and a host of other variations on these themes. What is common to all of these approaches is that the reward is linked to a specific EEG pattern, which may be very simple (e.g., C3 beta) or quite complex (coherence of cortical volumes defined with inverse methods such as LORETA).

[9] We do not consider passive neurofeedback methods, such as “pacing” EEG oscillations with injected transcranial electrical currents (e.g., the LENS method) here as these likely work at a more physiological than behavioral level, if at all.

- While the number of possible EEG patterns one may use for biofeedback is huge, the number of associated cognitive states a person experiences during EEG biofeedback is relatively small and divides into two broad classes, each containing a few “canonical” states. In the first class, there are external and task-oriented states, which include monitoring the environment (attention to external stimuli, attending to other people, watching, listening, observing, examining), task engagement (attending to task requirements, performing a task), task disengagement (withdrawing attention from tasks, ending or pausing task performance), etc. In the second class there are internally-directed states, including thinking about one’s self, remembering past events, re-living experiences, mind wandering, meditating, imagining future events, day dreaming, theorizing about things, including other people’s behavior, etc.
- The sequence of external and internal canonical cognitive states is continually woven into a strong autobiographical episode that is both emotional and social, which are stored in episodic memory and may become the object of future reminiscence.
- Underlying each canonical cognitive state there is a specific global pattern of network activity, complete with sequences of neuronal excitation and inhibition, emerging local and global oscillations and associated functional connectivity throughout the cortex. During these sequences, macroscale EEG oscillations may distinguish short- and long-range connectivity by inverse relationship to EEG frequency, e.g., delta, theta, alpha → long-range connectivity; beta, gamma → short-range connectivity. A guiding principle is that some low-frequency oscillations, such as alpha rhythms, reflect inactivation of regional networks, such as the appearance and disappearance of the posterior rhythm with the closing and opening of the eyes, or the interruption of central μ-rhythm by the movement of limbs.
- The mapping of cognitive states to EEG patterns is many-to-one, such that the patterns may distinguish different canonical states (task performance, vs. day dreaming) but not different states within the same canon (visualizing the face of your aunt or your grandmother)
- During EEG Biofeedback training, a limited number of EEG patterns (which reflect the sequences of canonical states) occur in distributed cortical networks, including loci other than the training sites. The activation/inactivation sequences of these networks may in some but not all cases be estimated by multiway (tensor) EEG patterns defined in space (a weighted array of electrodes, or voxels of an inverse model, such as LORETA), frequency of oscillation (a spectral band, or bands), and time (an episode, or period during which the pattern appears and disappears).[10]
- We can estimate these EEG patterns efficiently with multiway methods such as parallel factor analyses or PARAFAC, but they may also be estimated in other ways.[11] When using

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[10] There are many ways that EEG pattern recognition methods can fail to faithfully reflect specific brain network activity patterns. These include minimally, lack of precision due to noise and artifact as well as direct estimation problems such as superposition of sources, invisibility of sources from the surface, cancellation of source potentials, and volume conduction effects. Converge of various methods and agreement with other methods, such as fMRI can help disambiguate EEG pattern recognition methods.

[11] PARAFAC is one multiway method that allows for simultaneous estimation of EEG patterns in space, frequency and time. One may approximate multiway solutions with a series of two-way

PARAFAC atoms as the estimate of an EEG pattern, we may regard the time series of atom activations as mirroring the activation of specific networks, including networks that go on and off during EEG biofeedback training. A network may function through a sequence of neuronal firings that require more than one atom to model, such as if a distributed network links oscillators with different frequencies and different regions.

- The hidden and unobservable behavior that EEG biofeedback conditions is a sequence of activations and deactivations of specific networks, such as the Default Mode Network or the Dorsal Attention Network, and this is mirrored in the activation/deactivation of related EEG atoms.
- Repeated conditioning of this sequence reinforces a “canonical-state control habit,” consisting of a sequence of canonical states, which includes at a minimum, internally directed attention (Default Mode), switching to external attention (Dorsal Attention) and processing external biofeedback reward stimuli (visual or auditory perception). This demystifies and simplifies EEG biofeedback by suggesting that the particular patterns being trained are less important than the process of exercising internal behaviors of sequenced canonical cognitive states. Differences in the effectiveness of various EEG training patterns in our model would arise from the ease or difficulty with which the trainee can “access” them with cognitive states that alter their strength or probability of occurring. This also suggests that similar benefits provided with EEG biofeedback could be achieved without EEG by using other methods to reinforcing and rehearse beneficial sequences of canonical cognitive states.
- We speculate that widespread and lasting changes in cortical connectivity may result from reinforcing habits of canonical state control. When training is over, the EEG atoms activated and deactivated by sequences of cognitive sates return to pre-training amplitude distributions. The effect of changing connectivity instead is to facilitate repetition of the learned sequences of canonical states beyond the training period.
- A necessary and key component of canonical state control is the Default Mode Network, which constitutes a monitoring system that weaves together sequences of canonical states and their corresponding network activations in an autobiographical episode.

Experimental Analyses of EEG recorded during Biofeedback Episodes

The Solving the Mystery of EEG Biofeedback add-on project provided a small direct budget for investigating EEG phenomena recorded during EEG biofeedback sessions from Experiment 1 (Andrew Hill’s experiment). We focused analyses on two interpretations of the experimental effects: 1) test the notion that EEG biofeedback produces temporary alteration of EEG atoms, as expected from the training networks that follow the biofeedback signal, 2) test the notion that

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solutions such as principal components, common factor analysis, or independent component analysis. With two-way solutions atoms are estimated in frequency and space then projected in time by fitting the two way components to the EEG at a series of times. Or fits may be done in space and time and then frequency spectra are measured at different time intervals using spectral analysis of the various components’ time series. The difference with multi-way methods is that time itself is one of the dimensions of each component and is uniquely estimated jointly with space and time dimensions.

EEG atoms dynamically follow the biofeedback reward signal, momentarily cycling through a series of atom activations as networks follow the sequencing of canonical cognitive states set out in our model.

Methodological Developments

As a prelude to both analyses we further developed APECSgui and related codes to extract EEG segments corresponding to high absolute or relative atom activation patterns. The PARAFAC equivalent measure of an atom activation during a specific EEG epoch is called the "time score," which is a component loading that the PARAFAC algorithm solves for in the time dimension. For example we may define EEG epochs of high alpha activation as those in which the alpha atom time scores exceed the 85th percentile of all alpha atom time scores. Similarly, EEG epochs of high relative alpha activation are those in which the relative alpha time score (alpha time score / (sum of all atom time scores)) exceeds the 85% percentile.

After extracting EEG epochs matching atom activation criteria we developed code to interface our EEG records with the sLORETA program of the Key Institute for 3-D source localization. EEGs as measured on the scalp represent a summation of post-synaptic neuronal processes at the cortical level. sLORETA is a technique for solving EEG the inverse problem; that is, an estimate of cortical activation corresponding to the scalp EEG. The atoms themselves cannot be localized as they are a summary of space-time-frequency information for an interval of time, in this case a 1-second epoch. Instead the raw EEG for the epoch containing a high atom score is used to compute the sLORETA source voxel map, a map of estimated current source densities, or CSDs. Then if desired we may average the LORETA CSDs for all time points in each epoch or across multiple epochs that match the time score criteria. The method and its application are subject of the paper attached as Appendix A.

Representative Results

First, using data from seven C3-Beta trained subjects and two SHAM subjects from Experiment 1, we analyzed EEG of the eyes-open condition recorded prior (Pre) and after (Post) the BFB training. Using the PARAFAC algorithm in APECSgui we searched for day- and condition-based spatial-frequency atoms. We observed stable day-to-day atoms reflecting theta, alpha, SMR, low beta and high beta in all subjects during both Pre- and Post- eyes-open condition sessions. An example of the low beta atom extracted separately for each of four training days is depicted for S120 in Figure 11 and S123 in Figure 12, both of whom received C3-beta training. For S120 slightly increased frontal activation can be seen in the topo-plot for the sixth day; however, the atom spectra clearly reflect the range of low beta with peak at around 17 Hz for this subject. We observed the same stability of the low beta atom when grouping all four days together and when Pre- versus Post-BFB eyes-open conditions were compared. This was true for all subjects, days, recording conditions and all considered atoms.

Next, we separated EEG into segments based on the PARAFAC atom score values. This allowed us to investigate cortical patterns corresponding to different atomic activations. Grouping together eyes-open condition data of four subjects (two C3-Beta trained and two Sham subjects) recorded during four days we estimated the low beta, alpha and theta atoms. We did this for Pre- and Post-BFB training sessions separately. For every set of EEG segments we computed sLORETA CSDs and in the post-processing analysis we averaged them. Finally, we computed the difference of averaged sLORETA CSDs for Pre- and Post-BFB training eyes-open conditions.

In Figure 13 the average CSD computed from segments of EEG data corresponding to the high activation/scores of the low beta atom (EEG data segments corresponding to the PARAFAC time score greater than 85 percentile were used) is depicted for one of the C3-Beta trained subjects. Increase of the cortical activation after BFB training can be seen in the Brodmann areas 5 and 7 and in the precuneus. This increase was observed neither for the other C3-beta trained subject nor for the two Sham group subjects.

Using the alpha atom scores to determine the selection of the EEG time epochs for sLORETA, similar to Figure 13, an increase of CSD after the BFB training was observed for subject 123 only. The other three subjects (one C3-Beta and two Sham) have shown no increase in CSD between Pre- and Post-BFB sessions. Finally, for the theta atom a decrease in CSD was observed for subject 123 in the right Brodmann area 7 (Figure 14). Note that the training criterion in Experiment 1 for increasing low beta training was linked with simultaneous inhibition of the theta rhythm (4-7 Hz).

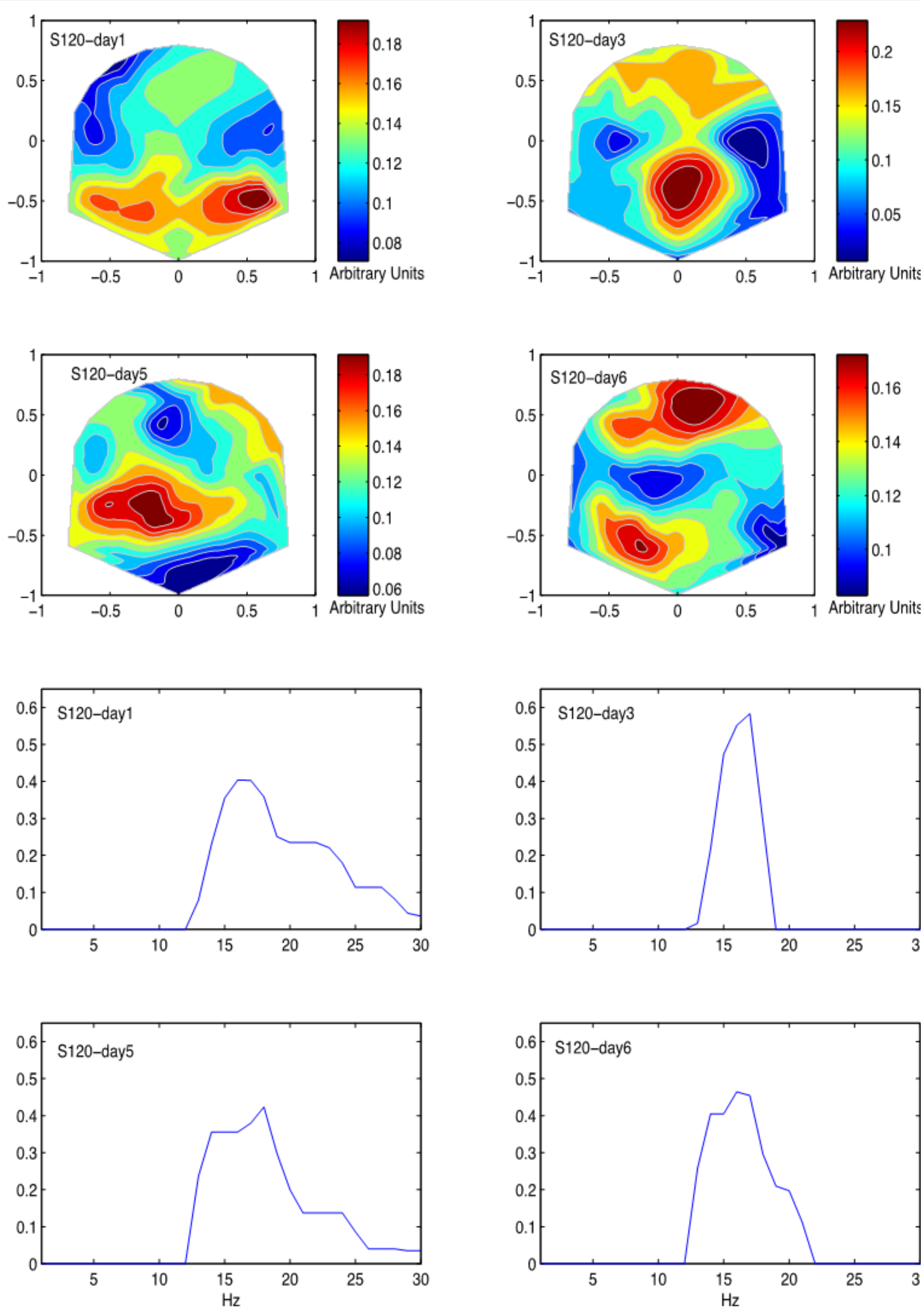

Figure 11. Topo plots with corresponding spectral loadings for the low beta atom of the subject 120. The atoms were extracted separately for each day, by running the PARAFAC model with non-negativity constraint for time and spatial scores, and uni-modality constraint for the frequency component.

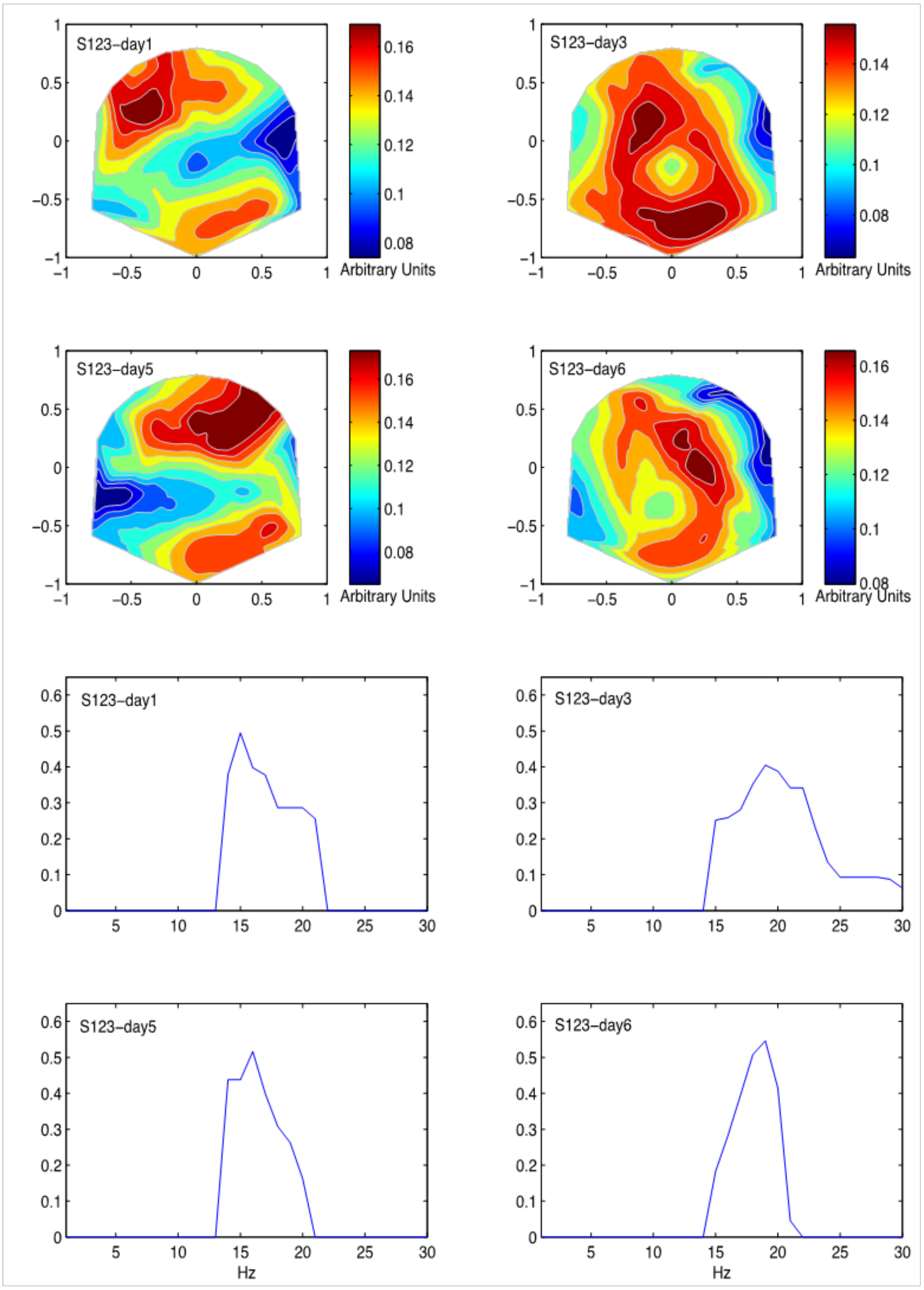

Figure 12.

Topo plots with corresponding spectral loadings for the low beta atom of the subject 123. The atoms were extracted separately for each day, by running the PARAFAC model with non-negativity constraint for time and spatial scores, and uni-modality constraint for the frequency component.

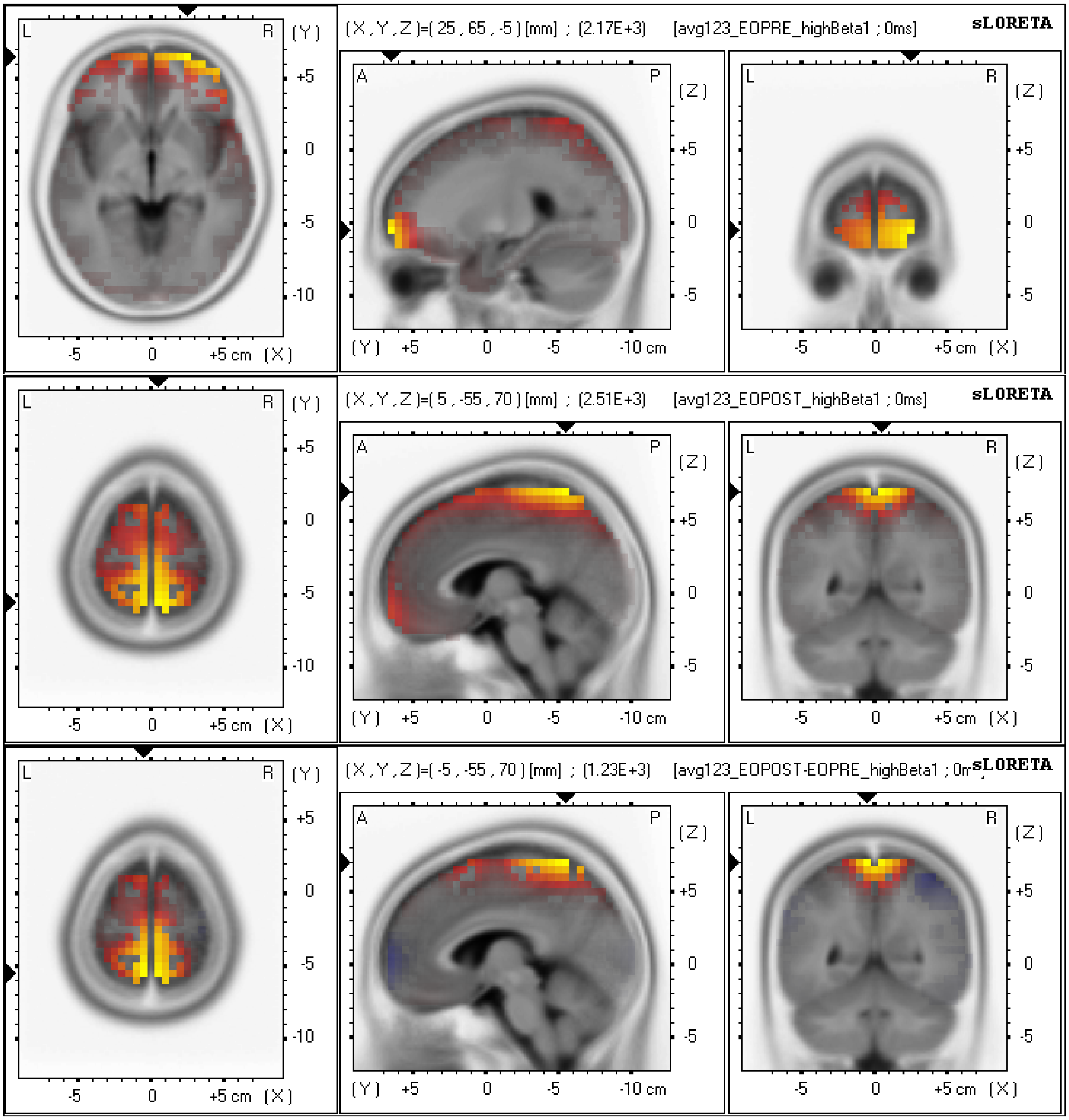

Figure 13. Subject 123 trained with the C3-Beta BFB protocol. Averaged sLoreta corresponding to high activation of the low beta atom is depicted. Top: Pre-BFB training eyes-open condition. Middle: Post-BFB training eyes-open condition. Bottom: Difference between the Post- and Pre-BFB training eyes-open condition.

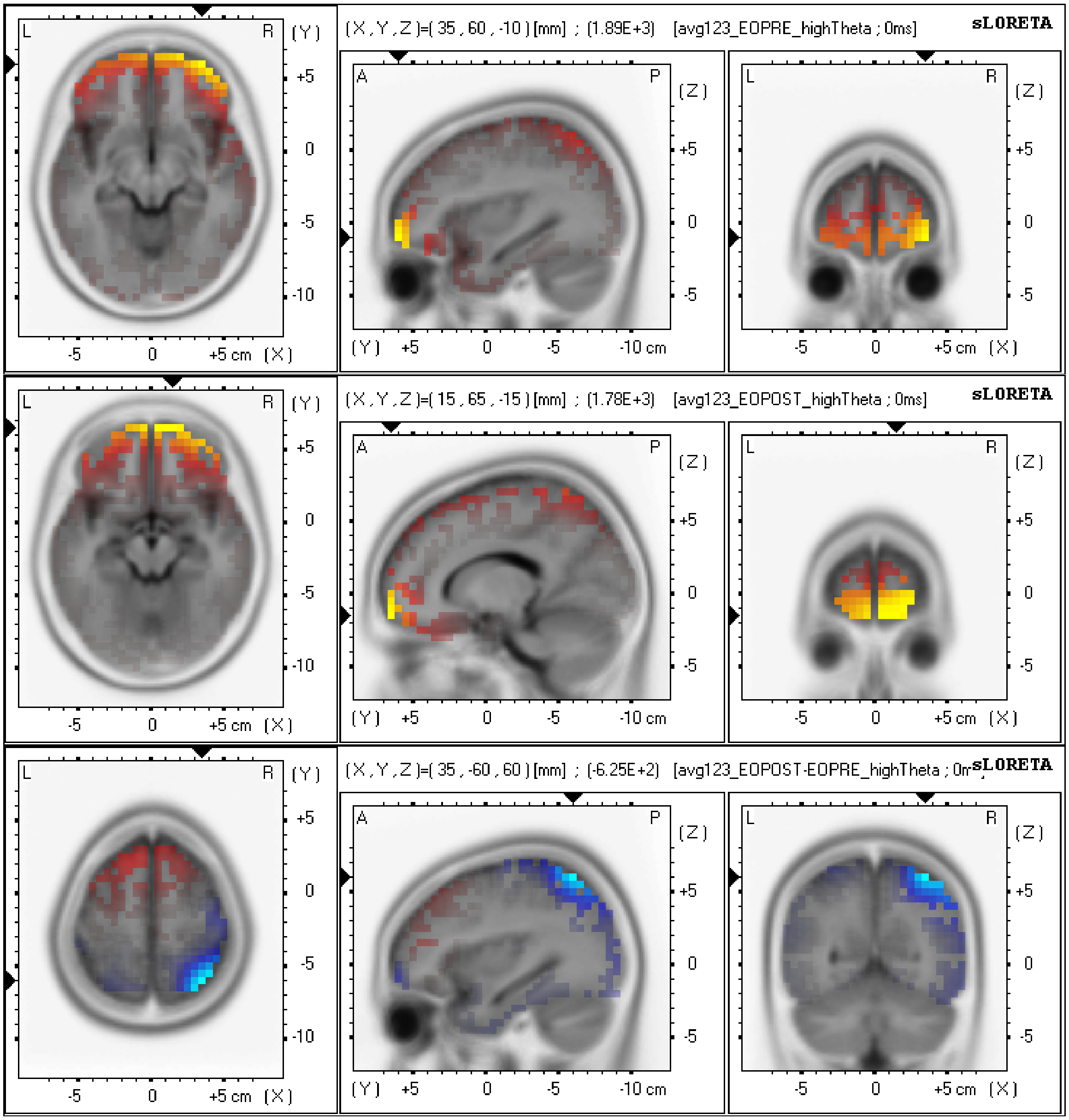

Figure 14. Subject 123 trained with the C3-Beta BFB protocol. Averaged sLORETA corresponding to high activation of the Theta atom is depicted. Top: Pre-BFB training eyes-open condition. Middle: Post-BFB training eyes-open condition. Bottom: Difference between the Post- and Pre-BFB training eyes-open condition.

These results show that our APECSgui PARAFAC + sLORETA method is powerful enough to identify EEG segments corresponding to specific atom activation patterns and to compare these patterns across conditions where we may expect to see changes resulting from EEG biofeedback or BFB. In one subject (S123), we found evidence of heightened low beta atom activations in the eyes-open segment at the end of the BFB session as compared to the eyes-open segment at the beginning. In the same subject we found evidence of reduced theta atom activation in the eyes-open segment after the BFB session as compared to the beginning. We have not yet tested whether there was any trend towards persistent increases across days using the sLORETA method. However, earlier direct tests of atom activation scores showed no persistent changes across BFB training days (Figure 15). This is consistent with Andrew Hill's analysis of classic EEG band powers, which showed no lasting changes at the trained EEG electrode sites. We also tested atom activation scores for eyes-open and eyes-closed conditions only contrasting Pre-BFB and Post BFB values (Figure 16). Again there is no evidence of temporary movement of atom scores from the beginning to the end of the BFB session. Overall, these observations support the notion in our model, that the mechanism of EEG biofeedback does not require lasting changes in EEG atom activations.

We are continuing the application of this atom-sLORETA method to more subjects and conditions and will report on these results in a future separate progress report.

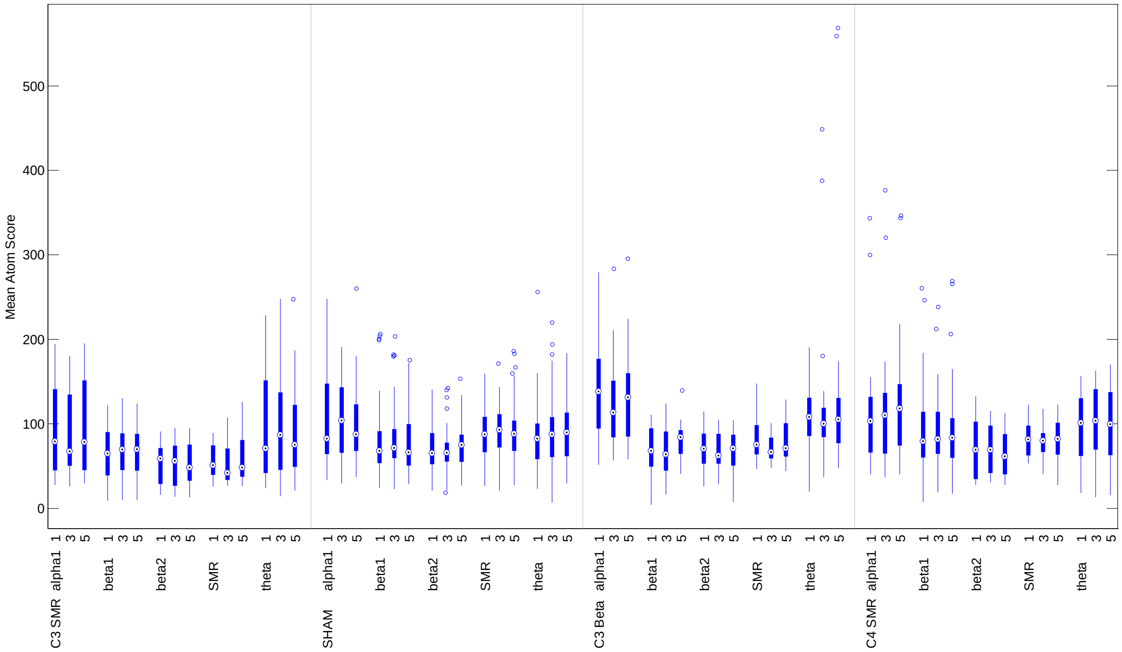

Figure 15. Boxplot showing atom-score median and dispersion metrics; 25th and 75th percentiles for thick line and whiskers marking +/–2.7σ or 99.3% coverage if the data are normally distributed. Outliers marked as single points. The plot is for all subjects in Experiment 1 on test days 1, 3 and 5 of BFB training (training also occurred on days 2 & 4). In each test group C3 SMR, SHAM, C3 Beta and C4 SMR we tabulated the scores of "standard" atoms (Figure 4) alpha1, beta 1, beta 2 and theta and SMR. The boxplot shows no evidence whatsoever of a training-related change in any atom score as a function of training. The atom scores were averaged across all conditions (EO, EC, LANT and BFB, pre- and post).

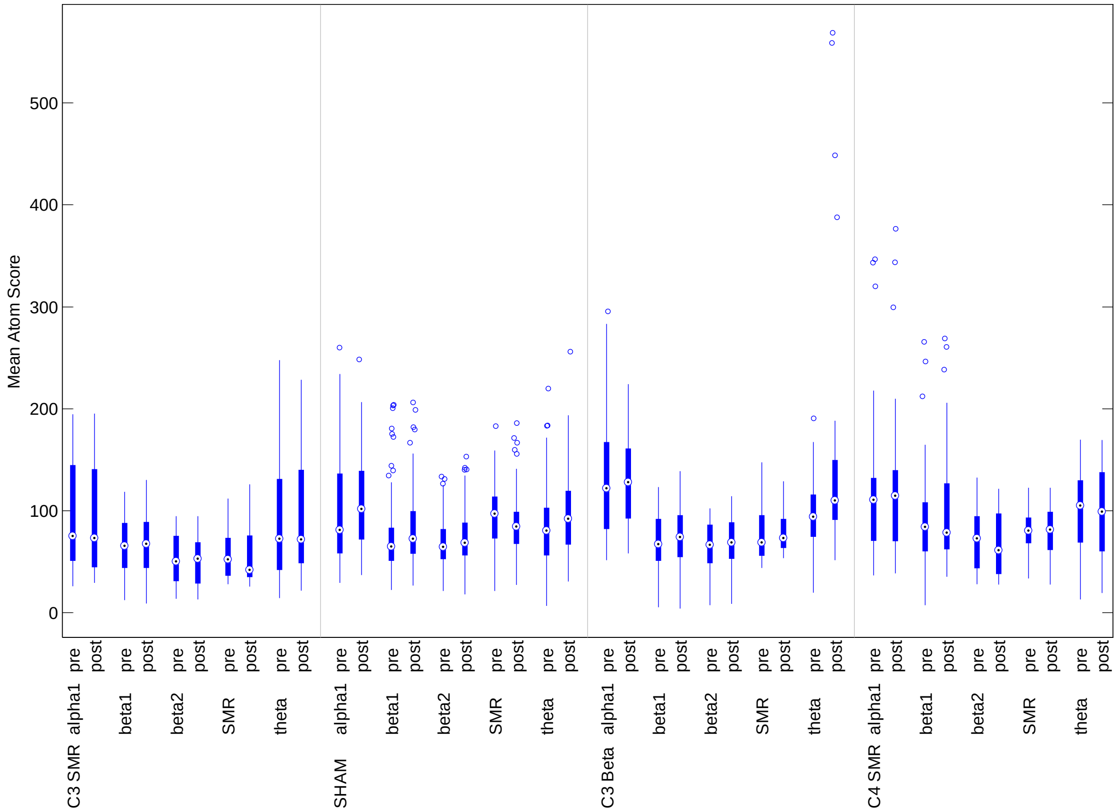

Figure 16. Boxplot showing atom-score median and dispersion metrics; 25th and 75th percentiles for thick line and whiskers marking +/–2.7σ or 99.3 coverage if the data are normally distributed. Outliers marked as single points. The plot is for all subjects in Experiment 1 on test days 1, 3 and 5 of BFB training (training also occurred on days 2 & 4). In each test group C3 SMR, SHAM, C3 Beta and C4 SMR we tabulated the scores of "standard" atoms (Figure 4) alpha1, beta 1, beta 2 and theta and SMR. The boxplot shows no evidence whatsoever of a training-related change in any atom score from pre- to post BFB training session . The atom scores were averaged across Days 1, 3 & 5 for the EO and EC conditions.

Experimental Analyses of EEG recorded during Biofeedback in Experiment 3

In addition to the analyses in the preceding section of Experimetn1, the UCLA team analyzed biofeedback related changes in LANT performance, EEG SMR atoms and ERP from Experiment 3. This experiment was focused on multiple sessions (up to 20) in a small number of subjects (n-4). Training used the SMR enhancement protocol pioneered by Barry Sterman. Additional training parameters included suppression of theta, high beta and EMG bands. Details of the methods and analyses appear in Appendix H.

These analyses led to the following conclusions:

1. SMR training has definite effects on the hemispheric networks of attention. However, training showed clinically significant (cumulative) effects on attention in only few cases.
2. We discovered two distinct types of SMR atoms operating in the context of SMR training. This is perhaps the most important discovery of our EEG biofeedback research thus far. SMR-3 is symmetric in both hemispheres whereas SMR-1 is strongly lateralized to a single hemisphere. The combination of SMR 1 and SMR 2 may allow for different

degrees of right hemispheric dominance and it provides a natural computational scheme for relating attention in the two hemispheres to each other during tasks such as the LANT.

3. The size and the change of sMR-1 with eyes open correlate with reduced scores in hemispheric attention networks and these changes always involve the right hemisphere to some extent (left hand, LVF, or both). By contrast, the size and the change of SMR-2 with eyes open correlates both positively and negatively with hemispheric attention networks. The atomic decomposition of the SMR atoms during eyes open seem to have “built-in” hemispheric selectivity following training, consistent with their localization.
4. There was a remarkable relationship between changes in the two SMR atoms during training and subsequent changes in hemispheric attention networks. In particular, we found that the relationship was stronger with the previous training session than with the one immediately preceding the administration of the LANT. Most dramatically, there were three correlations that were significant between hemispheric attention networks of the LANT and the following training session (Next). This suggests that the administration of the LANT primes the two SMR atoms and engages their training. This is particularly important because it “solves” one of the mysteries of EEG Biofeedback. Namely how does the brain “know” which behaviors to relate to changes in SMR.
5. Participant 004, trained at electrode C3, showed a selective ability to benefit from EEG biofeedback training using the C3-SMR protocol. There are three outstanding features in the resulting pattern of data.
    a. Participant 004 exhibited successful conditioning but the control participant who had training at C4 (006) did not.
    b. Conditioning successfully modified the alpha-2 and theta atoms, resulting in improved right hemisphere control of the conflict resolution.
    c. Remarkably, there was no evidence in any participant for the SMR atoms during performance of the LANT. It follows that modulating the SMR atoms during EEG-biofeedback resulted in changes in the alpha-2 and theta atoms, which were associated with the reduced conflict resolution in the right hemisphere. This most likely reflects changes introduced by EEG biofeedback training in the activation and connectivity of other atoms.
6. The results demonstrated that there are large individual differences in EEG-biofeedback training. Successful training can result in changes in atoms other than the ones targeted by the training protocol and centered in locations other than the training electrode. During the SMR protocol, Participant 004 showed evidence for simultaneous changes in two separate SMR atoms whose net effect is a systematic increase in right hemisphere SMR via suppression of the left hemisphere SMR. We call this pattern the “contralateral training effect” and it can serve as a model for recovery of function. Following focal damage to one hemisphere by activating homologous regions in the contralateral hemisphere.
7. ERP analyese of the LNAT trials from Partiicapnbt 004 were performed to validate expected interhemisphereic transfer effects expected in the LANT. The analyses focused on three components, P100, N160 and P360. Analyses of peaks and latencies showed a significant asymmetry in the transfer of visual information from left to right and then from right to left. The data support the general conclusion that the LANT paradigm in participant 004 is valid and yields evidence for systematic changes in performance, associated with a specific time period during trial performance.

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Appendix A

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Measuring attention in the hemispheres: The speeded Lateralized Attention Network Test (sLANT)

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Author Note

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Abstract

The Lateralized Attention Network Test (LANT) is a brief test that evaluates independent networks of attention within each hemisphere. We constructed a speeded version of the LANT to optimize use in an Event Related Potential (ERP) paradigm. We evaluated the ability of this new test to behaviorally measure LANT attention networks as well as identify corresponding physiological characteristics of these networks. Speeded trial presentation and increased numbers of trials improved sensitivity of

behavioral accuracy measures versus the LANT documented in Greene, et al, 2008. The speeded-LANT (sLANT) validly measured executive Conflict and spatial Orienting in behavior, although omitted an estimate of Alerting in favor of increased trial count. ERP components of N1, P2, and P3 correlated with behavioral latency and accuracy of Conflict and Orienting networks; differences between ERP components distinguished networks. The scalp distribution of these ERP components lends weight to existing theories of hemispheric and modular attention networks.

Introduction

Hemispheric Specialization of Attention and its Assessment

Existing research suggests that aspects of selective attention are lateralized and that hemispheric specialization may be observed for both covert orienting of spatial attention and executive response conflict. Evidence comes from both behavioral and physiological research in typical and clinical populations (Posner & Petersen,1990). Behavioral findings suggest that each hemisphere has it's own independent attention system and that each hemisphere may differ in component networks (Zaidel,1995). In contrast, physiological results often emphasize exclusive specialization of one hemisphere for specific components of attention, as seen in hemifield neglect. There is also abundant evidence of an anterior/posterior division of attention resources, suggesting parietal cortex is involved in orienting while frontal areas are involved in executive attention. For example, violations of expectation created by conflicts in information processing (Botvinick, Braver, Barch, & Cohen, 2001) are attributed to anterior cingulate cortex and dorsal frontal areas (Fan, McCandliss, Fossella, Flombaum., & Posner, 2005). The right hemisphere may also have a dominant role in orienting attention to locations in space, especially parietal areas (Corbetta & Schulman. 2002). Lateralized attention models suggest each hemisphere is biased towards contralateral space (Spencer & Banich, 2005) although the right hemisphere has greater competence to attend to ipsilateral space (but see Zaidel, Clarke, & Suyenobu, 1990; Zaidel, & Iacoboni, 2003). The right hemisphere may also serve additional attention control and salience tuning functions (Corbeta & Schulman, 2002). This suggests that components of attention are separable along both anterior/posterior and left/right divisions of the cortex, although shared resource models are not ruled out. For this paper we will consider Posner's model of selective attention, including three component networks, namely executive Conflict, spatial Orienting, and Alerting to a stimulus. To measure these constructs Posner combined an Eriksen Flanker Task (Eriksen & Eriksen, 1974) with the Posner paradigm for measuring covert Orienting of spatial attention in a computerized test called the Attention Network Test (Fan & Posner, 2004). The Eriksen flanker task produces response Conflict between targets and incongruent distractors (flankers). Cues are used to estimate both Orienting and Alerting. Orienting is provided by a spatial cue preceding each target while Alerting is estimated by non-spatial cues.

Zaidel developed a variation of the ANT labeled the Lateralized Attention Network Task (LANT; Greene, Barnea, Herzberg, Rassis, Neta, Raz, and Zaidel, 2008). The LANT presents cues and subsequent targets with flanking distractors, with a force choice identification of the target direction. Target and simultaneous flankers are flashed to one visual field using tachistoscopic presentation. Presenting test stimuli to one hemifield and examining responses made with the ipsilateral hand enables the LANT to estimate Conflict, Orienting, and Alerting in each hemisphere separately. Adding cross-hemifield cue-target sequences enable separating out Orienting Cost from spatial Orienting, as a resource cost from attending to invalid cues; examining trials for the response hand contralateral to target visual field may also distinguish interhemispheric from intrahemispheric resources.

Cue and Flanker effects are present in the ANT and LANT. Targets with congruent flankers produce faster and more accurate responses than those with incongruent flankers (executive Conflict). Predictive validity of spatial cues facilitates performance (Orienting effect). Cued targets are also faster and more accurate than targets without a cue (Alerting effect). The LANT adds a neutral spatial cue (center or bilateral cue) to the spatially valid or invalid cue presentation. Invalid cues facilitate covert attention to the visual field where a subsequent target will not occur. Performance differences across valid cues versus invalid cues compared to neutrally cued trials refine Orienting into components of Orienting Benefit and Orienting Cost. Several studies have used variations of the ANT or LANT to measure attention networks. Greene, et al (2008) compared the ANT and LANT and demonstrated that the LANT provides valid and reliable measures of attention networks which are similar to networks as measured by the ANT. Reaction time measures were found to be more sensitive in the LANT, with behavioral accuracy apparently near ceiling.

ERP Correlates of Attention Networks

While performance on the LANT is well characterized, ERPs are not, but may be critical for validating hemispheric results observed in the behavior. Existing theories of attention physiology also often suggest anterior resources provide executive function and posterior source serve sensory function. This division is supported by ERP scalp amplitude differences (Fan, Byrne, Worden, Guise, McCandliss, Fossella, & Posner, 2007) and supports our theory of prefrontal control of inhibitory processes serving Conflict versus posterior sensory and visual cortices acting to Orient visual attention. The degree to which attention can modify the corresponding ERP components is also a relevant question. Combing fMRI and EEG, Di Russo, Martinez, and Hillyard, (2003) showed that early components (50-90 ms) evoked in the visual cortex are unaffected by attention, although subsequent components (150-225 ms) in the same calcarine sources are moduled by attention. The early evoked components are interpreted as representing spatial effects of early selective attention (Luck, Woodman, Vogel, 2000). Later component modulation may be interpreted as salience sensitization by attention via input from non-striate occipital and parietal cortex. Visuospatial attention networks may thus be divided into detection of target occurrence followed by spatial orienting of attention to the target.

Evidence from concurrent fMRI and EEG suggest that a P3 component in this later time range indexes both the activation of a ventral attention network at target onset as well as sustained activation of the dorsal attention network (Mantini, Corbetta, Perrucci, Romani, and Del Gratta, C., 2009) interpreted as "Orienting" here.

Both N1 and P3 components (occurring > 100 ms) are sensitive to attention processes, as shown in recent study by Neuhaus, Urbanek, Opgen-Rhein, Hahn, Ta, Koehler, Gross, and Dettling, M, (2010) using a version of the ANT. Neuhaus demonstrated a parietal N1 that responds with increased negative amplitude for spatially relevant versus spatially neutral cues. Other authors suggest this N1 may be modified by selective attention (Luck et al, 2000), or bottom up processes. This may suggest an early stage of sensory processing is driven by the spatial cue and not as an effect of cognitive stimulus evaluation. Other researchers have shown increased amplitude for early negative ERP components are produced by flanker incongruity (Van Veen, & Carter, 2002) and have tied its activation to anterior cingulate sources. Again, this suggests a frontal scalp source for executive attention network activity.

In contrast to the N1/P2, the later N2 and P3 components are often interpreted as indexing cognitive evaluation of a stimulus (Luck, et al, 2005) and may be sensitive to stimulus salience changes. It is clear that these components are related to attention, although some theories suggest the attention resources indexed by these two ERP features are separable. Using a combined flanker and go-no/go task, Enriquez-Geppert, Konrad, Pantev, and Huster, (2010) illustrated an N2 mainly affected by executive response conflict while a P3 amplitude showed the effects of motor inhibition. Neuhaus (2010) also suggests that parietal P3 amplitude (~ 500 ms) is reduced for incongruent versus congruent targets (Conflict), and showed a slightly later frontal P3 (~ 400 ms) exhibiting increased amplitudes to incongruent targets. Rueda, Posner, and Rothbart, (2005) have also shown an increased P3 (~ 400 ms) amplitude to incongruent flankers. They identified an anterior distribution for this component in adults but a more diffuse anterior/posterior distribution in children. Given maturational lag of prefrontal areas in children, this also supports an anterior network of executive attention. Other studies investigating the effect of incompatible or incongruent flankers on the P3 have found increased amplitudes at both Fz and Pz electrodes in adults (Wild-wall, et al, 2008) or just Pz (Kopp, et al, 1996). Kopp also shows increased N2 amplitude with incongruent flankers.

This paper explores the relationship between behavior and evoked EEG of attention networks. Specifically, we will demonstrate the first systematic study of behavioral and ERP components of LANT attention networks, including Conflict, Orienting Benefit, and Orienting Cost.

Methods

Participants

40 right-handed UCLA undergraduates (17 men, 23 women, M = 22.65, SD 2.6, age 18-30) were recruited from the UCLA undergraduate population, for behavioral testing with EEG monitoring. Participants were selected to be strongly right handed using a modified version of the Edinburgh Handedness Questionnaire, (Oldfield, 1971) with a cutoff score of 12 out of 14. Exclusion criteria included any

current use of psychiatric medication, any history of learning disability or attention deficit, any psychiatric or neurological history, non-corrected vision, or lack of native English fluency, evaluated by self-report. Testing sessions lasted one hour, and participants were compensated $25 for their time. Three participants were excluded for chance behavioral performance and one from an EEG data recording error.

Behavioral task: evaluating hemispheric attention networks

Participants were given a new lateralized test of attention. A speeded version of the Lateralized Attention Network Task was developed to evaluate networks of attention in each hemisphere. Continuous EEG recording was performed during the task, and speeded-LANT (sLANT) event-locked ERPs were created to evaluate time and frequency evoked changes to task events and behavior.

sLANT: A "speeded" Lateralized Attention Network Test

The LANT (Greene et al, 2008; Hill, Barnea, Herzberg, Rassis-Ariel, Rotem, Meltzer, & Zaidel, 2008) measures covert orienting of spatial attention and provides a measure of Orienting Benefit due to a valid spatial cue and a measure of Orienting Cost due to a spatially invalid cue, both relative to a neutral (center) cue. The LANT also evaluates response Conflict using a lateralized flanker task. Conflict and Orienting are measured by manipulation of Flanker Congruity, Target Visual Field, and Cue Validity. Targets are presented with either congruent or incongruent flankers; cues predict target visual field validly, invalidly, or not at all (center cues). By subtracting reaction time and accuracy difference for averaged trials of Incongruent versus Congruent targets, we cacluate Conflict. Orienting Cost subtracts trials with Invalid Cue and Center Cue; Orienting Benefit is the difference between trials with Center Cue and Valid Cue. We developed a version of the LANT with faster timing than Greene, et al, and also eliminated neutral flankers and double (both visual field) cues. The sLANT also discards the "no cue" condition, eliminating the Alerting measure. The first reason for these modifications was to optimize the LANT for ERP data; an ERP study requires many trials of the same behavior type. The LANT presented by Greene, et al., 2008 only has 16 trials of each of 24 unique trial types (Visual Field (2) x Flanker (3) x Cue (4)). In a pilot ERP study being written up separately, the authors of this paper and Greene ran an ERP pilot study on a LANT without neutral flankers.That modification produced enough (~ 96) trials for each LANT variable level combination, but required almost an hour of testing time (10 five minute blocks plus self-paced breaks) and introduced fatigue and EEG quality issues.

sLANT Design

Our goals with the sLANT included shorter administration time, increased test effort, and increased trial count for each unique stimulus combination. Eliminating Alerting allowed us to increase Orienting and Conflict component trials, and changed the LANT factorial design from 3 (Flanker congruency: congruent, neutral, incongruent) x 2 (Target Visual Field: left, right) x 4 (Cue validity: none: center, double, valid) as in Greene to a new sLANT factor design of

2 (Flanker congruency: congruent, incongruent) x 2 (Target Visual Field: left, right) x 3 (Cue validity: none, valid, invalid). Also, the LANT has shown accuracy rates above 90% (Greene, et, al, 2008); often much higher (Eran Zaidel, personal communication). To increase sensitivity in the accuracy domain, the sLANT decreased trial time and added variability to make stimuli less predictable and increase test difficulty. LANT trials used an 850 ms SOA between Cue and Target; the sLANT implements a 350 ms SOA Cue to Target. The LANT also uses 1000 ms padding per trial after response while the sLANT implemented padding of 1000 ms minus reaction time, which adds variability to the inter-trial interval. This approach also produced faster next trial onset after a slow response, effectively speeding or "rushing" the participant. A central feature of the LANT is the vertical, lateralized target/flanker arrow set. The sLANT retained these stimuli as well as the LANT presentation eccentricity of 2 degrees for cue and target stimuli.

- Insert Figure 1 about here –

Measures: Data acquisition and signal processing

EEG & sLANT recording: Dense array EEG was recorded using a BioSemi / ActiveTwo system (64-channel QuickCap plus ear electrodes), with cap CMS-DRL for active reference and ground. Digital codes for sLANT unique trial type were sent from E-Prime computer to BioSemi computer via parallel cable. Trial codes were embedded in the EEG record at target+flanker stimulus onset.

EEG preprocessing: Before analysis, the 66-channel data set was visually inspected to remove EMG artifact and excessive noise. A small number of bad electrodes were removed and interpolated. EEG was filtered to remove frequencies below 0.16 Hz and above 50 Hz, and referenced to averaged ears ((A1+A2)/2) for analysis.

ERP Analysis: Three-second epochs were constructed from the continuous EEG, +/-1500 ms to each sLANT target event. Each unique trial type was averaged in the frequency domain to produced ERPs and averaged in the time domain to produce Event Related Spectral Perturbation (ERSP), or event related frequency changes. A pre-target baseline of −500 to −400 ms was used for ERP epochs to avoid contamination of target locked ERPs with cue-evoked activity before target onset. Within-participant ERP component peak latency and peak amplitude were measured for waveform regions that varied by sLANT stimulus type across the trial interval. N1, P2, and P3 components were measured at 150, 250, and 550 ms respectively. A time window for 100 ms was used around the center of the N1 and P2 waveforms. The P3 component was measured across a 500 ms window from 300-800 ms after target onset.

Combination of ERP and Behavior: The ERP component measurements and sLANT behavioral measures to Cue and Target effects were subjected to separate ANOVAs. In addition, we performed a Pearson correlation between ERP measures and behavioral performance on different sLANT stimuli types (N = 37; 36 df). Given the large number of correlations possible across ERP components and sLANT stimuli, we restricted our analysis to correlation between electrophysiology and behavioral measures for identical sLANT trial types.

Estimating scalp EEG measures of sLANT: On finding significant but similar ERP components for all sLANT variables, we created subtraction waves to mimic the sLANT construct of Orienting Benefit, Orienting Cost, and Conflict. Testing individual participant data using repeated measures ANOVAs on combinations of ERP and behavioral data (post hoc) may increase Type I errors. Adding additional electrodes to a general linear model would also increase the risk of Type 1 error by adding multiple comparisons. We implemented an alternative method for ERP statistical analysis that considers scalp distribution, as implemented by David Groppe's "Mass Univariate Toolbox" for EEG (Groppe, Urbach, & Kutas, 2011). To determine if significant differences in scalp distribution existed between ERPs for these sLANT measures, the following difference waves were created: Conflict waves were created from valid- flankers minus invalid-flanker, Orienting Cost was produced for center-cues minus invalid-cues, and Orienting Benefit was produced for center-cues minus valid-cues. N.B. We subtracted from center or valid for all of these waves to enable visual comparison. The ERPs from these sLANT analogs were submitted to a repeated measures, two-tailed permutation test based on the tmax statistic (Blair & Karniski, 1993) using a family-wise alpha level of 0.05. Identical time windows were used for the subtraction waves as the trial averaged ERPs although the sign often changes in the subtraction. For all sLANT measures, windows of 100-200 ms, 200-300 ms and 300−800 ms were used. All time points for the time window at 64 scalp electrodes were included in the test (i.e., 3328 total comparisons for N1 or P2 component, and 16448 total comparisons for the P3). 2500 random within-participant permutations of the data were used to estimate the distribution of the null hypothesis (that there is a real difference between conditions used to produce the difference wave). This permutation analysis was used to supplement our earlier ANOVA-based findings because it provides better spatial and temporal resolution than conventional ANOVAs when used to across multiple electrodes, while maintaining a desired family-wise alpha level. The tmax statistic we used here has also been shown to have relatively good power for data whose dimensions are highly correlated (Hemmelmann, Horn, Reiterer, Schack, Susse, & Weiss, 2004). The highly correlated of points along an ERP waveform suggest that tmax may be a more appropriate measure than an ANOVA, as ERP component measurements data will violate the strict independence requirement of the GLM. To ensure this measure was stringent we chose 2500 permutations to estimate the distribution of the null hypothesis; this is over twice the number recommend by Manly (1997). Based on these tmax estimates, critical t-scores of +/- 3.94 (df=35) were derived for N1 and P2, which corresponds to a test-wise alpha level of 0.000371. For the P3 component critical t-scores were determined at +/- 4.17, corresponding to a test-wise alpha level of 000193. Therefore any differences that exceeded the relevant t-score were deemed reliable.

Apparatus & Testing Procedure

Participants were seated in front of a computer. A BioSemi / ActiveTwo system was applied to the participants head, and 66-channel EEG was recorded using (64-channel QuickCap using CMS/DRL reference, plus ear electrodes). Several minutes of resting baseline EEG was recorded and then instructions for the sLANT were given. General instructions emphasized both speed and accuracy, as well as maintaining visual fixation on a crosshair in the center of the screen. The main task instruction was to report the direction of a middle arrow in lateralized vertical line of 5 arrows. sLANT stimuli were presented via E-Prime on a PC with a 2.1 GHz CPU, running Windows XP. Stimuli were presented at 57 cm from participant on a 17” LCD monitor with a refresh rate of 70 Hz and a resolution of 1280 * 1024 pixels. Participants performed 4 blocks of the sLANT, with 156 trials per block. A total of 624 trials were presented in a random order within blocks that alternated by response hand, counterbalanced among participants. Unimanual responses were gathered using a serial mouse held at 180 degrees by the non-responding hand. This allowed consistency of the responding hand to indicate ‘‘up’’ with the index finger and ‘‘down’’ with the middle finger, regardless of hand used. Trials and thus blocks were of variable length; Blocks ranged from 4-6 minutes based on reaction time differences. The sLANT provided self-timed breaks between blocks, which participants often limited to a few seconds.

Before analysis, sLANT trials with reaction times less than 100 ms or greater than 800 ms were discarded, removing 2.5% percent of trials. The remaining trials had a mean reaction time of 326 ms (median 305, SD 121). Three participants were excluded for accuracy below

60%. One subject was excluded due to a loss of behavioral session data. Mean accuracy for the reduced N = 36 was 0.74.

Results

Behavioral Results

We carried out repeated measures ANOVAs on data for 36 participants. The design was a 2 Target Visual Field (TVF: Left, Right), x 3 Cue Validity (Center, Valid, Invalid), x 2 Flanker Congruity (Congruent, Incongruent) ANOVA. We ran separate ANOVAs for behavioral reaction time and accuracy. In these results we will ignore the significant interactions between Flanker and Cue, due to the theoretical complexity of this second order interaction. Examining accuracy, we show main effects of TVF, of Cue Validity, and of Flanker Congruity, as a significant interaction of Target Visual Field with Flanker. Tables 1 and 2 summarize the significant sLANT variables that show up for reaction time and accuracy.

- Insert Table 1 & Table 2 about here -

Laterality of accuracy performance suggests left visual field targets (*M* = 0.759) were responded to significantly more accurately than right visual field targets (M=0.739, F = 7.663, p = 0.009). Performance to Center cues (*M* = 0.739) was significantly more accurate than to Invalid cues (*M* = .718, F = 6.411, p = 0.016), and performance for Center cues was also significantly less accurate than for Valid cues (*M* = .774, F = 21.874, p < 0.001). Congruent Flankers produced more accurate (*M* = 0.870) performance than incongruent flankers (*M* = 0.618, F = 296.232, p <0.001). Furthermore, Target Visual Field (TVF) and Flanker interactions highlighted a larger difference between Congruent and Incongruent flankers in the right visual field (*M* =

.281, F = 87.189, p <.001) than in the left visual field (*M* = .215 ms, F = 79.596, p < 0.001).

Latency performance failed to show a main effect of TVF (F = 0.039, p = 0.845) although did show main effects of both Flanker and Cue. Congruent flankers produced significantly faster responses (*M* = 315 ms) than incongruent flankers (*M* = 359 ms, F = 113.452, p < 0.001). Performance to Center cues was significantly different than performance to Invalid and Valid cues; Center cues produced significantly faster responses (M = 367.25 ms) than did Invalid cues (M = 375.19 ms, F = 8.809, p = 0.005) and significantly slower responses than Valid cues (M = 367.25 ms, F = 14.604, p = .001).

Electrophysiological Results

Continuous EEG gathered during sLANT administration was used to produce Event Related Potentials from epochs time locked to the sLANT target onset. We chose an averaged- ears ((A1+A2)/2) reference to minimize any hemispheric effect of reference while preserving ERP amplitudes at vertex electrodes. The resulting ERPs demonstrate posterior amplitude changes at electrodes including P3, Pz, & P4 in the first 300 ms after the target. An N1/P2 complex was elicited at these parietal sites by the target stimuli and modified by the cue type. Frontal electrodes, including FP1, FP2, and Fz, showed the largest amplitude changes with a later P300 post-target component that lasted from about 300 to 800 ms.

Changes in this posterior P300 tended to vary by Flanker. Given these observations, electrodes of Fz and Pz were chosen as representative of test-evoked activity for measurement and statistical testing. Central electrodes of C3, C4, and Cz were also analyzed to validate visual field effects of Cue and Target. For these 5 electrodes we considered ERP components of N1, P2, and P3 as described in the Methods section. Figure 2 shows the evoked waveforms for Cue and Flanker as they vary around the Fz electrode. ERP components have similar timing at all electrode sites, although patterns of laterality and anterior / posterior differences in ERP components can be observed.

- Insert Figure 2 about here -

When considering all 64 electrodes, the ERP components evoked by both cues and targets show a clear lateralized pattern of scalp distribution. Even cursory inspection shows that ERP components are evoked contralateral to the visual field of sLANT stimuli. Examining instantaneous amplitudes near the middle of the N1, P2, and P3 time windows (150 ms, 250 ms, and 550 ms respectively) we can observe a similar pattern in the scalp distribution across Cue Validity and Flanker Congruity for N1 (Figure 3), P2 (Figure 4), and P3 (Figure 5)

- Inset Figure 3, 4, 5 about here -

The above figures show that N1 and P2 components are more strongly lateralized than the P3 component. Considering only the N1/P2, we see the N1 has a more anterior/posterior scalp distribution (showing a largely central anterior negativity) while the P2 shows more strongly lateralized activation of temporal and posterior scalp sources. Aside from these gross laterality effects driven by visual field of stimuli, scalp distribution of evoked patterns appear to be largely similar across cues and targets.

When examining ERPs at specific electrodes, Target evoked components appear at most electrodes, visible in waveform and scalp distribution above as an N1, P1, N2, and P3. Each evoked component was measured as the dependent variable for a 2x3x2 ANOVA with the same design as above (TVF x Flanker x Cue). The N2 component largely echoed the significant effects of the P3 component, so only the N1, P2, and P3 components was considered. Measurements included peak amplitude, peak latency, and mean amplitude. Mean amplitudes were found to be redundant with peak amplitudes, so only peak latency and peak amplitude was considered. In addition, components in the cue to target interval will not be discussed here, although did include a main effect of Cue (P1 amplitude: $F = 8.76$, $p = .044$) and an interaction of TVF x Cue (P1 mean area: $F = 8.76$, $p = .016$; P1 amplitude: $F = 7.90$, $p = .001$). These visual field and cue validity effects on early ERP components are unsurprising and suggest early automatic processes.

The ERP components that interact with attention at time of target bear more scrutiny, and significant post-target ERP components were found at all electrodes examined. Peak latency was more often significant than peak amplitude, although this varied by electrode considered. Parietal (Pz) and left central (C3) electrodes showed the largest number of significant effects. Frontal (Fz), and right central (C4) electrodes also showed many significant peak latency effects, but fewer peak amplitude effects.

The sLANT showed patterns of significant test variable that diverged by electrode and ERP component. Target Visual Field was significant at all three ERP components at both peak amplitude and latency, although the test statistic was largest for P2 amplitudes (C3: $F = 59.10$, $p < 0.001$; C4: F 22.66, $p < 0.001$; Pz: $F =11.323$, $p = 0.002$). Cue validity only demonstrated significant effects on peak latency, and varied by electrode considered (C4 N1: $F = 3.62$, $p = 0.032$; Cz N1: $F = 3.21$, $p = 0.046$; Fz P3: $F = 3.24$, $p = 0.045$; Pz N1: $F = 5.66$, $p = 0.005$; Pz P2: $F = 7.26$, $p < 0.001$). Flanker congruity had significant effects on both peak amplitude and peak latency at Pz (N1 amplitude: $F = 4.50$, $p = 0.041$; P2 amplitude: $F = 6.61$, $p = 0.002$; P3 latency: $F = 37.99$, $p < 0.001$). For the other electrodes around the vertex, Flanker congruity showed only peak latency effects on the P3 component (C3: $F = 18.84$, $p < 0.001$; C4: $F = 43.52$, $p < 0.001$; Cz: $F = 39.00$, $p < 0.001$; Fz: $F = 30.12$, $p < 0.001$). Interactions of sLANT variables also showed significant effects on peak amplitude and latency. TVF * Cue validity interactions on peak amplitude were found at C3 (N1: $F=5.91$, $p = 0.004$; P3: $F = 4.11$, $p = 0.021$), Fz (N1: $F = 3.25$, $p = 0.045$; P3: $F = 4.88$, $p = 0.01$), and Pz (N1: $F = 3.29$, $p = 0.043$). TVF * Cue also showed significant peak latency of the P3 component at C3 ($F = 5.15$, $p = 0.008$) and C4 ($F = 4.2$, $p = 0.019$). TVF * Flanker interactions showed significant effects on N1 peak latency at C3 ($F = 9.28$, $p = 0.004$), C4 ($F = 14.59$, $p < 0.001$), and Pz ($F = 9.94$, $p = 0.003$).

ERP validity & scalp distribution of Orienting Benefit, Orienting Cost, Conflict

Instead of examining unique variable combinations (trial types), the sLANT provides for creation of difference measures to evaluate Conflict, Orienting Benefit, and Orienting Cost. As described in the Methods, the Mass Univariate Toolbox for EEG (Groppe, Urbach, & Kutas, 2011) was used to examine the first positive peak in the sLANT subtraction based components during the 300 – 800 ms post-target interval. Figure 6 shows the difference waves for Conflict and Orienting Cost in each TVF. Orienting Benefit was just below significant for the 300 – 800 ms time region. Conflict and Orienting Cost showed significant changes in the difference waveforms however, e.g. Conflict demonstrated a P3 (peaking ~ 440 ms) distributed parietally and contralaterally to the TVF as well as a later negativity (~ 700 ms) that was broadly significant across central and parietal electrodes. Orienting Cost showed significant differences in the Cue to Target interval (~ 180 ms, not labeled) as well an early P3 (~ 280 ms) in parietal electrodes, contralateral to TVF (i.e. effect of the preceding Invalid Cue). Orienting Cost also evoked a later P3 (~ 440 ms) significant at posterior electrodes bilaterally or ipsilateral to the target.

- Insert Figure 6 about here -

Figure 6 shows a clear pattern of statistically significant ERPs and their spatial distribution to targets presented in each visual field. The upper panel for each sLANT measure contains the ERP waveform of an sLANT subtraction measure, grand averaged across all participants (N=36), with Target Visual Fields presented side by side. The corresponding lower plot demonstrates an output of the tmax test for that waveform. T-test plots that exceed the red dotted threshold indicate significant differences from the null hypothesis. Each scalp plot shows data corresponding to the waveform time point selected by the vertical black.

The subtraction waves for Conflict (P3) showed stronger anterior scalp amplitude differences but greater posterior statistical differences in flanker type, ipsilateral to Target Visual Field. There was also right parietal activity during Confllict, regardless of TVF. Orienting Benefit (P3) showed anterior scalp distribution and only a weak (non-significant) difference between valid and center cues. Orienting Cost showed frontal and central ERP distribution without strong laterality for invalid versus center cues, although a suggestion of greater contralateral activation than seen in Conflict. We observe from Figures 6 that the laterality of this P3 ERP component is separable across Conflict and Orienting Cost. Using similar methodology to examine subtraction regions for earlier components (not shown) also demonstrated the expected contralateral visual field effect of N1 and N2 evoked by cue.

Correlation of Electrophysiology with Behavior

With these well-behaved differences in trial level and subtraction measures of attention networks across both electrophysiology and behavioral results, we subjected the ERP components defined above to separate Pearson correlations with performance latency or performance accuracy. When only considering the correlations between behavior and physiology to the same sLANT trial, we found many strong correlations between latency and accuracy performance and both ERP peak amplitudes and latency. Given the large number of possible correlations (sLANT trial type (12) * Behavior DV (2) * ERP Component (3) by Component Measure (3)) we chose to only highlight correlations significant at $p > .01$, or a

Pearson R value > 0.42 for d.f. = 34. With this restriction, a clear pattern of Accuracy versus Latency emerged. Significant changes in N1 and P2 amplitude correlated with sLANT behavioral accuracy, while P3 component latency instead correlated with sLANT reaction times. Both visual fields showed this effect across flanker congruency and cue validity for all three ERP components, although N1 and P2 effects appeared at frontal and central sites while the P3 component demonstrated latency effects at both fronocentral and parieal electrodes. Given the large number of positive correlations between sLANT performance latency, accuracy, and

evoked N1, P2, & P3 components across all sLANT unique trial types, it would not be useful to list all correlations. The most statistically stringent of these correlations showed P2 ERPs correlating with sLANT Accuracy. For example accuracy to LVF Incongruent flankers with Center cues correlated with P2 amplitude at Fz (r = 0.543, p <.001) and to trials with Incongruent flankers and Valid cues with P2 amplitude at Cz (r = 0.512, p < .001). sLANT LVF reaction time measures correlated with P3 latency. Reaction time to LVF Incongruent flankers with Center cues correlated with P3 latency at C3, C4 (r = 0.529, 0.489; p < 001, .002) and reaction time to RVF Congruent flankers with Invalid cues correlated with P3 latency at Cz (r = 0.613, p < .001). At these values, the observed Pearson correlations indicate a strong positive relationship between the behavior and physiology of attention processes as measured by the sLANT. Significant positive correlations obtained between both peak amplitude and latencies, and different ERP components and electrode sites showed different patterns of behavioral sensitivity (reaction time versus accuracy). Before restricting to only the most significant correlations, we observed a large number of significant effects at Pz (not shown). When considering the more stringent p value, most remaining significant effects are observed at C3, Fz, and C4. This suggests a frontocentral executive component of attention networks is highlighted by this correlation. In contrast, as we saw in the scalp distributions of the Orienting and Conflict difference waves earlier, the significant differences between waveforms of sLANT “subtraction measure” constructs were largely parietal.

Discussion sLANT Validity

The sLANT introduced a modified LANT and demonstrated a valid measure of three networks of lateralized attention in each hemisphere. Behavioral findings were similar to what has been shown in prior work. Main effects for Conflict, Orienting Benefit, and Orienting Cost were found on our speeded version, with significant effects in both performance latency and performance accuracy. We also showed differences in hemispheric performance on test accuracy, demonstrating some right hemisphere superiority for these attention tasks. This is consistent with prior LANT and other flanker task research.

We chose to compress test timing from prior LANT iterations. This provided increased trial numbers in a shorter time, although risked overlapping ERP components. Given the relatively short epoch (~ 1500 ms after a 100 ms baseline) and the quick succession of sLANT trials, interactions were indeed possible; this is one reason we restricted our analyses from 0 to 800 ms after target onset. With the main effects on N1 & N2 amplitude at Pz, and main effects on P3 at Pz and Fz for both peak amplitude and peak latency, it is clear that the sLANT can distinguish different trial and stimuli type by ERP component. The sLANT attention networks were reasonably tracked by changes in the evoked EEG. In addition, many sLANT trial types showed correlation between behavior and physiology that exceeded a Pearson correlation of 0.4 or 0.5. We also presented several significant interactions (Cue, Flanker) with Target Visual Field. These obtained for TVF * Flanker on performance accuracy; for EEG we showed an interaction of TVF * Cue in earlier ERP components (N1) at Pz and a later component (P3) at Fz. We chose not to discuss additional interactions of Cue * Flanker, although increased difficulty or loading of the test variables (e.g. Invalid Cue and Incongruent Flanker) may be demonstrated as additive Conflict/Cost effects; the ERP components for those trials were also strongly positively correlated with behavior (not shown). This suggests an interaction Conflict and Orienting Cost modules of attention, but requires further study.

sLANT versus LANT in measuring behavior

By removing non-cued trials we lose the LANT Alerting measure but retain cue-driven measures of Orienting Benefit and Orienting Cost. Reducing cue improved Orienting and Conflict, but eliminated a direct vigilance measure. The sLANT may not have measured Alerting well even if non-cued trials were retained; the fast-paced sLANT requires careful attending without stimulus-free intervals necessary to capture a decrease in vigilance. If vigilance measures are important, a Continuous Performance Test (CPT) may be used (Ricco, et al, 2002) alongside the sLANT. We took this approach and will report on a novel lateralized CPT in a separate paper.

Both LANT and sLANT show similar reaction time and accuracy effect on cue validity and flanker congruity. This sLANT data also showed a left visual field / right hemisphere advantage in overall accuracy. This right hemisphere advantage is usually found in other versions of the LANT as well as the ANT.

By establishing the validity of these three measures of Conflict, Orienting Benefit, and Orienting Cost, the sLANT shows a mean accuracy that is much lower than the LANT, and has more variability. The speeded nature of the sLANT may increase task difficulty, reducing accuracy from a possible “ceiling” as reported by Greene. The absolute measures of Conflict and Orienting are also reduced slightly. This appears to be an effect of shortening trial timing, and may be an effect of attention network interactions, simple task difficulty, or a scale effect based on forcing participants to consistently respond quickly.

The ERP Correlates of Lateralized Attention

This sLANT with full-head EEG recording is the first systematic study of a lateralized flanker task looking at combined behavioral and electrophysiological indexes of attention networks in each hemisphere. These measures provide a useful window into understanding stimulus-evoked attention resources, although illustrate a complex interaction of brain laterality and attention network distribution. As mentioned in the introduction, ERP literature often finds Conflict and Orienting in anterior and posterior sources respectively, and finds a right hemisphere bias for attention performance. Our results provide a pattern of significant ERP components suggesting stages of information processing and dissociable effects of Orienting and Conflict. The N1 and P2 responded to variations in VF of the Target as well as validity of the preceding Cue. The later P3 that occurred at both anterior and posterior sites is a more complex component. The effects summarized suggest that the P3 peak latency is more affected by Flanker, while TVF and Cue variation instead drive changes to peak and mean amplitudes of the P3. Given the larger amplitude of P3 and absence of earlier N1 (and N2) components at frontal sites, it is plausible that these parietal N1 amplitude changes correspond to the sLANT construct of Orienting. In contrast, the P3 may serve to index both Orienting (in amplitude changes) and Conflict (in peak latency changes). We intepret this as early Orienting resources being driven by parietal and occipital sources, while Conflict occurs slightly later (peri-response) and localizes to central and frontal electrodes. While we did not find a largely right-hemisphere network of attention, we did find asymmetrical EEG response in Conflict and Orienting Cost, as well as strong visual field effects of Cue and Flanker.

Behavioral Latency versus Accuracy and sLANT ERPs

The sLANT ERP components showed significant effects across all measurements, even when we eliminated duplicates that did not add to the picture (e.g. N2 was largely redundant with P3 measures; component mean amplitude was redundant with peak amplitude). Comparing different ERP components also illustrated different stages and aspects of attention processing. Speed or accuracy of behavior was also clearly related to the latency or amplitude of an ERP. As mentioned earlier, P3 amplitude is thought shows a relationship of cognition to behavior, changing with the either the speed or accuracy of a decision variable. In the sLANT, we saw both latency and accuracy effects on the P3 component (at both Pz and Fz). The behavioral and ERP correlations we demonstrated suggest that frontal (Fz) ERPs are largely driven by performance latency (RT) differences, while posterior (Pz) ERPs are driven by both reaction time and accuracy. We interpret these accuracy effects on the ERP as reflecting a decision process, while reaction time effects may have been due to ancillary sensorimotor resource constraints or a task-relevant decision process. As N1 and P2 effects on amplitude correlated with RT, we interpreted these early components as indexing something that is affecting the speed of a complex attention process. There may be some underlying process that shares resources with our attention networks (e.g. “Attention”) or this may have indicated changes in processing speed or sensory activation. For example, if a sensory or motor process is fast, this may also affect latency in later ERP components; this interpretation was supported by statistical effects on the N1 and P2 obtaining for later N2 and P3 components as well.

Scalp Distribution of Conflict, Orienting Cost, and Orienting Benefit

When exploring a tmax analysis of ERP difference waves in the sLANT, we observed distinct patterns in each sLANT component. Most of these patterns showed an anterior/posterior distribution of amplitude, but also laterality evoked by visual field of cue and target. It is interesting to note that Orienting Cost (which involves cueing the wrong visual field) has a *more* strongly lateralized effect than pure Orienting Benefit (which only cues one hemisphere). For example, an OC trial has an RVF cue followed by an LVF target. A similar OB trial has an

LVF cue preceding an LVF target. In both cases the LVF target activates the right hemisphere visual cortex, but in Orienting Cost the ERP is more strongly lateralized to this right hemisphere when the left hemisphere is first probed by the invalid spatial cue.

Summary & Initial Conclusions

The sLANT demonstrated valid measures of spatial Orienting Cost and Orienting Benefit and executive response Conflict in each hemisphere. It has shown distinct and unique patterns of ERP components that change with LANT variable types. The speeded trials of the sLANT successfully produced both behavioral and ERP changes to the task variable levels, and the behavioral accuracy captured by the sLANT appears more sensitive than the earlier LANT. The sLANT thus provides an increased ability to test models of hemispheric independence. We have confirmed discrete attention networks in each hemisphere, although the overall performance of attention networks in each hemisphere was somewhat the same.

The interaction of Cue * TVF suggested that Orienting Cost and Conflict share some resources. Aside from that interaction, the sLANT separately evaluated three networks of attention: two involved in spatial attention and one in executive attention. Thus, the sLANT may be useful in understanding attention from a research as well as clinical perspective and may be a powerful tool in assessment of complex hemispheric activity in normal and pathological brains. The data and interpretation presented above lends weight to the growing body of literature examining not only a right-hemisphere specialization for attention, but also the capacity of each hemisphere as well as interhemispheric function. We hope this introduction to the sLANT may prove useful to other researchers exploring the behavior and physiology of attention.

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Timeline of sLANT stimuli: Example shows a Valid Cue followed by a Congruent Target.

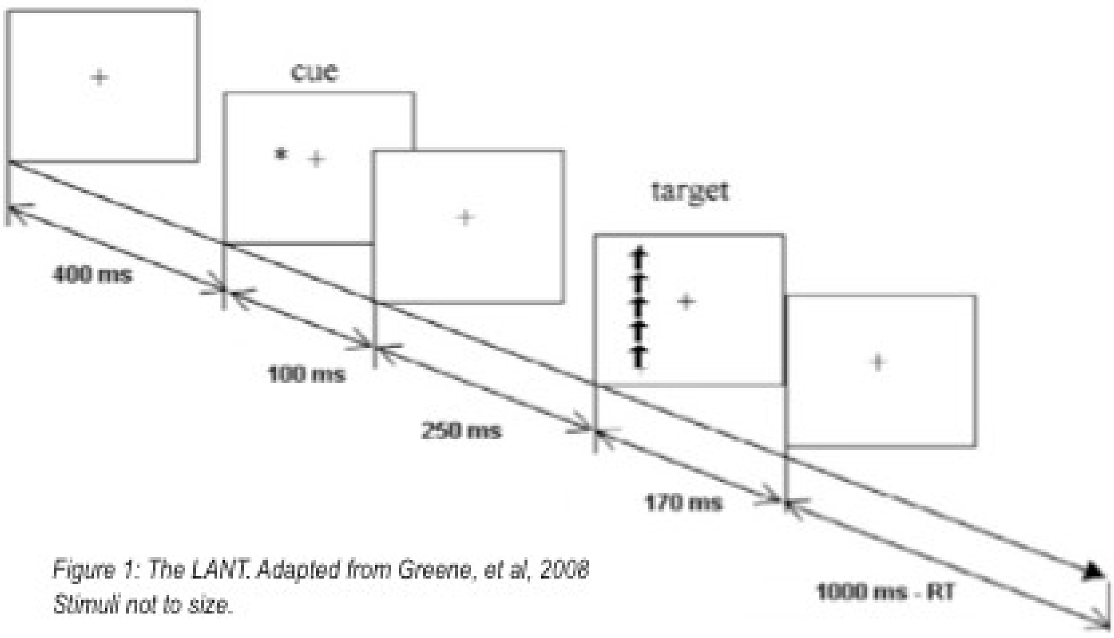


Figure 1: The LANT. Adapted from Greene, et al, 2008
Stimuli not to size.

Table 1: sLANT Performance: Reaction Time

sLANT 2x2x3 ANOVA (Reaction Time)		
Variable	F	P
Flanker	79.89	0.001
Cue	18.14	0.001
All results significant at p < 0.001		

Table 2: sLANT Performance: Accuracy

sLANT 2x2x3 ANOVA (Accuracy)		
Variable	F	P
Target Visual Field	7.66	0.009
Flanker	97.03	0.001
Cue	18.90	0.001
TVF * Flanker	7.32	0.01
TVF * Cue	7.48	0.001
All results significant at $p < 0.01$		

Figure 2: sLANT ERPs that vary by Cue Validity & Flanker Congruity

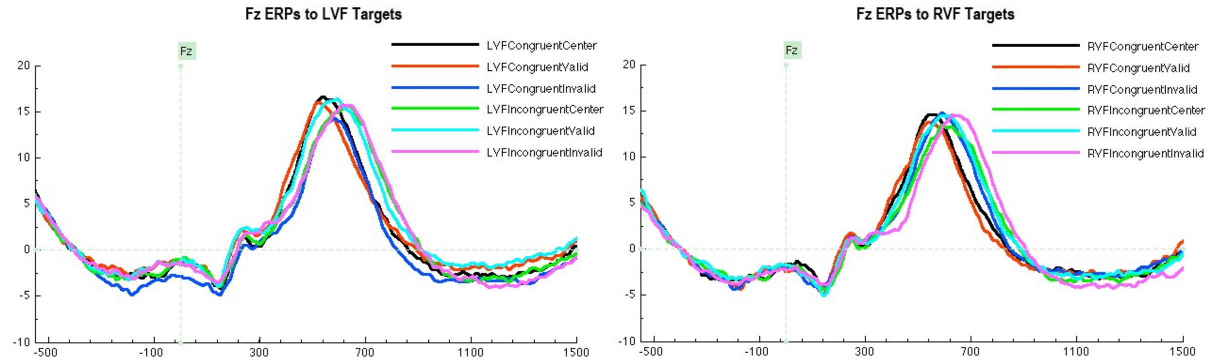


Figure 3: Scalp distribution of Nl ERP evoked by sLANT

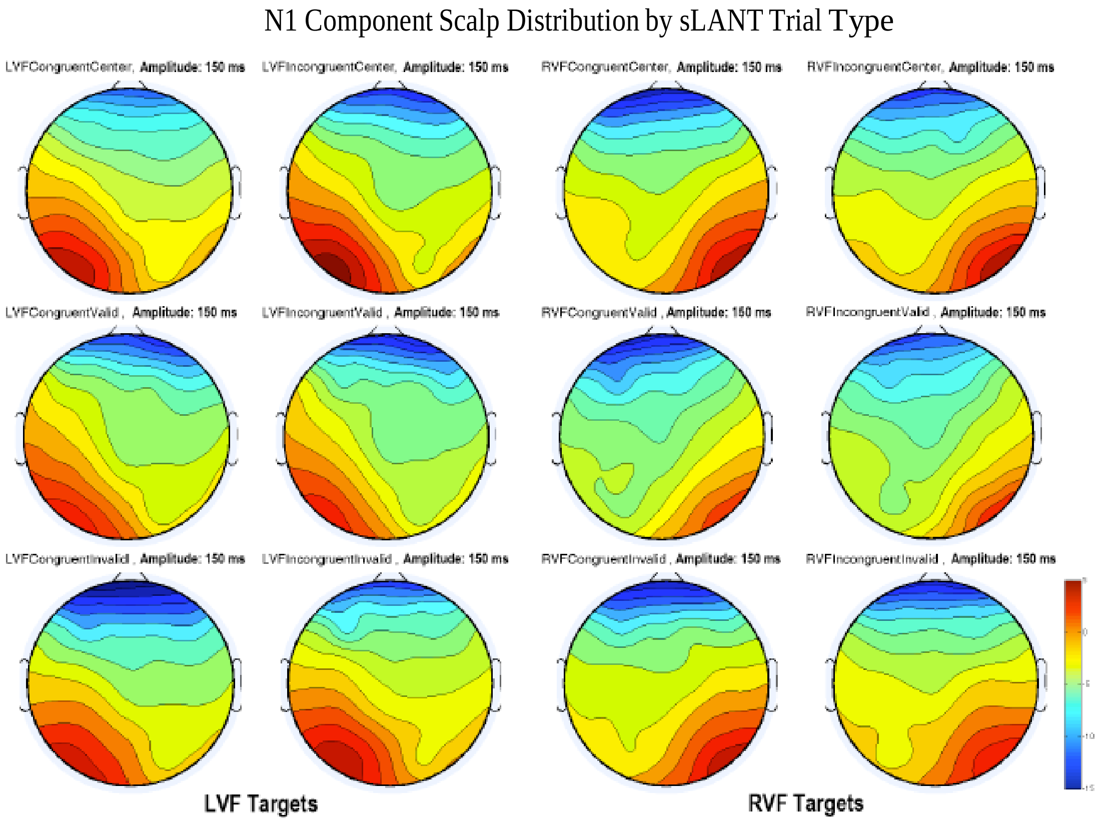


Figure 4: Scalp distribution of P2 ERP evoked by sLANT

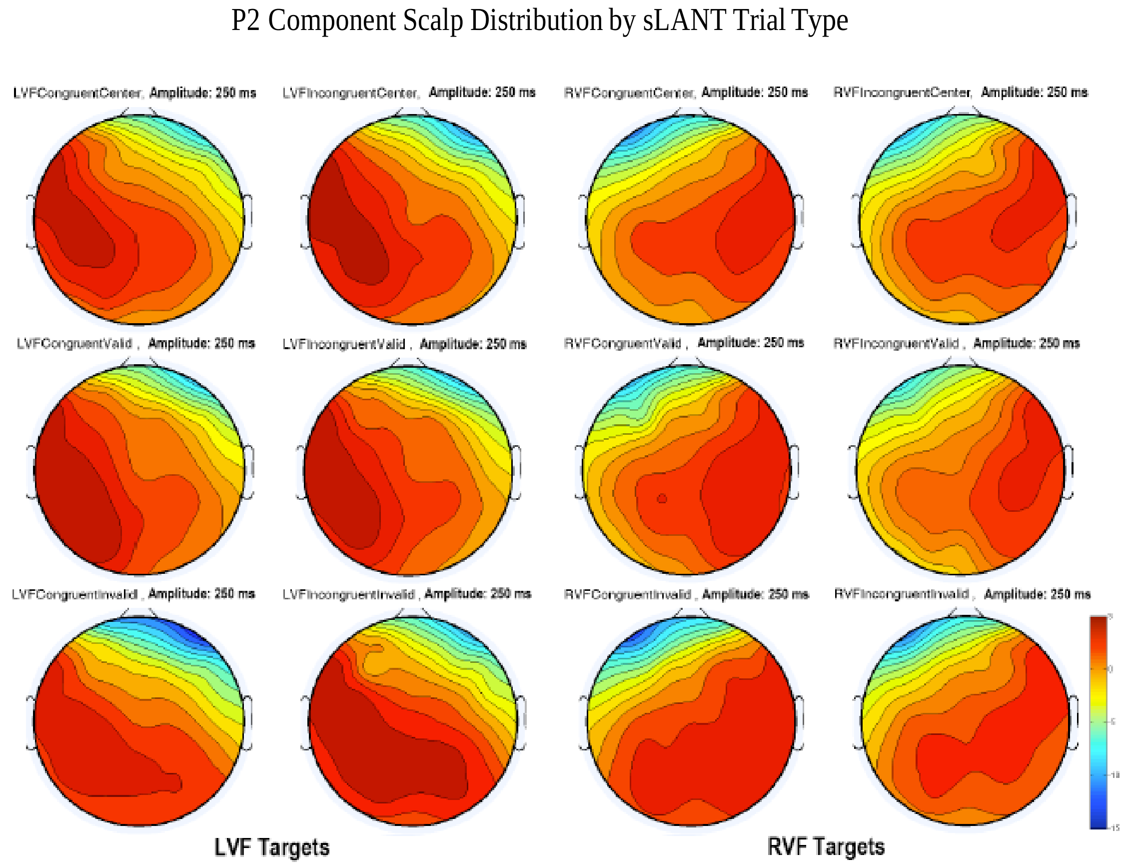
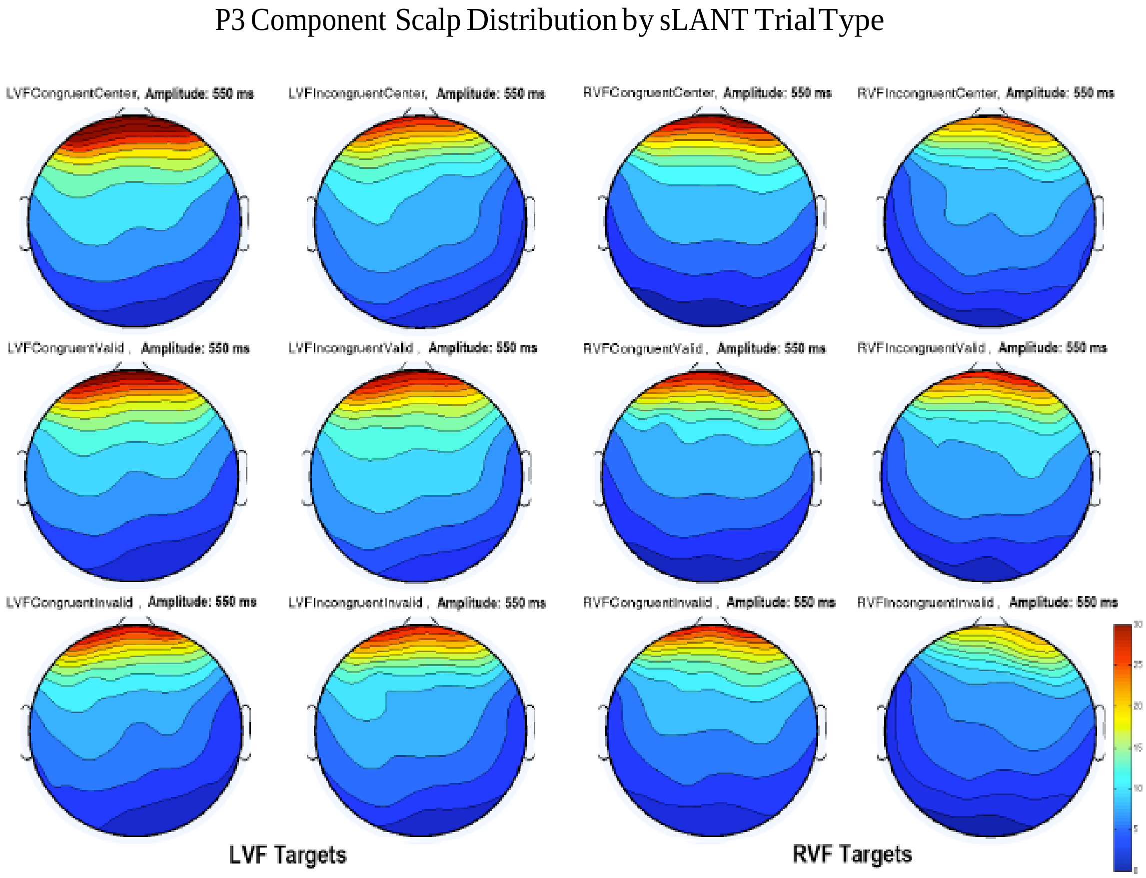


Figure 5: Scalp distribution of P3 ERP evoked by sLANT



P3 Component Scalp Distribution by sLANT Trial Type

LVFCongruentCenter, **Amplitude: 550 ms**

LVFIncongruentCenter, **Amplitude: 550 ms**

RVFCongruentCenter, **Amplitude: 550 ms**

RVFIncongruentCenter, **Amplitude: 550 ms**

LVFCongruentValid, **Amplitude: 550 ms**

LVFIncongruentValid, **Amplitude: 550 ms**

RVFCongruentValid, **Amplitude: 550 ms**

RVFIncongruentValid, **Amplitude: 550 ms**

LVFCongruentInvalid, **Amplitude: 550 ms**

LVFIncongruentInvalid, **Amplitude: 550 ms**

RVFCongruentInvalid, **Amplitude: 550 ms**

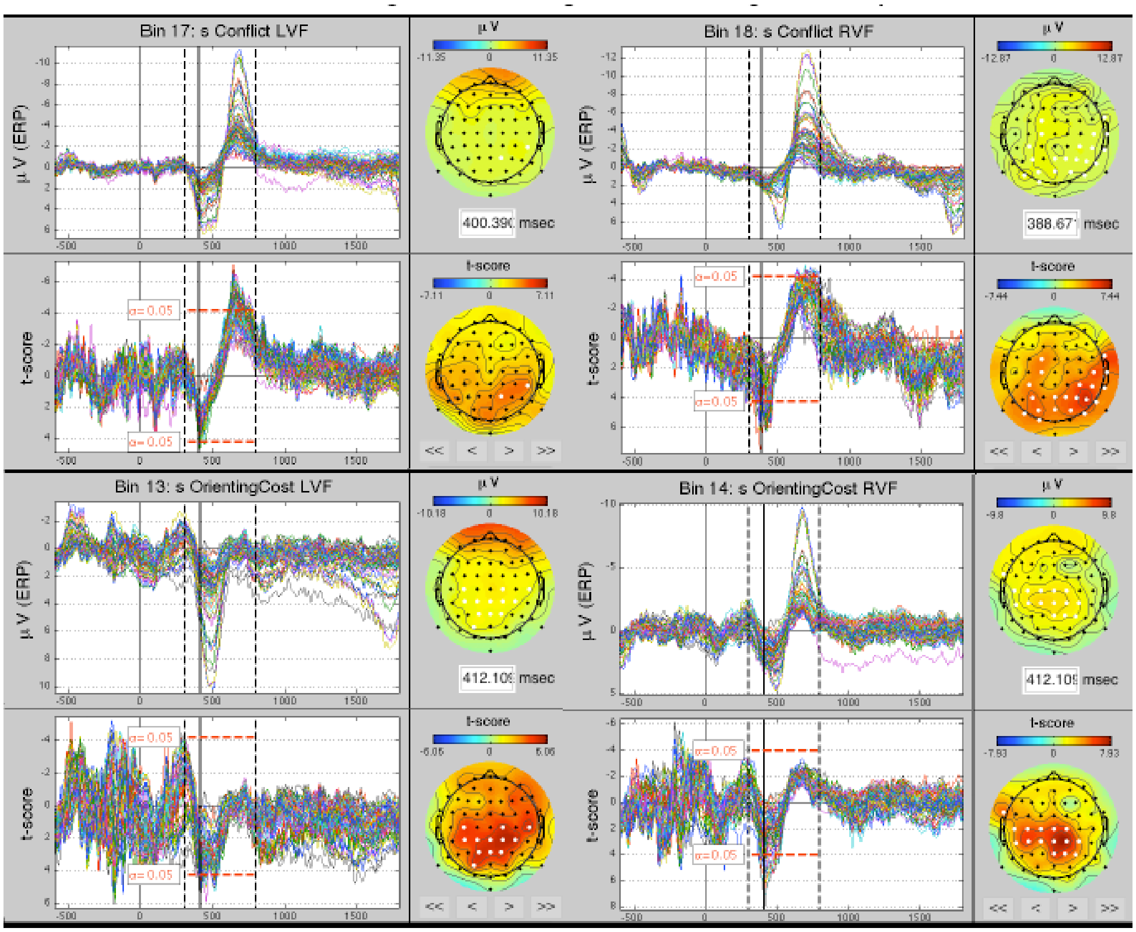
RVFIncongruentInvalid, **Amplitude: 550 ms**

LVF Targets

RVF Targets

Figure 6: Significant scalp differences of sLANT subtraction measures:

sLANT Conflict & Orienting Cost in each Target Visual Field: significant scalp distribution



Significant electrodes indicated by white dots. *Analysis and figures produced with Mass Univariate ERP Toolbox (Groppe, Urbach, & Kutas, 2011)*

Appendix B

Focus on the Positive: Anxiety Modulates the Effects of Emotional Stimuli on Hemispheric Attention

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Abstract

People with high levels of trait anxiety are said to orient attention selectively to threatening stimuli (MacLeod, *et al*, 1986; Bradley, *et al*, 1999), but this effect is sometimes difficult to replicate. We suggest the reason for this difficulty may be that past tests of the attention bias in spatial attention in anxiety failed to consider together: 1) the contribution of hypervigilance vs. failure to disengage from threatening stimuli, 2) whether the attention bias in anxiety is restricted to orienting or can also be observed in the conflict or alerting networks 3) the separate contributions of each hemisphere to the attention bias, and 4) the differential effects of positive and negative stimuli on attention in anxiety. Consequently, we used a lateralized version of Posner's Attention Network Task (Lateralized Attention Network Test) which distinguishes spatial Orienting Cost (due to an invalid cue; disengagement) from spatial Orienting Benefit (due to a valid cue; hypervigilance), and considers executive Conflict resolution and Alerting in addition to spatial Orienting in each hemisphere separately. We compared spatial cues consisting of schematic angry, happy, and neutral faces. We tested participants with high and low trait anxiety, measured by the STAI-TA (Spielberger, *et al*, 1983). Surprisingly, happy face cues rather than angry face cues interacted with target visual field and participant level of anxiety. Happy face cues presented to participants with low anxiety elicited maximal Orienting Benefit and minimal Orienting Cost for targets presented to the left visual field. Anxious individuals failed to benefit from happy cues in the left visual field. We suggest that lateralized happy face cues can provide a more sensitive index of attention changes in anxiety than is provided by centrally-presented threatening face cues.

Keywords: anxiety; attention; attention bias; emotion; hemispheric independence

Introduction

Despite the growing body of research on anxiety disorders, there is no comprehensive account of the cognitive consequences of anxiety to date. One of the best-documented correlates of anxiety is an attention bias toward threatening stimuli (MacLeod, Mathews, & Tata, 1986; Bradley, Mogg, White, Groom, & de Bono, 1999). This attention bias has been investigated extensively using the Emotional Stroop task (see Williams, Mathews, & MacLeod, 1996 for a review), the Visual Probe task (MacLeod, et al, 1986), and tasks of covert orienting of spatial attention (i.e., Fox, Russo, Bowles, & Dutton, 2001). These tasks attempt to differentiate two possible mechanisms underlying the attention bias: hypervigilance toward threatening stimuli and difficulty disengaging from threatening stimuli. Previous studies have shown conflicting evidence, alternately supporting hypervigilance (Koster, Crombez, Verschuere, Van Damme, & Wiersama, 2006), difficulty with disengagement (Yiend & Mathews, 2001; Salemink, van den Hout, & Kindt, 2006), or both (Koster, Crombez, Verschuere, & de Houwer, 2004; for a review of evidence, see Cisler & Koster, 2010). Indeed, opposite conclusions are sometimes reached from the same data using different analyses (Fox, et al, 2001; Mogg, Holmes, Garner, & Bradley, 2008). We propose that some of these inconsistencies may be due to the fact that the traditional tests of the attention bias measure only overall visual orienting, and do not consider the contribution of other components of attention, such as Conflict and Alerting.

Importantly, some studies of attention in low anxiety participants have found that, rather than a reduced bias to threatening stimuli, there is instead a bias toward happy stimuli (Waters, Nitz, Craske, & Johnson, 2007). This bias was explained as attentional avoidance of unpleasant or threatening stimuli. Others found similar results in participants with high anxiety, suggesting that highly anxious participants have developed a coping strategy of redirecting attention to happy stimuli because such stimuli are more likely to signal safety than threat (Derryberry & Reed, 2002; Eysenck, Derakshan, Santos, & Calvo, 2007). We tested this possible account by contrasting angry (threatening) face cues with happy face cues, both relative to neutral face cues.

The Role of the Right Hemisphere in Anxiety

There is evidence that the right hemisphere is specialized for processing emotion in general and for processing negative emotion in particular (Compton, Carp, Chaddock, Fineman, Quandt, & Ratliff, 2008; Schiffer, Teicher, Anderson, Tomoda, Polcari, Navalta, et al., 2007). This is attributable to right hemisphere specialization for activating the autonomic nervous system during fight-or-flight responses (EEG: Spence, Shapiro, & Zaidel, 1996; see Hugdahl, 1996 for a review). Moreover, the right hemisphere has been strongly implicated in orienting of attention both in the left visual field and in the right visual field (Heilman & Van Den Abell, 1980). The right hemisphere is therefore likely to mediate the attention bias in anxiety, and visual field of presentation must be carefully controlled when measuring the attention bias in anxiety in order to disentangle the separate contributions of each hemisphere. Failure to consider visual field of stimulus presentation in previous studies may have obscured the true nature of the attention bias in individuals with high anxiety, contributing to the observed inconsistent results.

In contrast to right hemisphere involvement in negative emotions, hemispheric competence for processing positive emotion is less understood. Two alternative models usually account for hemispheric differences in emotion processing. One view, the Right Hemisphere Hypothesis, states that the right hemisphere is activated for processing (both the identification and experience of) all emotions, regardless of valence (Borod, Kent, Koff, Martin, & Alpert, 1988; Dimberg & Petterson, 1999; Hagemann, Hewig, Naumann, Seifert, & Bartussek, 2005; Aftanas & Pavlov, 2005). An alternate view, the Valence Hypothesis, posits that the right hemisphere is specialized for processing negative emotions, and that the left hemisphere is specialized for processing positive emotions (see Demaree, Everhart, Youngstrom, & Harrison, 2005 for a review of hypotheses on the right hemisphere's role in emotion processing). Both hypotheses predict right hemisphere involvement in processing negative stimuli. However, the two hypotheses make opposite predictions about hemispheric contributions for positive emotions.

To distinguish these two hypotheses, we used an experimental paradigm which presents both positive and negative emotional cues to both visual fields. In this paradigm, we address the implicit effects of emotional state on hemispheric attention by examining the effects of spatial cues consisting of facial affects. The affects (angry, happy, neutral) were expressed in schematic cartoons, which should be equally perceptible to both hemispheres (Yashar, Herzberg, Fourney, Sopfe, Sin, Elperin, et al, 2008). We presuppose that each hemisphere can independently process the information projected to it (Zaidel, Clarke, & Suyenbou, 1990) resulting in a dissociation between the two visual fields and the valence of the face cues (cf. the "processing dissociation" criterion of independent hemispheric processing in the normal brain; Zaidel, 1983). There is by now compelling evidence that the two cerebral hemispheres constitute two separate cognitive systems that can process diverse stimuli in many perceptual-motor-cognitive tasks (e.g., Zaidel et al, 1990). We believe that lateralized presentations best tap the limits of independent competence of the two cerebral hemispheres in a given task (Zaidel, Iacoboni, Zaidel, & Bogen, 2003). This is in contrast to central presentations which may involve variable degrees of interhemispheric interactions.

An Alternate Measure of Attention: The Lateralized Attention Network Task

We used the Lateralized Attention Network Task (LANT), a modified version of the Attention Network Task (ANT), to measure separate components of automatic attention independently in each hemisphere. These components include executive Conflict Resolution (C), Alerting (A), and Orienting (O; Fan, McCandliss, Sommer, Raz, & Posner, 2002). Conflict Resolution (C) measures the ability to identify a target in spite of distracting incongruent flankers (cf. Eriksen & Eriksen, 1974). Alerting (A) measures overall arousal and response expectancy following a nonspatial cue. Orienting (O) is defined as the overall advantage in processing when attention is cued to the location of the impending target. The ANT has been shown to be a reliable and internally valid measure of attention, and it has been proposed as a clinical tool for assessing attention problems in psychiatric disorders (Fan, et al, 2002). The LANT is identical to the ANT in all but two respects. First, the LANT differentiates between Orienting Benefit (response facilitation by a valid cue; OB) and Orienting Cost (response inhibition by an invalid cue; OC). Orienting Benefit corresponds to the traditional measure of hypervigilance and Orienting Cost corresponds to the traditional measure of disengagement in spatial orienting paradigms. Second, the cues and targets are lateralized to the left and right visual fields, rather than appearing in the upper and lower fields. The LANT is a reliable measure of the independent attention networks in each cerebral hemisphere (Greene, Barnea, Herzberg, Rassis, Neta, et al., 2008).

Summary and Present Research

In this experiment, participants with high and low anxiety were given one of three versions of the LANT using happy, neutral, or angry faces as implicit spatial cues. The literature on the attention bias in anxious individuals leads to the prediction that angry face cues would increase OB and increase OC in participants with high anxiety relative to participants with low anxiety and relative to neutral faces in either group. This reflects both hypervigilance and difficulty in disengaging, respectively. At the same time, we measured two other aspects of spatial attention which may be affected by anxiety, namely, Conflict Resolution and Alerting. Furthermore, we manipulated the valence of the stimulus (positive, negative, and emotionally neutral) and the visual field of presentation (lateralized, tachistoscopic presentations). Due to the right hemisphere's known role in both negative emotions and spatial attention, we predicted that effects of anxiety on attention will be selective to the right hemisphere.

Methods

Participants

One hundred fifteen undergraduates (54 males) at the University of California, Los Angeles participated in the experiment as part of a class assignment. Anxiety level was measured with the trait portion of the State-Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1983). Anxiety scores ranged from 24-69, with a median score of 41. Handedness scores were not available. However, the short adaptation of the Oldfield handedness inventory (Oldfield, 1971) was administered for students in the same course for several different academic terms and the prevalence of non-consistent right-handedness was approximately 7%.

Apparatus

The experiment was performed on an IBM-compatible personal computer using E-Prime 1.1 presentation software (Psychology Software Tools, 2002). Stimuli were presented on a 17" Dell monitor with a refresh rate of 60Hz and a resolution of 1280 x 800 pixels/inch. The monitor was situated 57cm away from the participant's eyes. Participants made unimanual responses using a two-button computer mouse held in front of the participant at the midline. The mouse was rotated 90° (placed on its side) so that pressing a button with the index finger indicated the response "up", and pressing a button with the middle finger indicated the response "down".

Stimuli

Lateralized Attention Network Task (LANT). Targets consisted of a vertical arrow, pointing up or down, that appeared one degree to the left or right of fixation. Targets were flanked by two arrows above and two arrows below pointing in the same (congruent) or opposite (incongruent) direction and appearing equally often in the left visual field (LVF; 2° to the left of fixation at the closest edge) and in the right visual field (RVF; 2° to the right of fixation at the closest edge). The complete target stimulus (one central arrow plus four flankers) subtended a total of 3.09° of visual angle vertically and 0.57° horizontally.

An emotional cue preceded each target and consisted of a schematic happy, neutral, or angry face (cf. Öhman, Lundqvist, & Esteves, 2001). There were three versions of the test, each including cues of one valence type. Within each version of the test, the cues appeared equally often in one of three locations: at the same location as the target (valid cue), in the opposite visual field as the target (invalid cue), or at fixation (central, spatially neutral cue). There was also a fourth condition in which the cue did not appear at all (no cue). The cues subtended 1° of the visual angle vertically and horizontally. The neutral face cue in the central location constituted the baseline condition for this experiment: both spatially and emotionally neutral.

Each trial began with a fixation cross projected for either 400ms or 1600ms, varying randomly by trial. The temporal jitter was manipulated to avoid temporal expectation of cue presentations and thus pre-programming of the response. The fixation cross was followed by a 180ms cue, in which one of the emotional faces or no cue was presented. The cue was followed by a 150ms interstimulus interval, after which the target and flanker arrows were presented for 170ms. Participants had up to 1000ms to make a response after the target and flankers had disappeared from the screen, and their reaction times and accuracy were recorded. The fixation cross appeared unchanged throughout all trials and intervals. See Figure 1 for an illustration of trial events.

[Insert Figure 1 here.]

Procedure

Participants were randomly assigned to one of the three versions of the task: one with happy faces only, one with angry faces only, or one with neutral faces only. Cue Valence was a between subjects variable to limit the experiment to a practical length (approximately 35 minutes) and avoid the effects of fatigue. Each participant was first given a 20-trial practice block during which participants were given feedback on their accuracy and reaction time on each trial. This was followed by the two experimental blocks presented without feedback, separated by breaks after each run of 160 trials. Each block took approximately ten minutes. The length of each break was determined by the individual participant.

Participants were instructed to keep their eyes on the fixation cross at all times and to indicate the direction of the target arrow as quickly and accurately as possible. Participants clicked the mouse with either their left or right index finger if the target pointed up and they clicked the mouse with either their right or left middle finger if the target pointed down. Response hand alternated after each block, counterbalanced between subjects. The practice block and first trial block always used the same hand to respond. Response hand was included as a within-subjects variable in the experiment. However, the results showed no main effects or interactions involving Response Hand, Visual Field, Anxiety Level, or Valence. Consequently, Response Hand was excluded from further analysis.

The Orienting Benefit (OB) network was determined by subtracting response times to targets preceded by valid cues from response times to targets preceded by central cues. The Orienting Cost (OC) network was determined by subtracting response times to targets preceded by central cues from response times to targets preceded by invalid cues. The Conflict (C) network was determined by subtracting response times to targets with congruent flankers from response times to targets with incongruent flankers. The Alerting (A) network was determined by subtracting response times to targets preceded by a central cue from response times to targets preceded by no cue.

Results

Exclusion

Seventeen participants were removed from analysis because they failed to complete the State-Trait Anxiety Inventory. Overall accuracy for the LANT was 89% (SD = 19%). Participants who met any of the following criteria were excluded: 1) response times greater than two standard deviations from the mean of response times, 2) overall accuracy less than two standard deviations away from chance (50%) using the normal approximation to the binomial guessing distribution ($z < 1.96$, $p > 0.05$), or 3) large discrepancy in performance between congruent and incongruent flanker conditions (i.e., 90% or greater accuracy for congruent conditions, but 50% or less accuracy for incongruent conditions), showing that they could not do the task. This resulted in additional exclusion of 15 participants (12% of total). Eighty-four participants remained after exclusion (39 male). Overall accuracy following this exclusion was 95%. Due to the ceiling effect for accuracy in our remaining participants, we did not further examine the accuracy data.

Of the 84 remaining participants, 42 were categorized as high anxiety by median split1 on STAI-TA scores of the remaining participants (anxiety score > 40). See Table 1 for distribution of high and low anxiety in each participant group.

Handedness scores were not available for the participants in this experiment. However, the pattern of results in the LANT that involved hemispheric differences in each of the attention networks was similar in this class to previous academic terms, during which the Oldfield handedness questionnaire was administered and 7% of participants were non-consistent right-handers. Moreover, there were no effects or interactions with response hand. Taken together, we take the results in this experiment to represent the pattern expected from a representative population of right-handed participants.

Only reaction times for correct responses were included in the analysis. Response times below 100ms were considered errors of anticipation and were removed from analysis. Response times above 1000ms were considered lapses of attention and were not recorded in the experiment. All main effects and interactions were Greenhouse-Geisser corrected for violations of sphericity where appropriate.

Initial Analysis

We first performed a 2 (Flanker Congruity: Congruent, Incongruent) x 4 (Cue Position: Valid, Invalid, Central, None) x 2 (Target Visual Field: Left, Right) x 3 (Cue Valence: Happy, Neutral, Angry) x 2 (Anxiety Level: High, Low) mixed ANOVA with three repeated measures. Cue Valence and Anxiety Level were between-subjects factors. The dependent variable was reaction time (RT) measured in milliseconds (ms).

There was a significant main effect of Flanker Congruity showing that congruent targets (M = 323.67ms, SD = 1.75) were processed more quickly than incongruent targets (M = 401.43ms, SD = 2.24), F(1, 78) = 566.62, MSE = 3551.51, p = .000, ηp2 = .879. There was a main effect of Cue Position, F(2.61, 203.25) = 141.73, MSE = 998.44, p = .000, ηp2 = .645, showing that targets preceded by valid cues (M = 341.08ms, SD = 2.09) were identified more rapidly than those with central, spatially neutral cues (M = 353.95ms, SD = 1.99; t(83) = 5.83, p = .000, significant OB), which in turn were identified more rapidly than targets preceded by invalid cues (M = 365.60ms, SD = 2.16; t(83) = 5.91, p = .000, significant OC). Targets preceded by either cue, valid or invalid, were identified more rapidly than when there were no cues (M = 389.59ms, SD = 1.89). Cue Position also interacted with Target Visual Field, F(2.68, 209.36) = 5.89, MSE = 608.90, p = .001, ηp2 = .07 (see Figure 2), suggesting larger OC as well as OB in the right visual field (left hemisphere) than in the left visual field (right hemisphere).

[Insert Figure 2 here.]

There was no main effect of Anxiety Level, reflecting no systematic differences between the two participant groups, F(1,78) = 2.33, MSE = 500062.17, p = .131, ηp2 = .029. However, Anxiety Level did interact with Target Visual Field, F(1, 78) = 5.76, MSE = 1547.34, p = .017, ηp2 = .069. This showed no difference between responses to targets in either visual field in individuals with high anxiety. This is distinct from a pattern of increased reaction times to right visual field targets in individuals with low anxiety.

There was a significant interaction between Flanker Congruity and Cue Position, F(2.79, 217.74) = 35.54, MSE = 685.61, p = .000, ηp2 = .313. Given 1) our a priori predictions about the independent effect of anxiety on the separate attention networks in each hemisphere, 2) the observed interaction between Cue Position and Visual Field, and 3) the observed interaction between Anxiety Level and Visual Field, separate ANOVAs were carried out to investigate each of the four attention networks in each hemisphere.

Orienting Benefit

We used OB (i.e., response times to targets preceded by central cues minus response times to targets preceded by valid cues) as the dependent variable for this analysis. The critical interaction between Target Visual Field, Anxiety Level, and Cue Valence was significant, F(2,78) = 4.27, MSE = 433.10, p = .017, ηp2 = .099 (see Figure 3). There were no other significant main effects or interactions.

Planned comparisons for the three-way interaction were Bonferroni corrected to maintain p < .05. There was one significant contrast: in participants with low anxiety, happy faces presented to the left visual field (M = 22.32, SD = 18.27) elicited significantly higher OB than did happy faces presented to the right visual field (M = 4.91, SD = 13.51), t(15) = 3.07, p < .05. Importantly, this pattern is reversed in participants with high anxiety. Those participants showed higher OB to happy faces presented to the RVF (M = 21.96, SD = 21.62) than to the LVF (M = 6.58, SD = 21.77).

[Insert Figure 3 here]

Orienting Cost

We used OC (i.e., response times to targets preceded by invalid cues minus reaction times minus response times targets preceded by central cues) as the dependent variable for this analysis. There was a significant difference in OC between the left and right visual fields overall, F(1,78) = 6.70, MSE = 532.91, p = .011, ηp2 = .079. OC was lower in the LVF (M = 7.03, SD = .73) than in the RVF (M = 16.29, SD = .94). The critical interaction between Target Visual Field, Anxiety Level, and Cue Valence was again significant, F(3,78) = 2.23, MSE = 532.91, p = .045, ηp2 = .076 (see Figure 4). There were no other significant main effects or interactions.

Planned comparisons for the three-way interaction were Bonferroni corrected to maintain p < .05. There were two significant effects: 1) Happy faces presented to the LVF of participants with low anxiety elicited significantly smaller OC (M = -.41, SD = 16.67) than did happy faces presented to the RVF (M = 14.80, SD = 18.62), t(15) = 3.28, p < .05. 2) Happy faces presented to the LVF of participants with low anxiety elicited significantly smaller OC (M = -.92, SD = 12.31) than did happy faces presented to the LVF of participants with high anxiety (M = 24.96, SD = 21.76), t(12) = 5.15, p < .05. There was also a near-significant difference in participants with high anxiety between OC to happy faces (M = 24.96, SD = 21.76) versus neutral faces (M = -2.88, SD = 20.94) presented to the LVF, t(12) = 3.16, p = .06.

[Insert Figure 4 here]

Alerting

We used Alerting (i.e., response times to targets preceded by no cues minus response times to targets preceded by central cues) as the dependent variable for this analysis. Alerting also showed the critical interaction between Target Visual Field, Anxiety Level, and Cue Valence, F(2,78) = 3.21, MSE = 643.67, p = .046, ηp2 = .076. There were no other significant main effects or interactions.

Planned comparisons for the three-way interaction were Bonferroni corrected to maintain p < .05. Left visual field targets preceded by happy, central face cues showed a trend for eliciting greater Alerting in participants with high anxiety than in participants with low anxiety. However, there were no significant contrasts.

Conflict

We used Conflict (i.e., response times to targets with incongruent flankers minus response times to targets with congruent flankers) as the dependent variable for this analysis. Conflict showed no significant main effects or interactions.

Correlations with STAI-TA scores

The use of median split procedures to define participant groups simplifies the data in an attempt to enhance group differences, but is accompanied by a decrease in statistical power. Consequently, we correlated STAI-TA scores with OB and OC in each visual field to confirm the results of our ANOVAs. We furthermore compared these correlations for positive stimuli and for threatening stimuli. The only significant correlation following Bonferroni correction was between STAI-TA score and OC in the LVF for happy faces, r = .616, p = .000.

Reliability of the Neutral Condition

Targets preceded by central cues served as the spatially neutral condition, and therefore expected to have reaction times between those for targets preceded by the valid and invalid cues. Similarly, targets preceded by neutral face cues served as the emotionally neutral condition, and therefore expected to have reaction times between those for targets preceded by angry and happy face cues. The centrally presented cues satisfied this criterion for both high and low participants (see Figure 5). However, the emotionally neutral face cue did not satisfy this criterion separately for each participant group. In particular, the neutral face cue did not serve as an emotional neutral for participants with high anxiety (see Figure 6). This may be because participants with high anxiety interpreted the neutral face cue in a threatening way (Lee, Kang, Park, Kim & An, 2008).

[Insert Figure 5 here]

[Insert Figure 6 here]

Discussion

The goals of this study were to examine 1) the separate contributions of the three networks of selective spatial attention to the attention bias to threat in high anxiety discussed in the literature, 2) the separate contributions of each hemisphere to the attention bias, and 3) the differential effects of positive and negative stimuli on attention in anxiety. We determined that anxiety selectively affects spatial Orienting (including both OB and OC) compared to Alerting or Conflict. Only Orienting was explicitly sensitive to target visual field, valence, and anxiety level simultaneously. Based on traditional measures of the attention bias and on the traditional views of hemispheric specialization for emotional stimuli, we predicted that in anxious participants both hypervigilance (OB) and difficulty disengaging (OC) would be higher for angry cues than for nonthreatening cues and larger in the left visual field (LVF) than in the right visual field (RVF). We confirmed that sensitivity to emotional stimuli is selective to targets projecting to the LVF, i.e., the right hemisphere: targets projected to the right hemisphere showed differential effects depending on the cue valence for both OB and OC. By contrast, RVF cues elicited stable effects across cue valence. However, we found that the right hemisphere was specifically responsive to happy face cues rather than to angry face cues. Thus, participants with low anxiety showed overall response facilitation when happy cues were presented to the LVF (OB increased, OC decreased). This is in agreement with several studies which have shown that low anxious participants are more sensitive to positive stimuli (e.g. Waters, et al, 2007; Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn 2007; MacLeod, et al, 1986). By contrast, participants with high anxiety showed overall response inhibition when happy cues were presented to the LVF (OB decreased, OC increased). In sum, happy faces helped right hemisphere spatial Orienting in participants with low anxiety and hurt right hemisphere spatial Orienting in participants with high anxiety. Neither Alerting nor Conflict showed a significant effect of anxiety level with either happy or angry face cues, suggesting that neither provides as sensitive a measure of the attention bias in anxiety as does Orienting.

What Characterizes People with High Anxiety?

Participants with high anxiety are typically characterized by focused attention to threatening stimuli (MacLeod, et al, 1986; Bradley, et al, 1999). However, previous results have been inconclusive as to whether this is due to hypervigilance for threat or difficulty disengaging from threat. Our results do not support either of these accounts of the response to angry face cues compared to happy or neutral face cues: high anxiety showed both low OB and low OC in the LVF for angry faces (see Figures 3 and 4). Moreover, participants with high anxiety showed exceptionally high OC (strong difficulty disengaging) in the LVF when presented with happy face cues.

Taken together, our results suggest that the effects of threatening and happy stimuli in anxiety are independent of each other. This is in direct contrast both with 1) the standard theory of attention to threat in anxiety, which would predict a primary increase in OB to threatening stimuli (as well as an increase in OC to threatening stimuli), and 2) with attentional control theory (Eysenck, et al, 2007), which predicts a secondary increase in OB to positive stimuli (as well as an increase in OC to positive stimuli). Instead, positive stimuli demonstrated a primary increase in OB and decrease in OC in individuals with low anxiety and a primary decrease in OB and increase in OC in individuals with high anxiety. Threatening stimuli did not differentiate individuals with high anxiety from individuals with low anxiety. Importantly, this effect was found for Orienting in the LVF selectively, highlighting the necessity to differentiate the role of the two hemispheres when examining anxiety. This may have important implications for methods of clinical intervention for anxiety by targeting anatomical structures and processes in the right hemisphere.

Attention Bias to Threatening Stimuli

There are several potential reasons that our study produced novel results. First, our findings on emotional valence in anxiety apply to implicit (i.e., task-irrelevant) cues whose effects are measured by the indirect modulation of attention. This measure therefore has the advantage of being less sensitive to strategic, conscious, and other controlled state variables, and is more likely to reflect automatic, trait variables.

Second, the effects of threatening stimuli are known to occur earlier than for other stimuli (see Bar-Haim, et al, 2007 for meta-analysis). Therefore, it could be argued that the selective effects of happy face cues in anxiety result from slower perceptual processing of positive compared to threatening stimuli, However, physiological data using the N2pc event-related potential showed persistence in the effect of threat cues that does not diminish as the effect of positive cues rises (Holmes, Bradley, Nielsen, & Mogg, 2009). Furthermore, we presented positive cues and threat cues separately thus minimizing possible competing effects of valence processing in our data. Therefore, the effect of happy cues seen in our data cannot be attributed to slower processing of positive stimuli than of threat stimuli.

Third, it could be argued that we did not replicate the bias to threat because we lateralized stimulus presentations. These presentations are often considered “less natural” than other experimental paradigms. However, lateralized presentations have the advantage of distinguishing the lateralized cognitive processes which underlie observed behavior in natural conditions. This type of paradigm is ideal to measure the effects of anxiety on attention because the presumed component processes underlying this effect (namely, negative emotion and spatial attention) are strongly lateralized (see introduction). We believe lateralized paradigms are therefore uniquely suited to identify early implicit markers of a clinical state such as high trait anxiety.

Hemispheric Contributions to the Attention Bias

Our data failed to show a LVF advantage for all emotional cues, thus failing to provide strong support for the Right Hemisphere Hypothesis of emotion processing. Our data also failed to show a selective LVF sensitivity for negative emotional cues together with a selective RVF sensitivity for positive emotional cues, thus failing to support the Valence Hypothesis. However, the face cues did help performance (increasing OB, decreasing OC) in the LVF, whereas there was no sensitivity to the different valences of the faces in the RVF. We take this to provide partial support for the Right Hemisphere Hypothesis. It could be argued that this LVF sensitivity may in fact be due to right hemisphere specialization for processing and identifying faces. However, the face cues consisted of highly salient schematic cartoon faces that should be equally perceived in both hemispheres (Yashar, et al, 2008).

Generalizations and Extensions

Our results may be underestimated due to the relatively high exclusion rate. However, our sample size was able to convey statistically significant differences with some very large effect sizes ($\eta p2 > .60$; see Results). Nonetheless, these results should be replicated and extended in several ways.

First, it is important to show that the same results apply to patients with clinically diagnosed anxiety. Since STAI-TA scores are positively correlated with measures of clinical anxiety, it is reasonable to assume that the pattern observed here will extend to clinical populations. This is important to establish because it provides a model of the clinical condition in the normal population. The existence of such a model makes it easier to study the presentation, diagnosis, and treatment of the disorder.

Second, the deficit in performance following happy faces is more common in individuals with depression than with anxiety (Dalgleish & Watts, 1990). Given that the STAI-TA may provide a measure of depression as well as anxiety (Bieling, Antony, & Swinson, 1998), it is important to separate the contribution of anxiety and the contribution of depression in our results.

Third, our results showed that nonemotional cartoon faces do not serve as effective neutral stimuli to distinguish between positive and negative emotional faces for individuals with high anxiety. This point is particularly interesting because it invokes the question of how nonemotional stimuli are evaluated by individuals with high anxiety and, if nonemotional stimuli are evaluated as emotional, why do individuals with high anxiety automatically classify stimuli? Consequently, future studies should explore better candidates for neutrally-valenced stimuli. Future studies should also examine the possibility that evaluation of a nonemotional face may serve as an implicit measure of anxiety level.

Lastly, it is important to consider the role that individual differences play in our results. This includes more explicit measures of handedness which distinguish strong right-handers from nonconsistent right-handers and from strong left-handers, with and without familial sinistrality. This also includes consideration of sex (male/female) as well as gender attribution (masculinity and femininity). Consideration of sex is particularly important given that females are more likely to develop anxiety disorders than males (National Institutes of Mental Health, 2009). However, we did conduct separate analyses considering the effect of participant sex on these results, and found effects of participant sex that were completely separate from the effects of participant anxiety level. These results are currently being prepared for a separate publication (Wiens, Crump, & Zaidel, in preparation).

Based on our results, we suggest that the inability to benefit from positive experiences is an important part of the maintenance of anxiety. Studies have shown that it is possible to induce an attention bias to particular stimuli by making the stimuli predictive of target location (Frewen, Dozois, Joanisse, & Neufeld, 2007). A possible treatment for anxiety may be to induce an attention bias to positive stimuli in the left visual field in particular. This implicit change in behavior may teach individuals with high anxiety to attend to positive stimuli and experiences in everyday life, thus overcoming the maintenance of anxiety.

4.5 Conclusions

In summary, we examined the effects of emotional valence on separate networks of attention in anxiety independently in each cerebral hemisphere. We confirmed that the mechanisms underlying the attention bias occurred selectively in the Orienting, rather than Alerting or Conflict, attention network. We demonstrated that the two hemispheres make separate and independent contributions to the effect of anxiety on attention. Our results support a form of the Right Hemisphere Hypothesis in that we found right hemisphere sensitivity to positive stimuli but not to negative stimuli. Using a novel paradigm for measuring attention in anxiety, we found that attention in anxiety is primarily and independently affected by happy cues rather than by threatening cues. Thus, happy cues helped LVF performance in participants with low anxiety. By contrast, happy cues impaired LVF performance in participants with high anxiety.

Taken together, these results show that: 1) the Orienting network of the emotional LANT is sensitive to anxiety level, 2) the effects of positive cues provide a more sensitive measure of anxiety than the effects of threatening cues, and 3) a sensitive test of anxiety should distinguish its effects in each hemisphere.

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Footnotes

[1] We initially separated participants into three anxiety groups: high (STAI-TA score >50), intermediate (49 > STAI-TA score > 40), and low (STAI-TA score < 39). Results from this analysis showed no difference between high and intermediate groups, so we separated the participants by median split in the interests of parsimony.

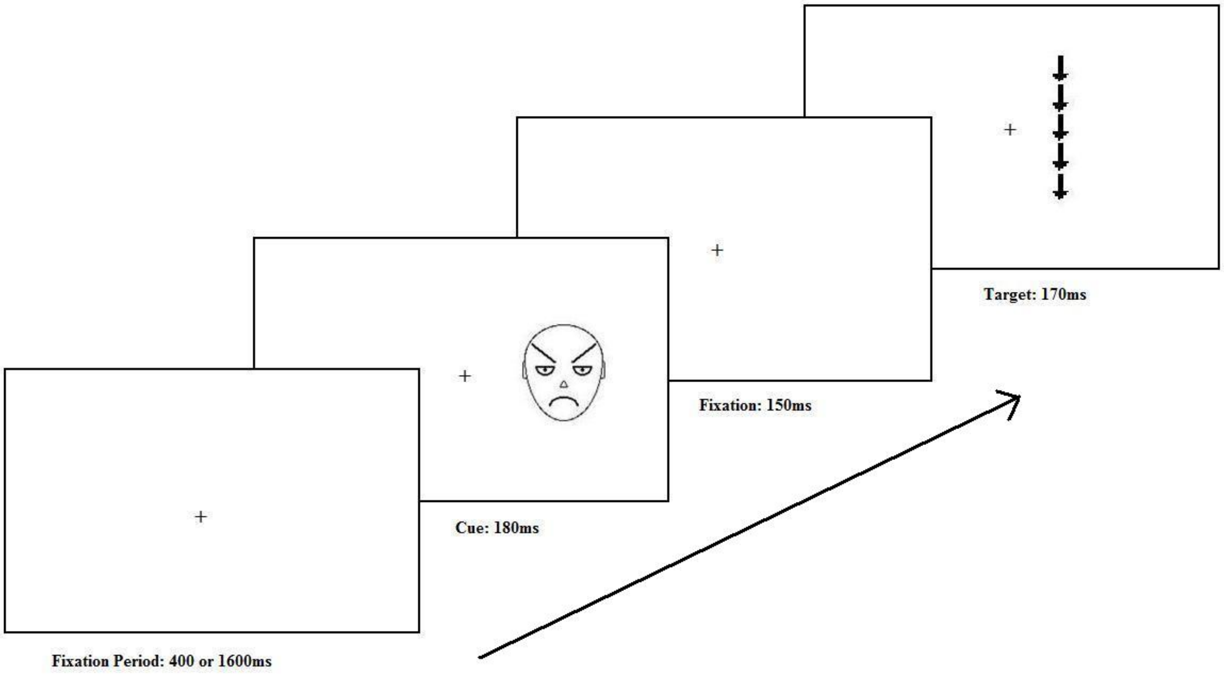

Fixation Period: 400 or 1600ms
Cue: 180ms
Fixation: 150ms
Target: 170ms

Figure 1.

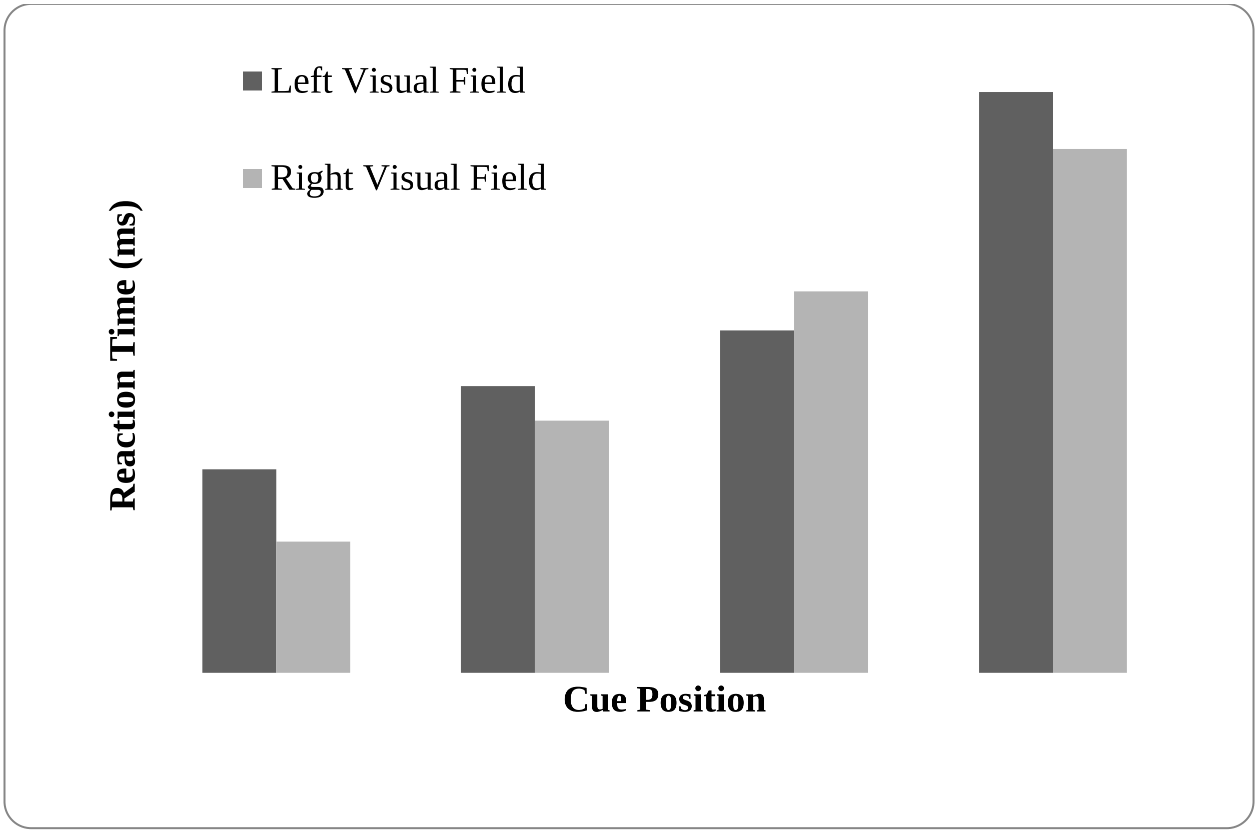
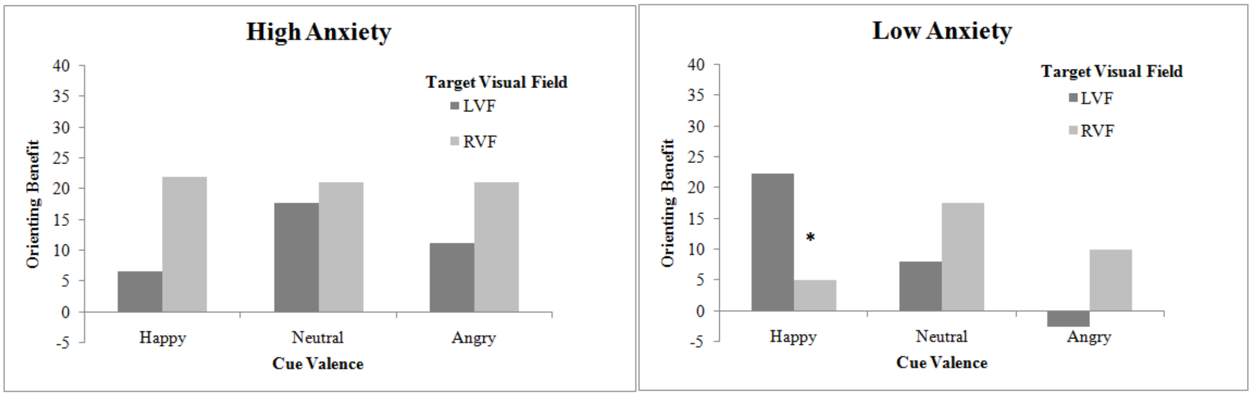

■ Left Visual Field
■ Right Visual Field
Reaction Time (ms)
Cue Position

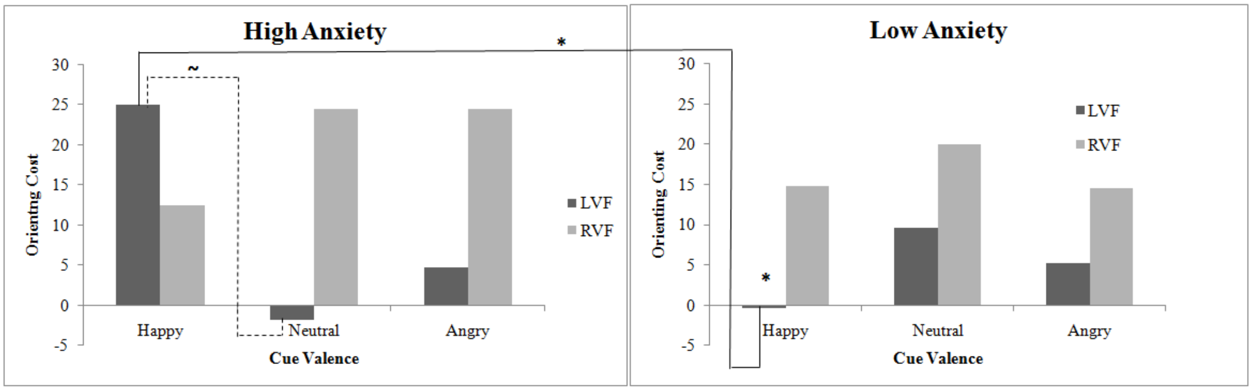
Figure 2.


High Anxiety

Low Anxiety

* = $p < 0.05$

Figure 3.



***** = $p < 0.05$

~ = $p < 0.06$

Figure 4.

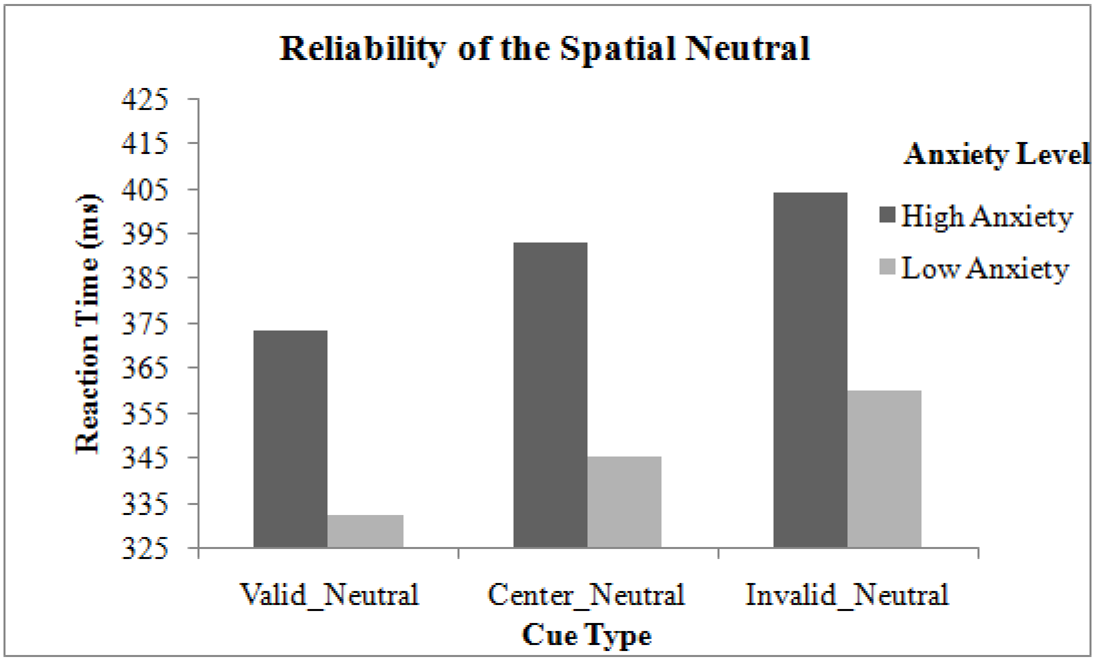

Reliability of the Spatial Neutral
Reaction Time (ms)
425
415
405
395
385
375
365
355
345
335
325
Anxiety Level
High Anxiety
Low Anxiety
Valid_Neutral
Center_Neutral
Invalid_Neutral
Cue Type

Figure 5.

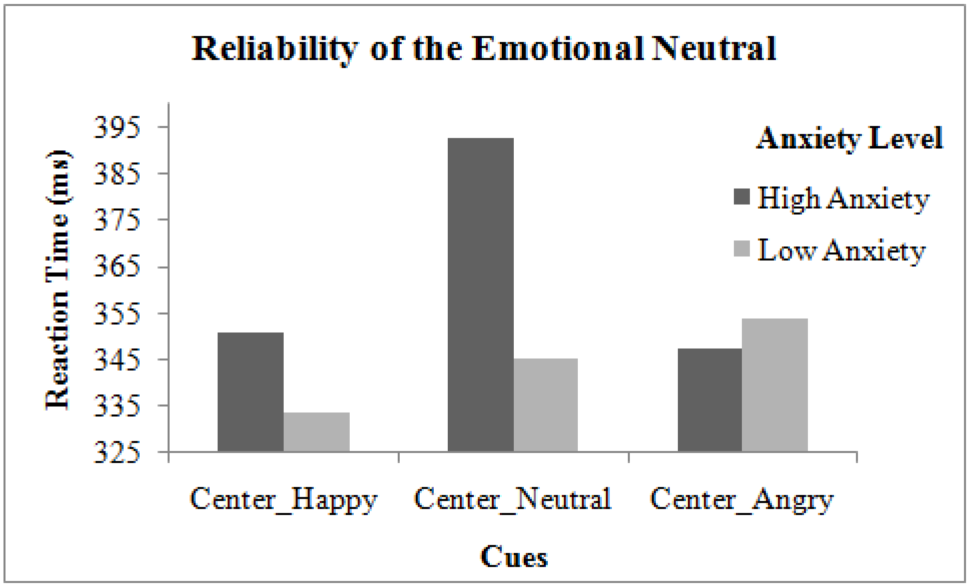
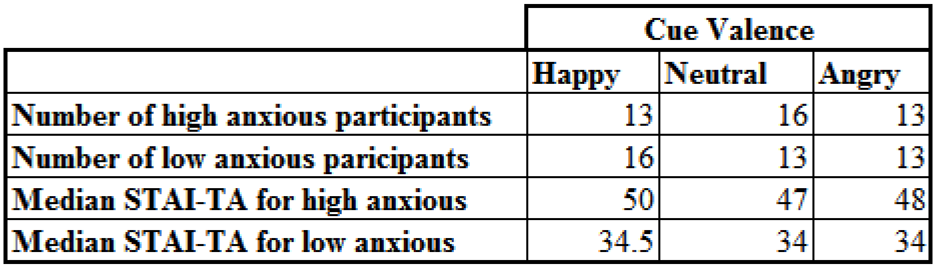

Reliability of the Emotional Neutral
Reaction Time (ms)
395
385
375
365
355
345
335
325
Anxiety Level
High Anxiety
Low Anxiety
Center_Happy
Center_Neutral
Center_Angry
Cues

Figure 6.



	Cue Valence		
	Happy	Neutral	Angry
Number of high anxious participants	13	16	13
Number of low anxious paricipants	16	13	13
Median STAI-TA for high anxious	50	47	48
Median STAI-TA for low anxious	34.5	34	34

Table 1.

Figure Captions

Figure 1. Schematic progression of the LANT experiment. Arrow represents progression of time.

Figure 2. Cue Position x Target Visual Field interaction in initial analysis. Results show no significant differences by Target Visual Field, but all differences between the four Cue Positions are significant at $p = .000$ within each target visual field.

Figure 3. Target Visual Field x Anxiety Level x Valence interaction for OB.

*Figure 4.*Target Visual Field x Anxiety Level x Valence interaction for OC.

Figure 5. Reliability of the spatial neutral. A reliable spatial neutral condition should fall somewhere between valid cues and invalid cues. This is the central, neutral face cue for all participants.

Figure 6. Reliability of the emotional neutral. A reliable emotional neutral condition should fall somewhere between happy faces and angry faces. This is the central, neutral face cue for participants with low anxiety but not for participants with high anxiety.

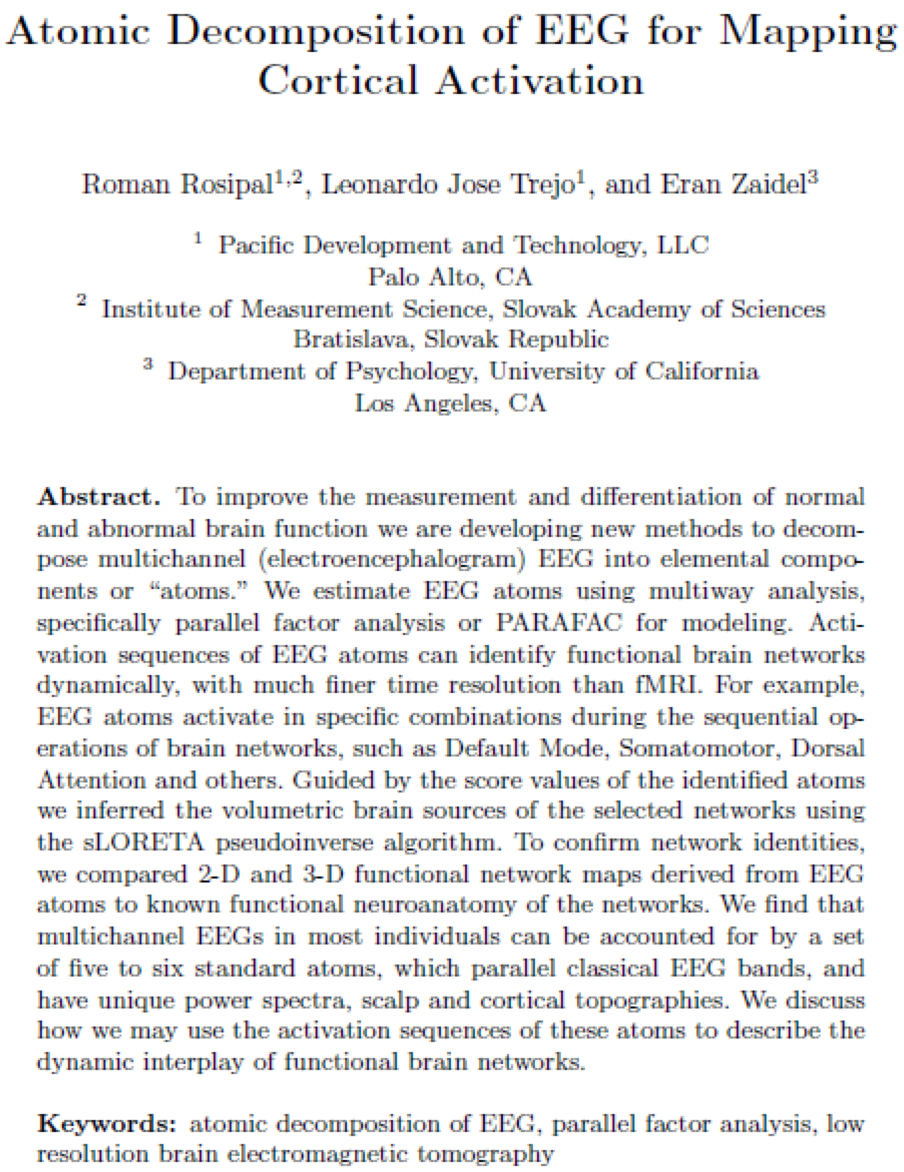
Table 1. Distribution of STAI-TA scores for each participant group and each cue valence.

Appendix C.

Atomic Decomposition of EEG for Mapping Cortical Activation

A full-text copy of this article is available on-line at http://publications.neurodia.com/Rosipal%20et%20al%202013%20Atomic%20Decomposition%20of%20EEG%20for%20Mapping.pdf.

Rosipal, R., **Trejo**, L. J. and Zaidel, E. (2013). Atomic Decomposition of EEG for Mapping Cortical Activation. Tensor Methods for Machine Learning workshop. Prague, September 27.



Atomic Decomposition of EEG for Mapping Cortical Activation

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Abstract. To improve the measurement and differentiation of normal and abnormal brain function we are developing new methods to decompose multichannel (electroencephalogram) EEG into elemental components or "atoms." We estimate EEG atoms using multiway analysis, specifically parallel factor analysis or PARAFAC for modeling. Activation sequences of EEG atoms can identify functional brain networks dynamically, with much finer time resolution than fMRI. For example, EEG atoms activate in specific combinations during the sequential operations of brain networks, such as Default Mode, Somatomotor, Dorsal Attention and others. Guided by the score values of the identified atoms we inferred the volumetric brain sources of the selected networks using the sLORETA pseudoinverse algorithm. To confirm network identities, we compared 2-D and 3-D functional network maps derived from EEG atoms to known functional neuroanatomy of the networks. We find that multichannel EEGs in most individuals can be accounted for by a set of five to six standard atoms, which parallel classical EEG bands, and have unique power spectra, scalp and cortical topographies. We discuss how we may use the activation sequences of these atoms to describe the dynamic interplay of functional brain networks.

Keywords: atomic decomposition of EEG, parallel factor analysis, low resolution brain electromagnetic tomography

Appendix D.

A copy of this presentation is available on-line at
http://publications.neurodia.com/Trejo%20et%20al%202013%20Modeling%20EEG-band%20Neurofeedback.%20Modulating%20Internal%20States%20without%20Conditioning%20of%20EEG%20Sources.pdf

Zaidel, E., Rosipal, R., Hill, A., Fernandes, N., Akbarut, R., Noh, S., and **Trejo**, L.J. (2013). Modeling EEG-band Neurofeedback: Modulating Internal States without Conditioning of EEG Sources. ISNR 21st Annual Conference. Dallas TX, September 18-22.

Modeling EEG-band Neurofeedback: Modulating Internal States without Conditioning of EEG Sources

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At least three neurofeedback techniques can produce measurable behavioral and neurophysiological changes. These involve modulating slow-cortical potentials (SCP), fMRI BOLD signals, or amplitude (or power) in narrow EEG bands. We think SCP neurofeedback may work indirectly by conditioning task-specific attentional focus, whereas fMRI neurofeedback directly conditions regional brain activity during task performance. However, the object of conditioning in EEG-band training is unclear because there is no overt task to perform and the electrophysiological and behavioral changes can occur rapidly. In a previous double-blind, placebo controlled experiment, we trained participants to increase EEG amplitude in narrow bands (C3-SMR, C4-SMR, C3-Beta, sham) using auditory rewards and 30-minute training sessions over five consecutive days. We observed widespread changes in ERP/ERSP patterns for reward stimuli *during* training. However, we did not find significant conditioning of trained bands within or across sessions. We also observed improved performance of a hemispheric attention task in the C3-Beta group *after* five sessions. To explain these and related results we are developing a four-part model: 1) Introspective tasks such as mind wandering during rest or autobiographical memory, engage a Switching Network which activates an internally-directed Default Mode Network and deactivates externally-directed problem-solving networks. 2) The DMN activates a “self-control” system which links rewards to internal states of arousal, motor activation, attentional focus, or cognitive engagement. 3) The internal states co-vary with synchrony in fundamental EEG “atoms.” We separately developed EEG atom metrics, where each atom represents one oscillatory EEG mode in the 1-40 Hz range, with a unique spectral envelope, topographical power distribution, and pattern of connectivity. 4) When the self-control system is engaged, neurofeedback rewards condition internal state modulations or “responses” which cause EEG atom synchrony levels to change accordingly. Thus EEG-band training conditions the self-control system, which can then manage internal states and global network connectivity.

Ghaziri, J., Tucholka, A., Larue, V., Blanchette-Sylvestre, M., Reyburn, G., Gilbert, G., Lévesque, J., Beauregard, M. Neurofeedback Training Induces Changes in White and Gray Matter. Clin EEG Neurosci. 2013 Mar 26. [Epub ahead of print].

Gruzelier JH, Egner T, Vernon D (2006) Validating the efficacy of neurofeedback for optimising performance. In: Neuper C, Klimesch W, Event-related dynamics of brain oscillations. Prog Brain Res 159:421–431.

Hill, A., Barnea, A., Herzberg, K., Rassis-Ariel, A., Rotem, S., Meltzer, Y., Li, Y.H., and Zaidel, E. (2008), Measuring and Modulating Hemispheric Attention. In Aboitiz, F., and Cosmelli, D. (Eds.) From Attention to Goal-Directed Behavior.

Rockstroh, B., Elbert, T., Birbaumer, N., Lutzenberger, W. 1990. Biofeedback-produced hemispheric asymmetry of slow cortical potentials and its behavioural effects. *International Journal of Psychophysiology*, 9(2), 151-165.

Ros, T., Théberge, J., Frewen, P.A., Kluetsch, R., Densmore, M., Calhoun, V.D., Lanius, R.A. 2013. Mind over chatter: Plastic up-regulation of the fMRI salience network directly after EEG neurofeedback, *NeuroImage*, 65, 324-335.

Appendix E.

Towards an Ecologically Valid Measure of Hemispheric Selective Spatial Attention:

A. Trait/State anxiety interacts with background emotions and with emotional cues in modulating the Orienting and Conflict Resolution components of the Lateralized Attention Network Test (LANT)

Introduction

In previous experiments, we have introduced the LANT in order to measure separately the Alerting, Spatial Orienting, and Conflict Resolution networks of selective attention in each cerebral hemisphere. We found that, in general, each type of network is rather similar between the two hemispheres (Greene et al., 2007).[12] Also, the Conflict Resolution measure is often larger in the left hemisphere (right visual field) than in the right hemisphere (left visual field), whereas the Orienting measure is often larger in the right hemisphere than in the left hemisphere.

In order to assess and incorporate the effects of individual differences in personality and in mood on the networks of attention in each hemisphere, we replaced the standard frame cues (which surrounded a possible location of the target) with cartoon facial affects (happy or angry) as peripheral spatial cues. We found that individuals with high anxiety (on the Spielberger Trait Anxiety Inventory or STAI, 1983)[13] show greater laterality effects, and emphasize a distorted version of right hemisphere processing. Moreover, individuals with high anxiety differed from individuals with low anxiety in failing to benefit from positive emotional cues, rather than in being selectively hindered by angry cues (Crump and Zaidel, 2013).[14] As a rule, individuals tend to process fastest stimuli that represent psychological conditions similar to their own, whether positive or negative, conscious or not. Moreover, psychiatric conditions can usually be represented along the normal continuum. Consequently normal individuals can be used as a model system for clinical populations. Thus, measures of anxiety on the STAI can serve as models of degrees of severity of clinical anxiety disorders.

In an attempt to increase the ecological validity of the LANT, we incorporated emotionally charged backgrounds (positive or negative emotional scene) into the test. We predicted that the emotion of the background will interact with the emotion of the cue and with the anxiety of the participant in modulating the Orienting and Conflict Resolution networks in each hemisphere.

Methods

We used a modified version of the LANT. Background Emotion was either a positive (happy elderly couple) or negative (menacing shark) scene selected from the International Affective Picture System (IAPS).[15] The two scenes were approximately matched for arousal level. Spatial cues consisted of either

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[12] Greene, Deanna J., et al. "Measuring attention in the hemispheres: The lateralized attention network test (LANT)." *Brain and cognition* 66.1 (2008): 21-31.

[13] Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press.

[14] Crump, Caroline, S. Aakash Kishore, and Eran Zaidel. "Focus on the positive: Anxiety modulates the effects of emotional stimuli on hemispheric attention."*Brain and cognition* 83.1 (2013): 52-60.

[15] Lang, P.J., Bradley, M.M., & Cuthbert, B.N. (2008). International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8. University of Florida, Gainesville, FL.

angry or happy cartoon faces presented at the possible locations of the visual targets in each visual hemifield. The targets consisted of arrows pointing up or down flanked above and below by congruent or incongruent distractors. Two-choice responses were indicated unimanually using a computer mouse. The experiment was presented using the E-prime software (Psychology Software Tools, Inc.) on a PC Computer. Cues were flashed for 150 milliseconds and, following a 100 millisecond delay, targets were flashed either in the same or opposite location for 150 milliseconds.

Eighteen UCLA undergraduate students between the ages 18 and 24 participated in experiments. All were right-handed as determined by a Modified Edinburgh Handedness Inventory, all had normal or corrected-to-normal vision and all reported no neurological or psychiatric histories. Individual levels of anxiety, a personality variable (trait anxiety) as well as a mood variable (state anxiety), were measured using the STAI-TA and STAI-SA subscales, respectively. Participants were classified as High or Low anxiety using a median split.

Our prediction was that there will be a significant interaction of the following form: [Orienting (Valid, Invalid cue) x Conflict (Congruent, Incongruent target)] x [Cue Emotion (Happy, Angry cartoon face) x Background Emotion (Happy, Angry)] x Target Visual Field (Right, Left) x [Trait Anxiety (High, Low anxiety by median split)]. In this design, at lease one element from each group (square brackets) must be present. Trait anxiety was a between-subject variable and all the other independent variables were within-subject. The dependent variable was response time.

Results

Accuracies were uniformly very high and consequently we focused on the reaction time data. Both hemispheres exhibited a “standard size” Orienting Network (42 ms) and a “standard size” Conflict Resolution Network (57 ms). As usual, there was a significant interaction between Orienting and Conflict. The responses were overall faster for trials with the positive emotion than with the negative emotion.

There were no overall differences between targets preceded by happy cues and targets preceded by angry cues. Trait anxiety interacted with Cue Emotion and with the Target Visual Field such that the high anxiety participants responded faster following happy cues in the left visual field and following angry cues in the right visual field. By contrast, participants with low anxiety responded faster following angry cues in the left visual field and following happy cues in the right visual field. Thus, the two groups showed opposite hemispheric specialization for the emotional cues.

There was also a borderline significant interaction (p=.057) between Trait Anxiety, Background Emotion, Orienting and Target Visual Field, showing that for low anxiety participants, Orienting was sensitive to the background emotion and to the visual field in which the target appeared. By contrast, people with high anxiety had similar Orienting regardless of the background emotion and of the visual field in which the target was presented. State anxiety showed fewer but similar significant effects.

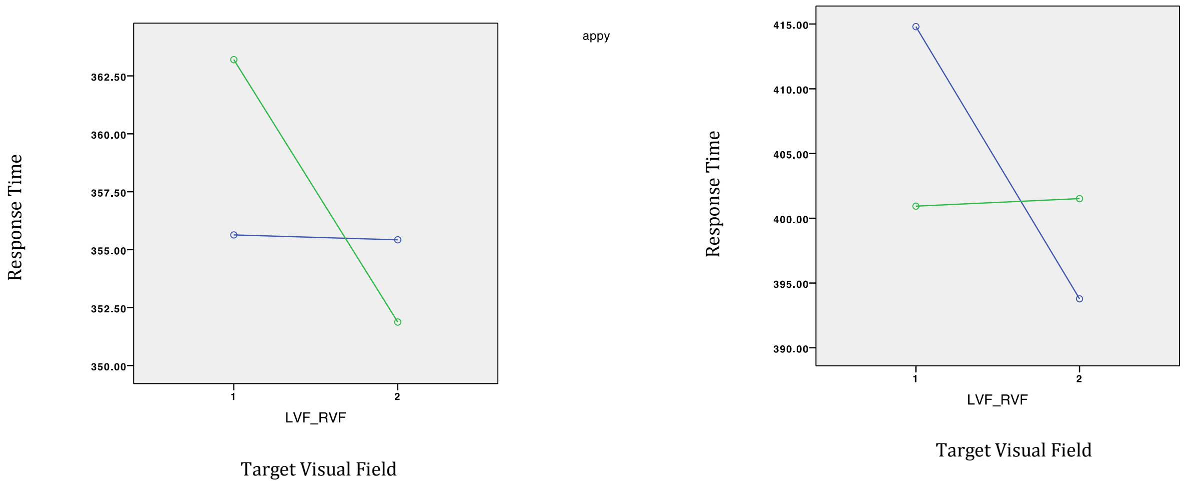

Figure 1: Cue Emotion x Target Visual Field x Trait Anxiety, P= .025

Table 1: Significant Interactions involving anxiety (Red), emotion of cue or of background (Blue), and attention network (Green).

Discussion

	Orienting	Conflict	Background Emotion	Cue Emotion	Orienting x Conflict	Anxiety x Cue Emotion x Target Visual Field	Anxiety x Background Emotion x Orienting	Anxiety x Background Emotion x Orienting x Target Visual Field
Trait Anxiety	+	+	+	-	+	+	-	~+ (p=.057)
State Anxiety	+	+	+	-	+	-	~+ (p=.064)	-

Note: A "+" indicates significant interaction involving attention network, emotionality and anxiety.

Discussion

The extended (ecologically valid) LANT demonstrates that the Orienting Network is sensitive to the emotionality of the background and of the cue as a function of the anxiety level of the participant. In particular, high and low anxiety participants often showed opposite hemispheric specialization patterns following positive and negative cues. Further, individuals with low anxiety exhibit more flexible shifts in hemispheric specialization following different emotional cues.

In sum, we found that trait anxiety, but not state anxiety, interacted with the emotionality of the background and of the cue, as well as with the Orienting Network. Numerous past experiments in our lab have confirmed that individuals are faster at processing information that describes their own states, regardless of whether those states are positive or negative and regardless of whether the individuals are consciously aware of them or not. Consequently, it is possible to “personalize” the LANT, thus making it sensitive to the participant’s temperament.

The LANT can be regarded as a perceptual test typical of army visual tracking tasks, but it can also be regarded as a general measure of the networks of selective spatial attention. It remains to be determined whether the LANT is indeed modality-specific or whether it measures the same general networks of attention regardless of the modality of the task and of its specific sensory-motor constraints. If the LANT does measure general networks of attention, then by modulating it one can modulate the rest of the cognitive system. The LANT can also be used to recreate situations from the participant’s own personal history using computerized virtual reality in order to promote superior performance or, alternatively, in order to diagnose and to treat traumatic psychiatric conditions, such as PTSD or general anxiety disorders.

B. “Weariness variables” interact with emotionality of the backgrounds and of the cues in modulating the networks of attention of the LANT

Introduction

An important component of our joint effort in the NOIT has been finding the behavioral and electrophysiological correlates of weariness and ways to minimize them. In order to assess the contributions of weariness variables to the LANT, we administered two surveys, the Profile of Moods Survey (POMS) and the T-MENTST (a PDT proprietary short survey of task related mental state focusing on energy, fatigue, and motivation), to participants before and after the administration of the LANT. Both surveys include several state variables, which contrast with personality variables such as trait anxiety, considered in part A. For each of the state variables, we will consider, in turn, the relationship between performance on the LANT and (1) the absolute level of the variable before administering the LANT, as well as (2) the proportion change of the variable following the administration of the LANT.

Methods

The experimental design was the same as in part A, with the exception that the median-split analysis of the between-subject independent variable Trait Anxiety (part A) was replaced by two separate ANOVAs for each of one of the state variables of the surveys at a time (part B). The surveys were administered before and after the LANT. The first ANOVA used a median-split of the pre-testing measure; the second ANOVA used a median-split of the proportion change following testing, where proportion change = (Pre-Post)/(Pre+Post).

Results

The results of the ANOVAs of the pre-test scores for the state variables of both surveys are presented in Table 2. The Anger and the Depression state variables of the POMS were excluded from the analyses because they did not show enough spread (variability) across participants (marked with x’s in Table 2). All state variables showed significant main effects of Orienting, Conflict, and Background Emotion. None of the variables, with the possible exception of proportion change analysis for the T-MENSTAT state variable Energy (p=.059), showed a significant main effect of the emotionality of the cue. The irritation scale of the T-MENSTAT showed the most extensive interactions across both the attention networks and the emotionality of the backgrounds/cues separately and simultaneously.

Figure 2 illustrates a significant interaction Irritation x Conflict x Background Emotion x Target Visual Field (p=.011). Figure 2a shows that with the happy background (happy elderly couple) participants with high levels of irritation had similar conflict measures in the two visual fields (hemispheres). Instead,

Figure 2b shows that with the same happy background, participants with lower irritation had much larger conflict in the left visual field (right hemisphere, RH) than in the right visual field (left hemisphere, LH). By contrast, Figure 2c shows that with the angry background (menacing shark) participants with high levels of irritation had a slightly larger conflict in the right visual field (LH) than the left visual field (RH), whereas figure 2d shows that participants with low levels of irritation had a much larger conflict in the right visual field (LH) than in the left visual field (RH). Together, this indicates that participants with low irritation are more likely to show a greater hemispheric difference, which switches completely between the happy and angry context.

The results of the ANOVAs using the proportion change in state variables following the test are presented in Table 3. Irritation remained the most "active" variable, but it was not involved with all the significant interactions of the form State Variable x Attention Network x Emotionality. Furthermore, the proportion change Irritation measure showed different effects than the pre-testing Irritation measure. Many of the effects that were significant in the proportion change ANOVAs, but not in the pre-testing ANOVAs, involved the emotionality of the cue.

Figure 2a

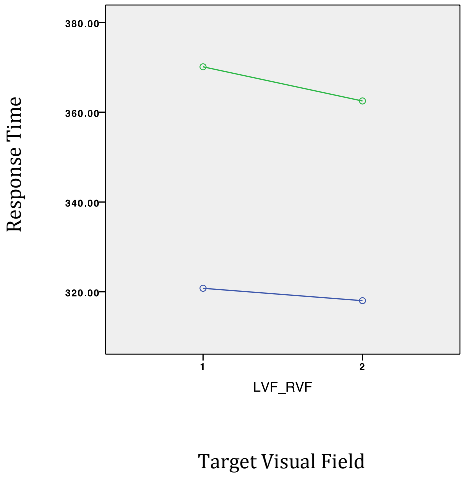

Figure 2b

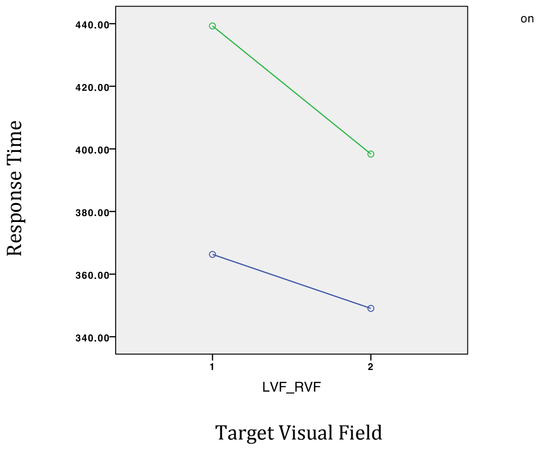

Figure 2c

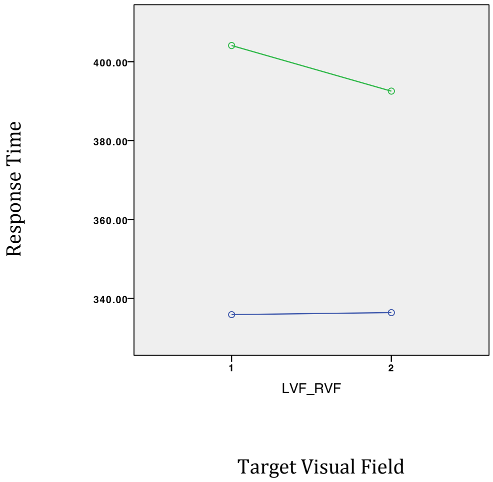

Figure 2d

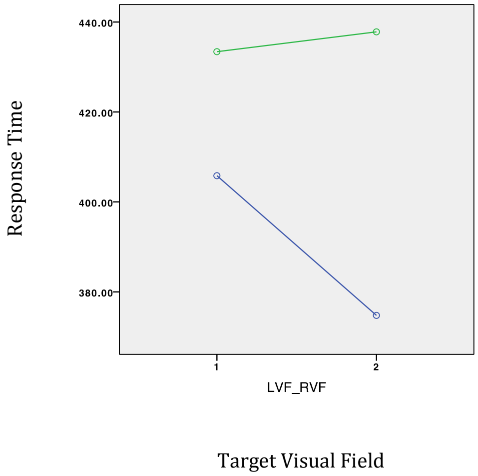

Table 2. Interactions of analyses of the pre-test scores of the "weariness" state variables (POMS + T-MENSTAT). A "+" indicates significant interaction involving attention network, emotionality and weariness; ; X == not available or range too narrow.

	Orienting x Background Emotion x Cue Emotion	Conflict x Background Emotion x Cue Emotion	Orienting x Background Emotion x Target Visual Field	Orienting x Conflict x Target Visual Field	Survey x Conflict	Survey x Orienting x Conflict	Survey x Orienting x Conflict x Target Visual Field	Survey x Background Emotion	Survey x Cue Emotion	Survey x Orienting x Background Emotion	Survey x Conflict x Background Emotion	Survey x Conflict x Background Emotion x Cue Emotion	Survey x Orienting x Background Emotion x Target Visual Field	Survey x Conflict x Background Emotion x Target Visual Field
Pre-Post/Pre+Post														
POMS														
Tension	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Anger	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Depression	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Vigor	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Fatigue	-	-	-	-	-	-	-	-	-	-	-	-	-	-
T-Menstat				-										
Energy	-	+	-	-	-	-	-	-	+	-	-	+	-	-
Fatigue	-	-	-	-	-	-	-	-	~+ (p=.055)	-	-	-	-	-
Irritation	+	-	+	-	-	-	+	-	-	-	+	-	-	-
Sleepiness	-	-	-	-	-	-	-	-	~+ (p=.055)	-	-	-	-	-

Table 3. Interactions of analyses of the proportion change scores of the "weariness" state variables (POMS + T-MENSTAT). A "+" indicates significant interaction involving attention network, emotionality and anxiety; X == not available or range too narrow.

	Orienting x Background Emotion x Cue Emotion	Conflict x Background Emotion x Cue Emotion	Orienting x Background Emotion x Target Visual Field	Orienting x Conflict x Target Visual Field	Survey x Conflict	Survey x Orienting x Conflict	Survey x Orienting x Conflict x Target Visual Field	Survey x Background Emotion	Survey x Cue Emotion	Survey x Orienting x Background Emotion	Survey x Conflict x Background Emotion	Survey x Conflict x Background Emotion x Cue Emotion	Survey x Orienting x Background Emotion x Target Visual Field	Survey x Conflict x Background Emotion x Target Visual Field
Pre														
POMS														
Tension	+		-	-	-	-	-	-	-	-	-	-	-	-
Anger	X	-	X	X	X	X	X	X	X	X	X	X	X	X
Depression	X	-	X	X	X	X	X	X	X	X	X	X	X	X
Vigor	+	-	+	+	+	-	-	-	-	-	-	-	-	-
Fatigue	+	-	+	-	-	-	-	-	-	-	-	-	-	-
T-Menstat														
Energy	+	-	-	~+ (p=.058)	-	-	-	-	-	-	-	-	-	-
Fatigue	+	-	+	+	-	-	-	-	-	-	-	-	-	-
Irritation	+	-	+	-	-	+	+	-	-	+	+	-	+	+
Sleepiness	+	-	+	+	-	-	-	+	-		+	-	-	-

Discussion

The results of Experiment 2B demonstrate that we selected sensitive behavioral measures of “weariness” that are associated with differential contributions both of the attention networks and of the emotionality of the backgrounds/cues when performing the LANT. In particular, we found that participants with low levels of weariness (e.g. Irritation) were more flexible in demonstrating and switching hemispheric asymmetry across test conditions. An important part of our joint research effort is to develop algorithms for automatic detection of “weariness” states and techniques to minimize and to reverse them. Towards that goal, we predict that the state variables that were “behaviorally active” in the analyses above, such as Irritation, will show corresponding electrophysiological correlates using our independent automated analyses of the ongoing EEG during the task.

Appendix F.

Analyses of Fatigue Effects in Mental Arithmetic

A full-text copy of this article is available on-line at http://dx.doi.org/10.4236/psych.2015.65055.
Trejo, L. J., Kubitz, K., Rosipal, R., Kochavi, R. L., & Montgomery, L. D. (2015). EEG-Based Estimation and Classification of Mental Fatigue. *Psychology*, *6*, 572-589.

Psychology, 2015, 6, 572-589
Published Online April 2015 in SciRes. http://www.scirp.org/journal/psych
http://dx.doi.org/10.4236/psych.2015.65055

EEG-Based Estimation and Classification of Mental Fatigue

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Abstract

Mental fatigue was associated with increased power in frontal theta (θ) and parietal alpha (α) EEG rhythms. A statistical classifier can use these effects to model EEG-fatigue relationships accurately. Participants (n = 22) solved math problems on a computer until either they felt exhausted or 3 h had elapsed. Pre- and post-task mood scales showed that fatigue increased and energy decreased. Mean response times rose from 6.7 s to 7.9 s but accuracy did not change significantly. Mean power spectral densities or PSDs of θ and α bands rose by 29% and 44%, respectively. A kernel partial least squares classifier trained to classify PSD coefficients (1 - 18 Hz) of single 13-s EEG segments from alert or fatigued task periods was 91% to 100% accurate. For EEG segments from other task periods, the classifier outputs tracked the time course of the development of mental fatigue. By this measure, most subjects became substantially fatigued after 60 min of task performance. However, the trajectories of individual classifier outputs showed that EEG signs of developing fatigue were present in all subjects after 15 - 30 minutes of task performance. The results show that EEG can track the development of mental fatigue over time with accurate updates on a time scale a short as 13 seconds. In addition, the results agree with the notion that growing mental fatigue produces a shift away from executive and attention networks to default mode and is accompanied by a shift in alpha frequency to the lower alpha band.

Keywords

EEG, Mental Fatigue, Alertness, Drowsiness

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[*]Corresponding author.

Appendix G.

Analyses of Fatigue Effects and EEG Correlates in Experiment 2

We analyzed the extensive EEG data collected during Experiment 2. The objective was to use the APECSgui algorithm for NPLS classification to identify multiway atoms that accurately track mental fatigue during performance of the eLANT task of Experiment 2. NPLS finds the multiway atoms defined similarly to PARAFAC atoms in terms of spatial, spectral and temporal loadings, but the atoms are selected with respect to a training criterion. In this case the criterion was a set of representative EEG segments taken during very early or late times on the task to accurately reflect alert and fatigue states.

We tested a total of 25 participants, of which a subset of 10 participants repeated the test session on a second day. A session consisted of five segments, 1) rest with eyes closed one minute, 2) rest with eyes open one minute, 3) a one-hour performance of the eLANT using two emotional spatial cues (happy or angry faces) and two emotional backgrounds (happy couple or a fierce shark), 4) rest for one minute with eyes closed, 5) rest for one minute with eyes open. We continuously recorded 64 channels of EEG and four channels of EOG using a Biosemi Active Two system during each of the five segments.

Methods

Preprocessing

- EEG artifacts were detected by a trained analyst and excluded in the analysis
- We manually labeled breaks between blocks of LANT within a session
- A spherical Laplacian was applied to emphasize local EEG sources and reduce volume conduction effects
- EEG recordings at 512 Hz were down-sampled to 128 Hz
- Segments consisted of 4 sec non-overlapping windows
- A 60 Hz notch filter was applied
- We computed the power spectral density functions using log power units by FFT (nFFT = 512, window: Hann) for echo segment
- The considered frequency range was 5 to 25 Hz.
- In all cases the same training strategy was used: an early 5 minute interval to represent alert states (1st to 6th minute) versus a late 5 minute interval to represent fatigued states (e.g. if the overall length of the LANT session was, e.g. 54.2 min, then the time between 49th to 54th minute was used for training but not the last 0.2 min of EEG).
- We used the training intervals to train a 4-atom NPLS model and computed the atom scores for all segments (but also submodels with 1, 2 , and 3 NPLS components were usually checked).
- We then used the computed NPLS atom scores to classify low and high fatigue using linear discriminant analysis, or LDA, which was trained using the training interval data
- We focused the analyses on the 10 subjects for whom we had both day 1 and day 2 LANT data. These are: 100, 101, 102, 103, 104, 105, 107, 110, 113, 999
- We computed the coefficient of variation (CV) of the reaction times, or RT, using a moving window of 10 values considered for each CV point. The first 10 values of RT were ignored after beginning of each break within the single LANT session.

- If there were more than one RT (CV) within an epoch an average of RTs (or CV values) is taken for the given epoch.

Results

As this was exploratory research that has never been attempted before, we used many different strategies of combining different subjects, sessions. We now report the results that we found most interesting.

Models trained on a single subject and a single LANT session. In almost all cases this worked reasonably well and it shows the fatigue changes one would expect. But we need to be careful because we train within the same session.

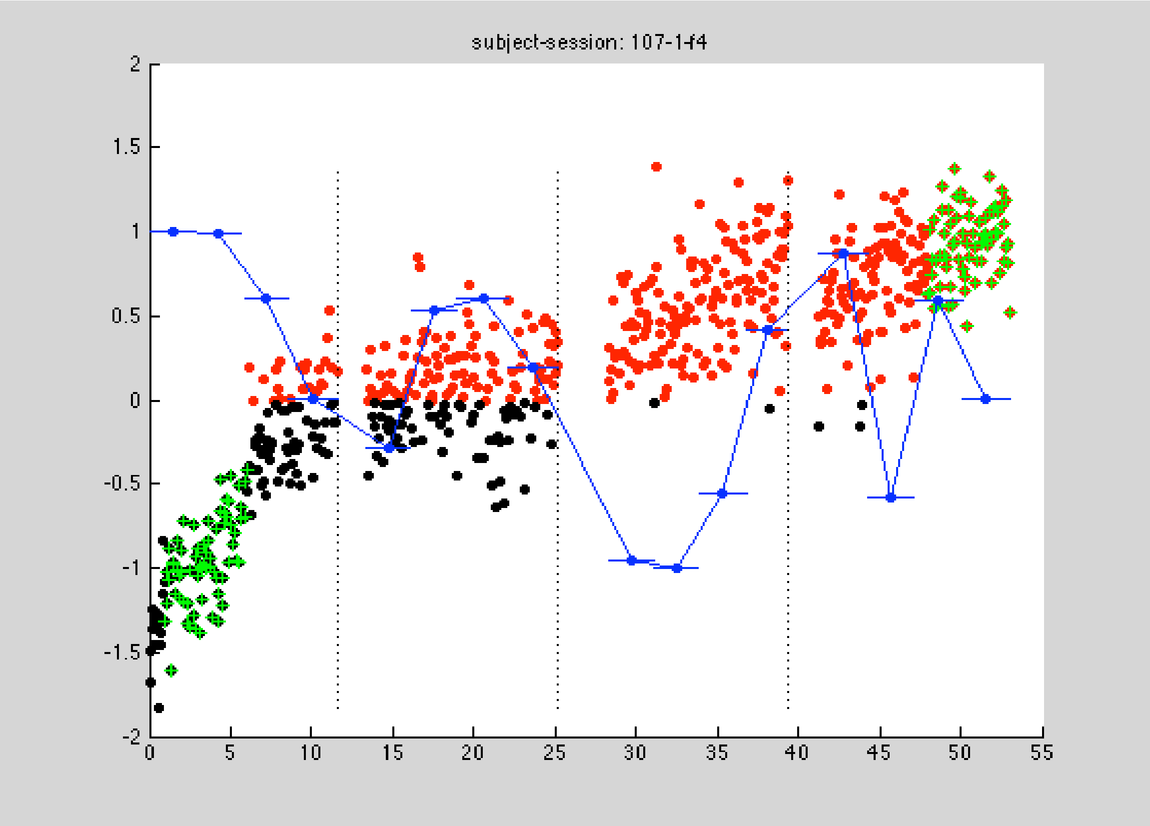

Fig. 1. S107, train: day1, test: day1, 4-atom NPLS. Vertical dotted lines indicate the beginning of breaks within the session. Green points are training data, **Black points** are predicted fatigue values belonging to the low fatigue class data and red points are predicted fatigue values belonging to the high fatigue class data as classified by LDA which was trained on green predicted fatigue values. Blue line is the coefficient of variation (CV) of the RT (10 values considered for each CV point) and 10 values of RT were ignored after beginning of each break within the single LANT session. If there is more than a single RT (CV) within an epoch an average of RTs (or CV values) is taken for the given epochs. Every block was divided into quarters and an average of CV values for a quarter was computed, these are short horizontal blue lines, dot on the lines serve only for connecting these quarter-based values for better visualization. Note that the EEG-based NPLS model tracks the development of fatigue in Block 1 and shows a leveling off of fatigue in Blocks 2-4. EEG-estimated fatigue seems largely unrelated to the variation in RT over blocks.

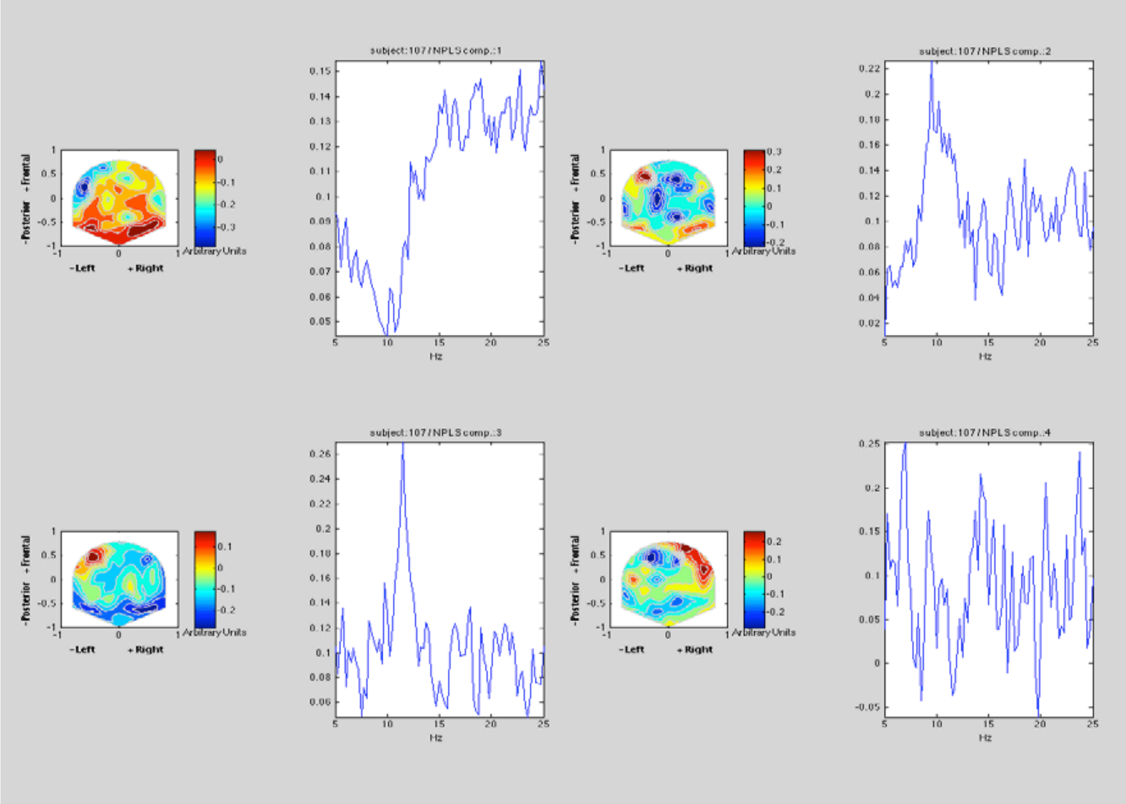

Fig. 2. The spatial and spectral loadings of the four NPLS atoms used in the model illustrated for S107 in Figure 1. The layout order of the atoms is matrix based: atom 1- (1,1), 2 - (1,2), 3 - (2,1), 4- (2,2)). Note that atom 1 has an occipital focus with a spectral dip near 10 Hz and may reflect alpha band activity. Atoms 2 and 3 have left frontal involvement and also show peaks in lower and upper alpha bands.

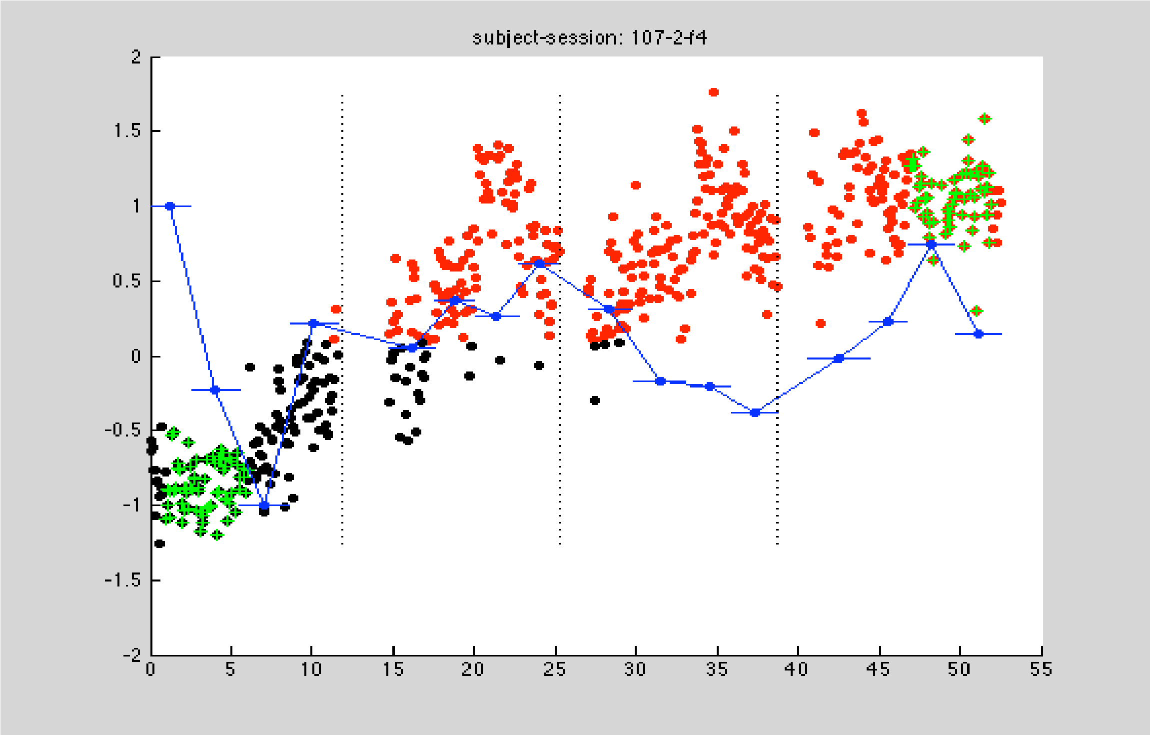

Fig. 3. S107, train: day2, test: day2, 4 NPLS. Conventions are the same as in Figure 1. As when training with day 1 data, the EEG-based NPLS model tracks the development of fatigue in Block 1 and shows a leveling off of fatigue in Blocks 2-4. Again, EEG-estimated fatigue seems largely unrelated to the variation in RT over blocks.

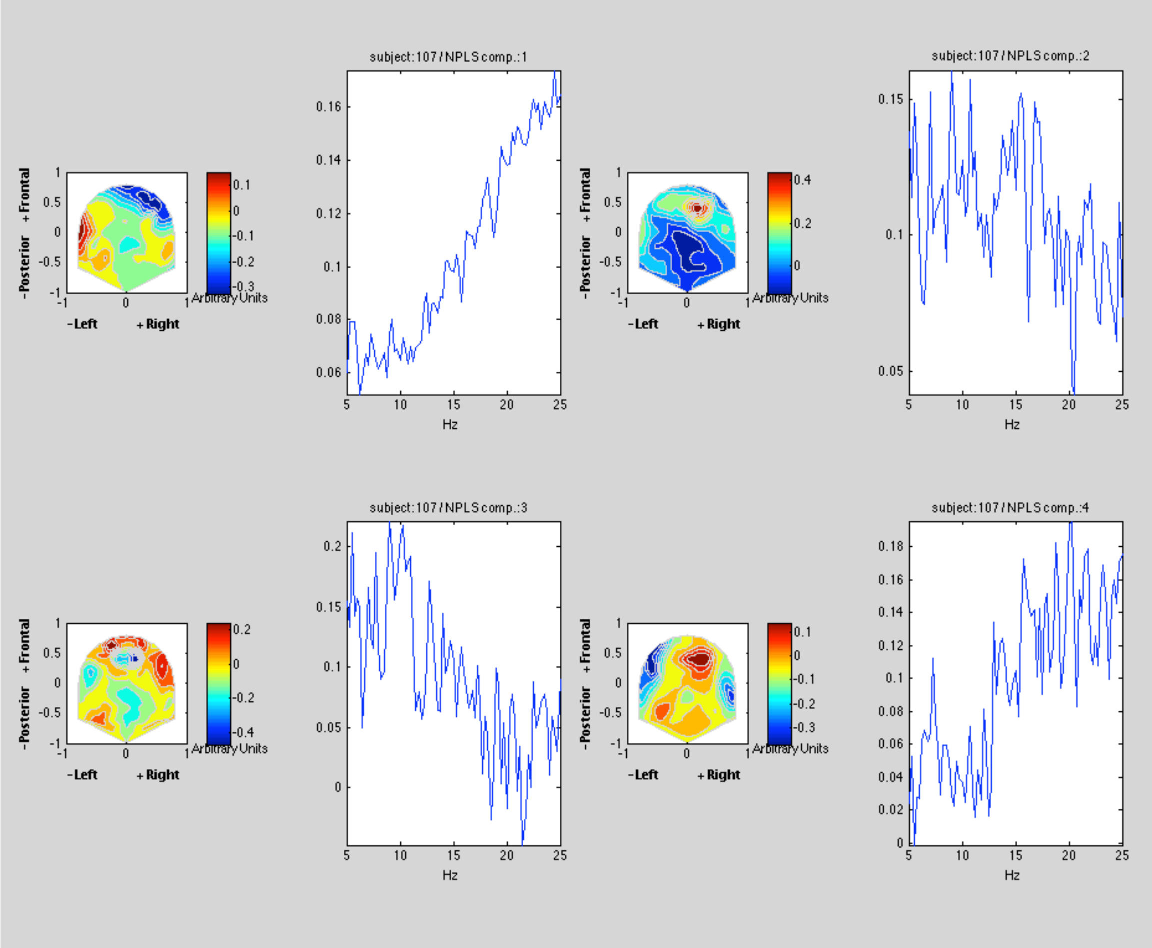

Fig. 4. The spatial and spectral loadings of the four NPLS atoms used in the model illustrated for S107 in Figure 3. Note that atoms for this analysis were trained using day 2 data and have a different focus and spectra than those for training with day 1 data in Figure 2. Atom 1 is broad band and may reflect EMG activity on day 2. Atoms 2 and 3 show high loadings in the alpha band and atom 4 shows a dip in the alpha band.

Models trained on a single subject both days LANT.

These models also appear to be successful. As an example, we show subject 107 again.

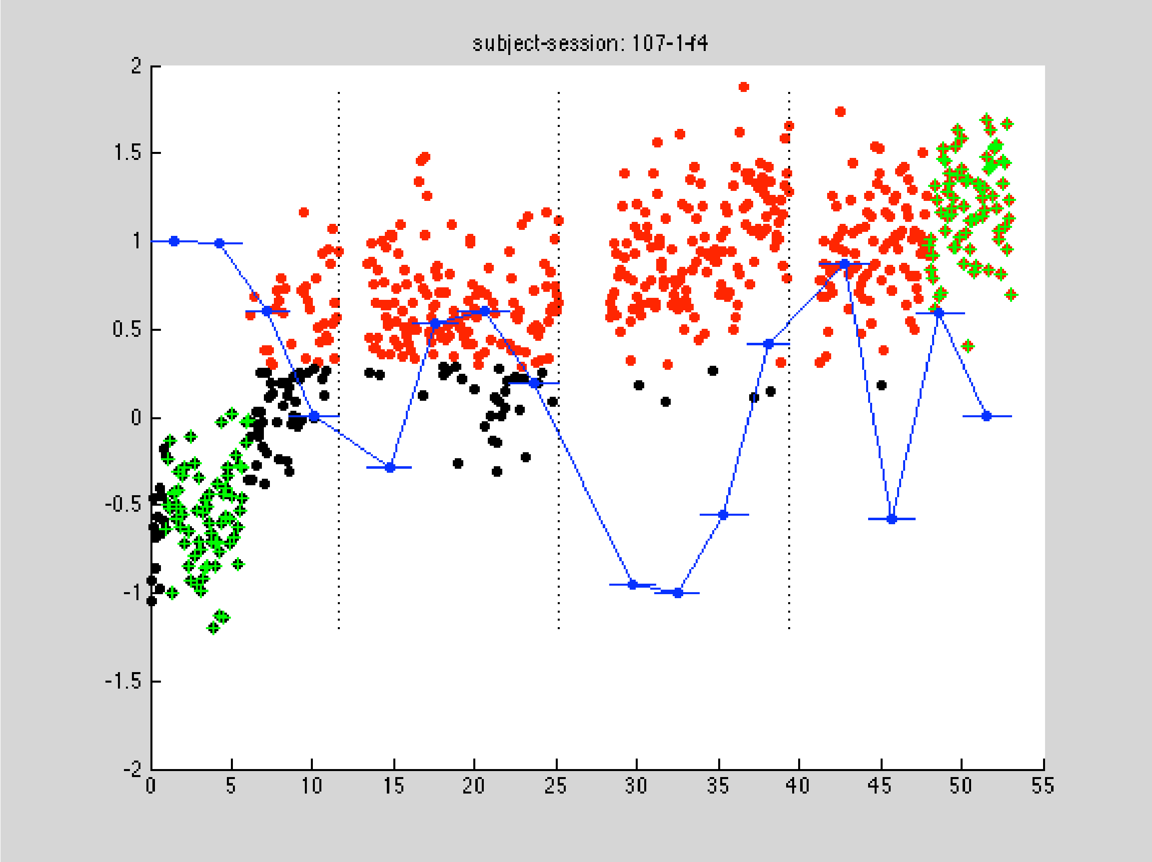

Fig 5: S107, train: day1 + day2, test: day1, 4 NPLS. Conventions are the same as in Figure 1. As when training with day 1 or day data alone, the EEG-based NPLS model tracks the development of fatigue in Block 1 and shows a leveling off of fatigue in Blocks 2-4. Again, EEG-estimated fatigue seems largely unrelated to the variation in RT over blocks.

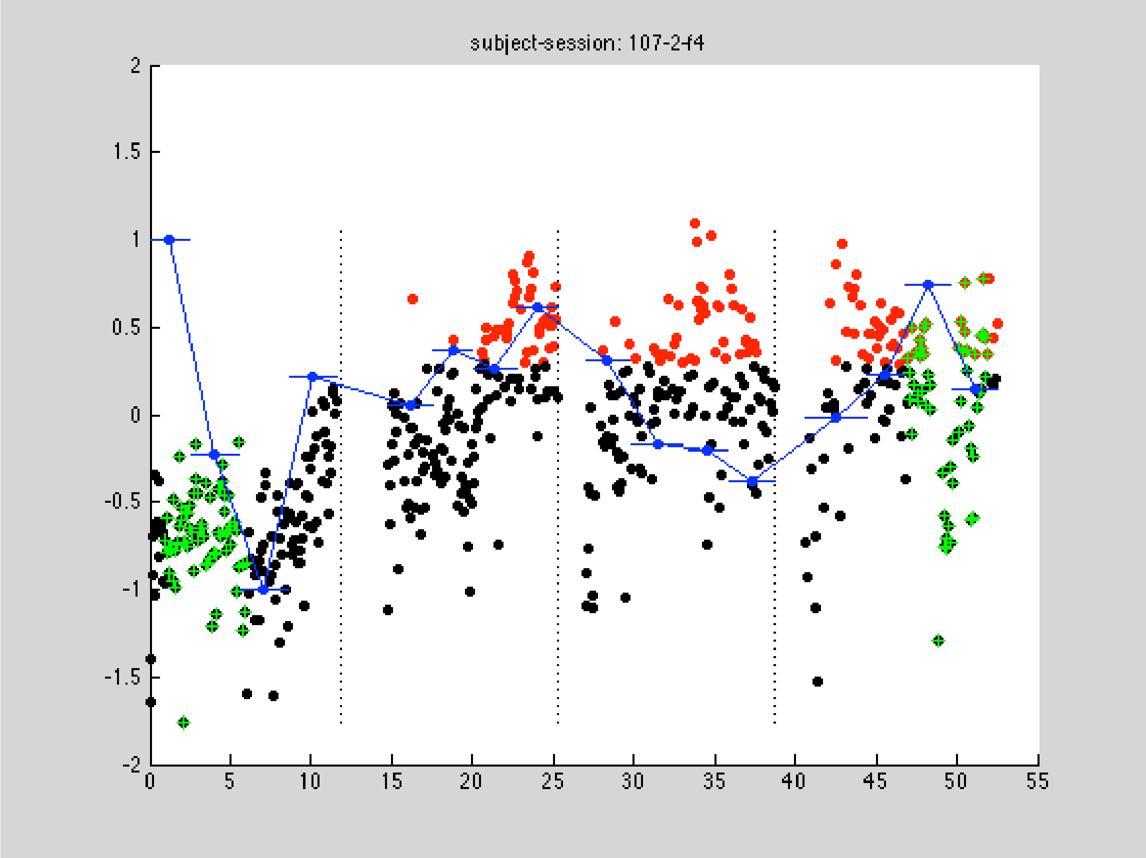

Fig. 6. S107, train: day1 + day2, test: day2, 4 NPLS. Conventions are the same as in Figure 1. As when training with day 1 or day data alone, the EEG-based NPLS model tracks the development of fatigue in Block 1 and shows a leveling off of fatigue in Blocks 2-4. In this case, EEG-estimated fatigue seems correlated with the variation in RT over blocks.

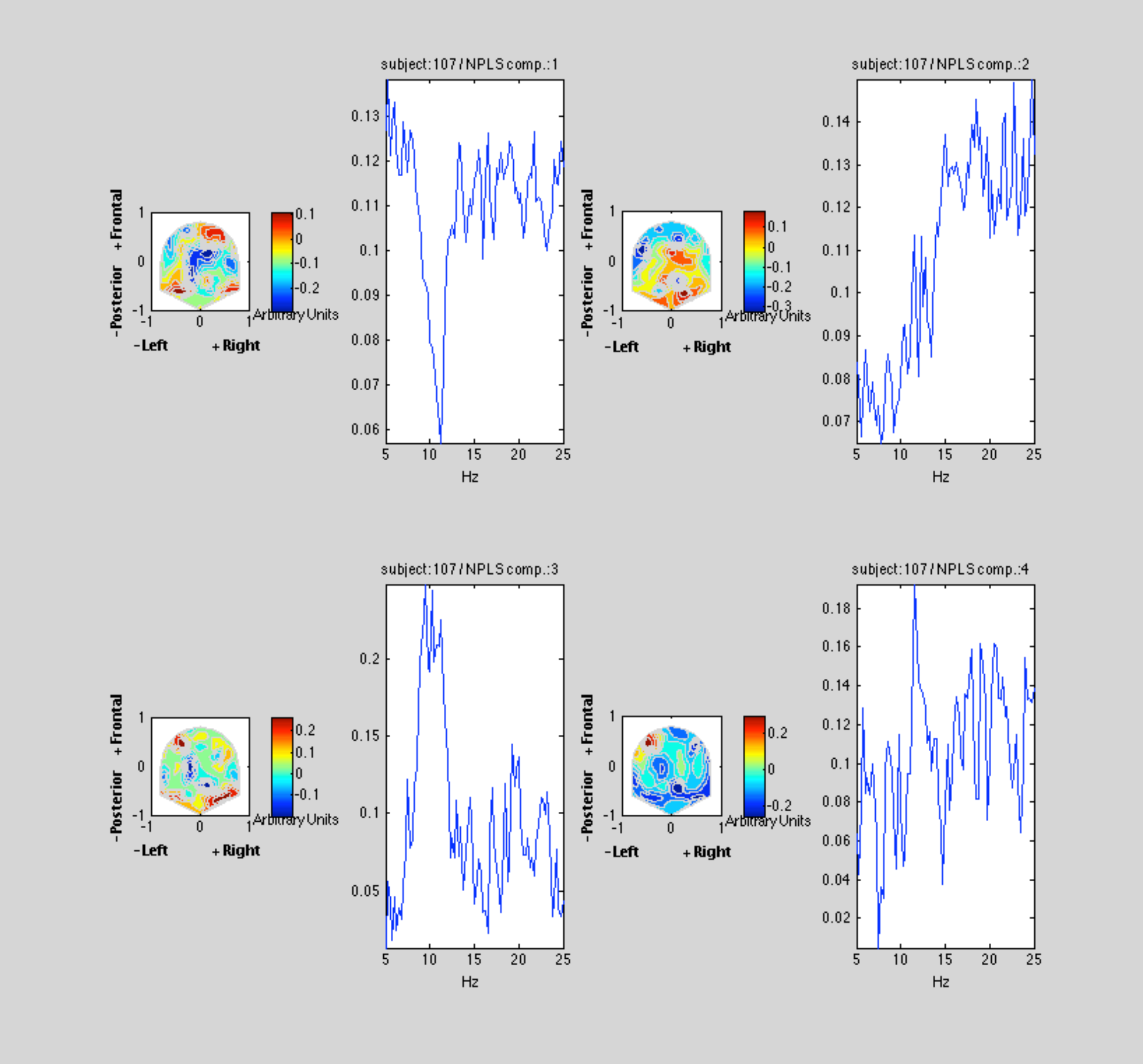

Fig. 7. The spatial and spectral loadings of the four NPLS atoms used in the model illustrated for S107 in Figures 5 and 6. Note that atoms for this analysis were trained using day 1 + day 2 data and have a different focus and spectra than those for training with day 1 data or day 2 data alone. The atom spectra are more highly focused in frequency with Atoms 1, 3 and 4 showing high loadings in the alpha band and atom 2 showing broad-band power suggestive of EMG.

Models trained on a single subject by taking one day for training and predicting the other day. This does not work that well for all subjects but it works quite well for some. Here we show results for S103.

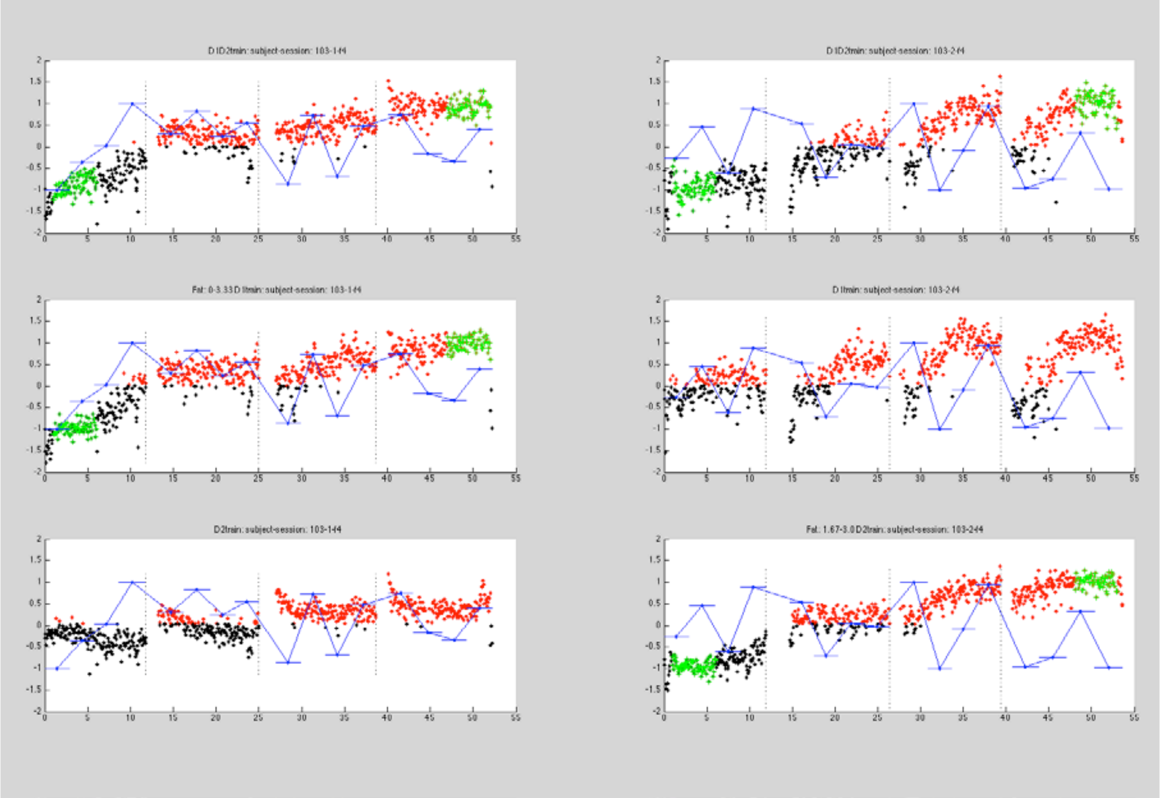

Fig. 8. S103. Training with both days compared to training with a single day to predict fatigue on both days. Green points mark data used for training, Layout: *Top row:* train: day1 + day2, test: day1, day2, 4 NPLS. *Middle row:* train: day1, test: day1, day2, 4 NPLS. *Bottom row:* train: day2, test: day1, day2, 4 NPLS.

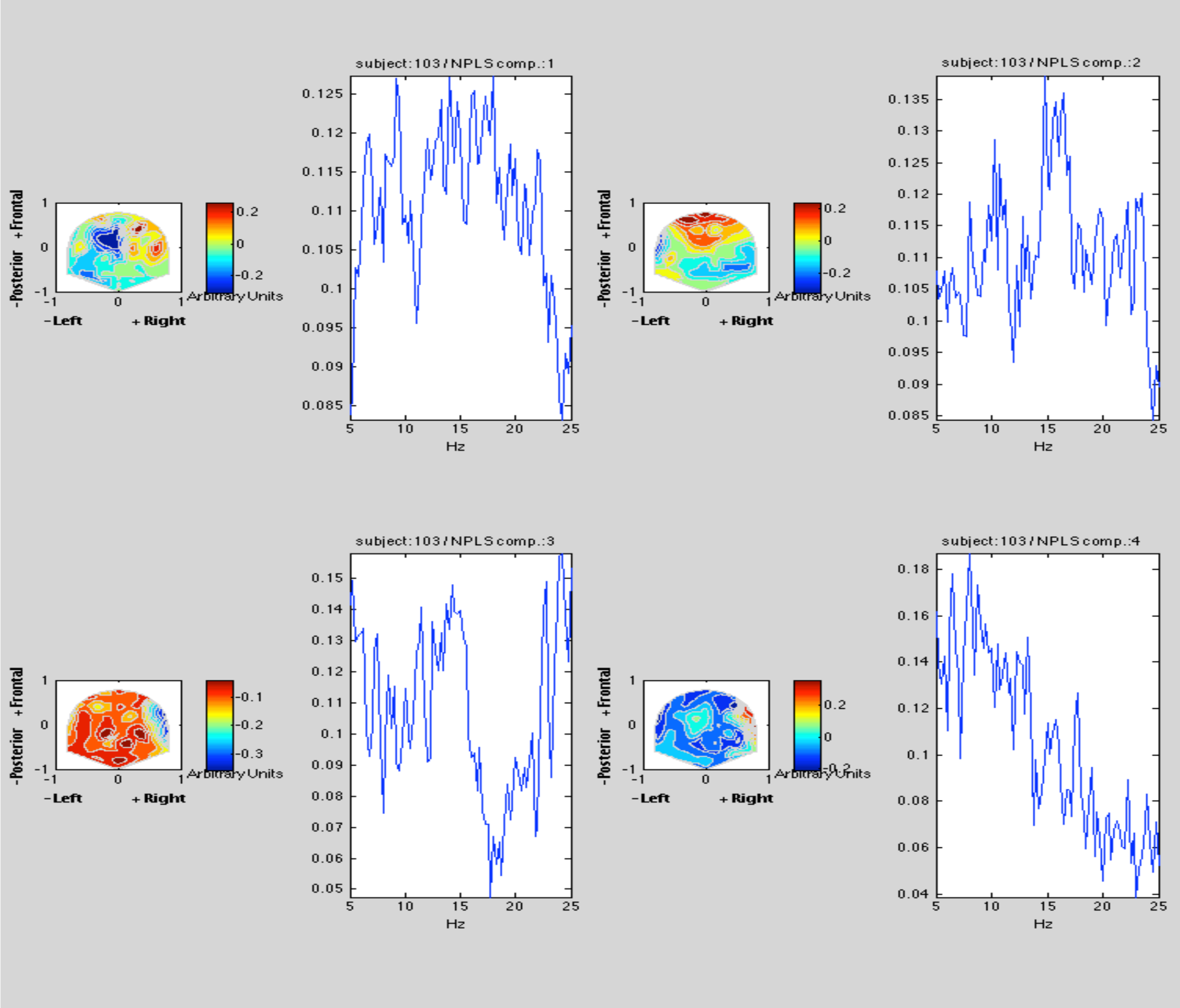

Fig. 9. These are the NPLS atoms for the first row of Fig. 8; that is day1 + day2 training.

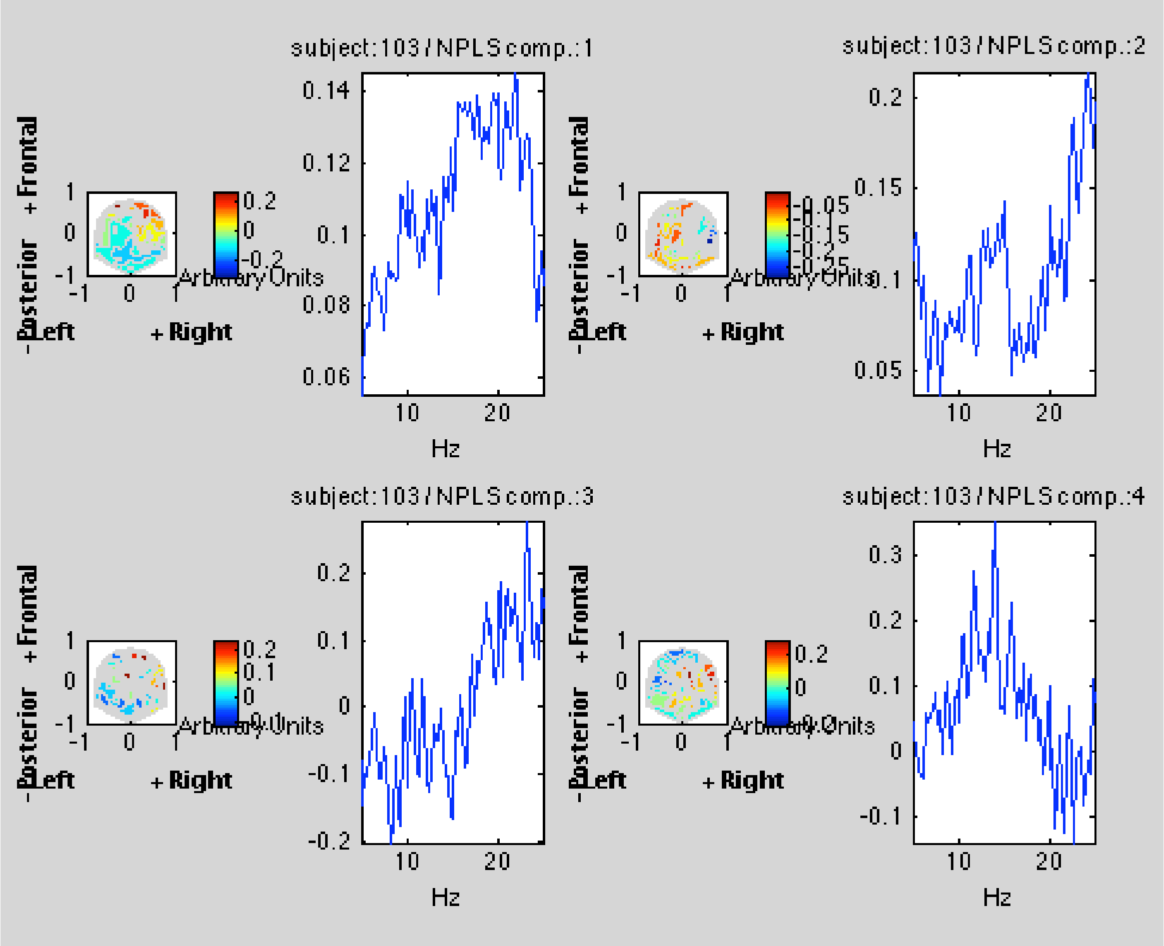

Fig. 10. These are the NPLS atoms for the second row of Fig. 8; that is day1 training.

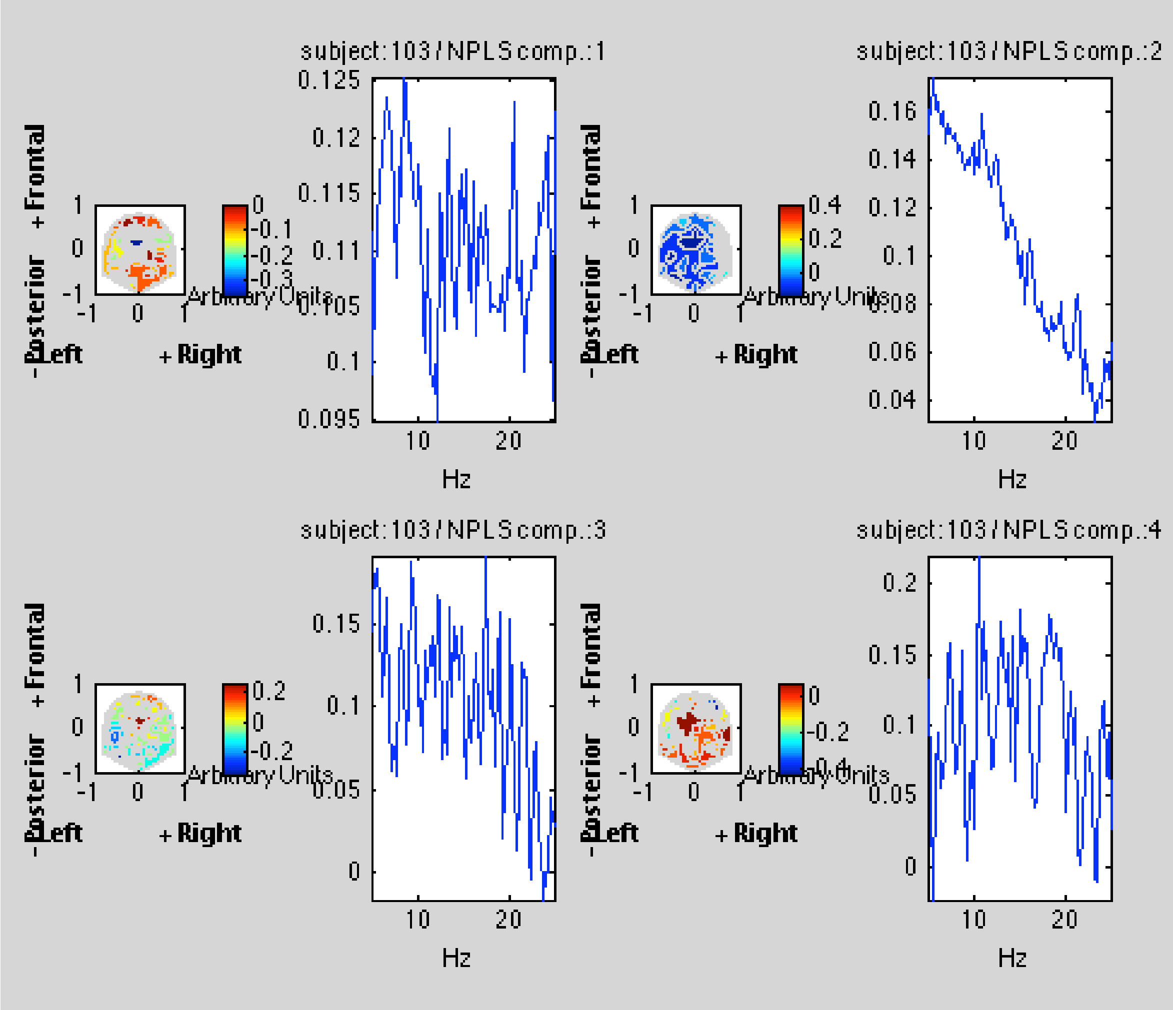

Fig. 11. These are the NPLS atoms for the third row of Fig. 8; that is day2 training.

Models trained by grouping subjects based on their T-MENSTAT fatigue scores at the beginning and end of the LANT session. **We ran** many different settings here, with 'better' or 'worse' results but overall this needs more work to get some consistent results. We report the case when we grouped data from day1 (first LANT session) of 5 subjects 100, 101,102, 105 and 107. This grouping was driven by the following criterion: T-MENSTAT fatigue of all 5 subjects was < 3.33 prior to the LANT and T-MENSTAT fatigue of all 5 subjects was > 5.67 post LANT. The list of fatigue scores was: S100 (pre – 2.00, post – 5.67); S101 (3.67, 6.33), S102 (0.33, 6.33), S105 (2.00, 5.33) and S107 (3.33, 6.67).

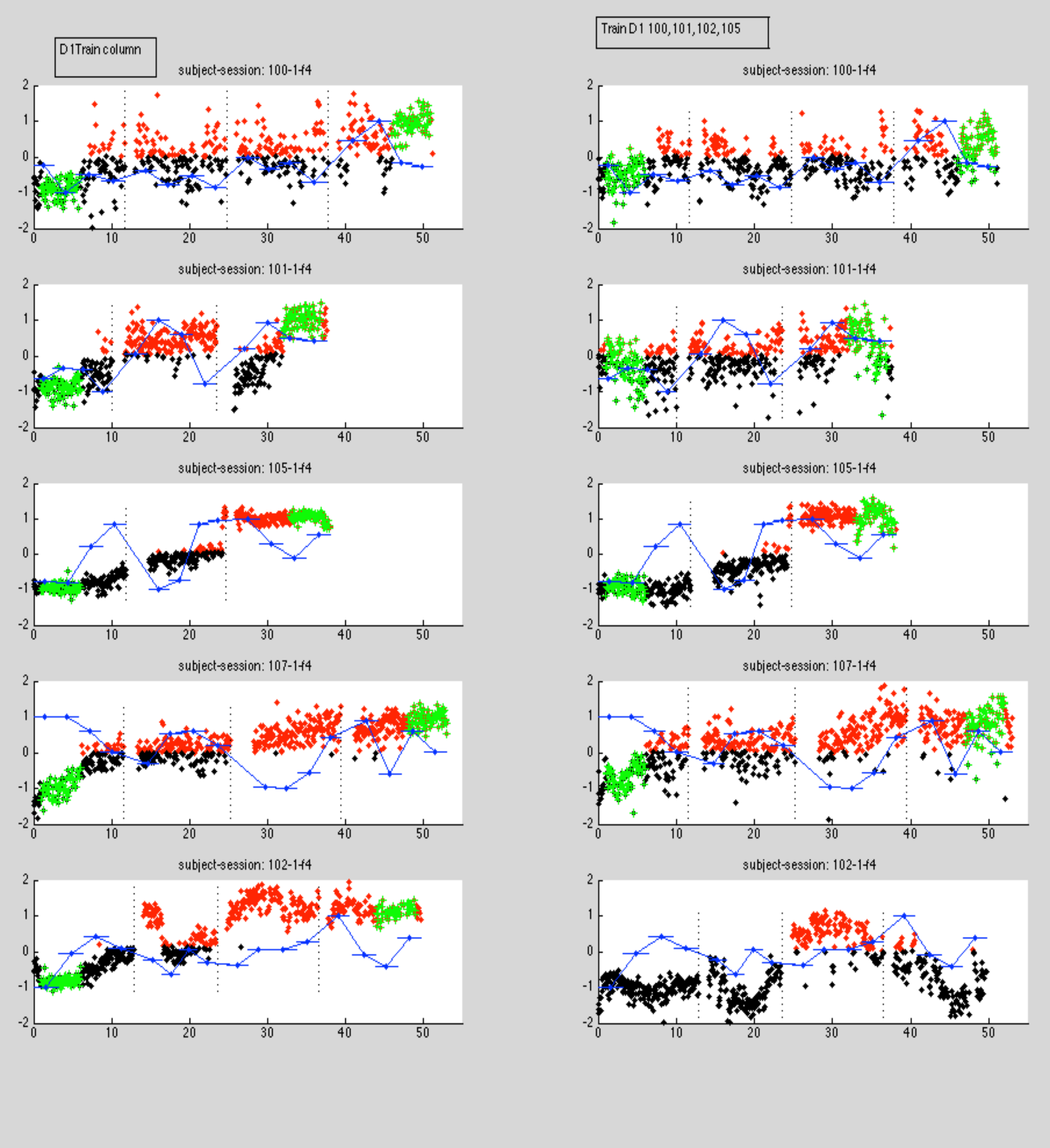

Fig. 12. Training with data from 5 subjects (100, 101, 102, 105, 107), day 1, T-MENSTAT fatigue pre < 3.33, T-MENSTAT fatigue post > 5.67. 4 NPLS components. *Left column:* first and last 5 min (green points) from all subjects were used to train the model, the other points were predicted. *Right column:* first and last 5 min (green points) from 4 subjects (all but 102) were used to train the model, that means 102 data were never seen during training, predictions for this subject are in the last row, right column (compare with the left column where the first and last 5 min of this subject were included in the training set). Leaving one subject out of the NPLS model had a negative effect on prediction accuracy for this subject but the model still captured the high fatigue condition in Block 3 and the relatively low fatigue condition in Block 2, or the two blocks that did not contribute training data to the model.

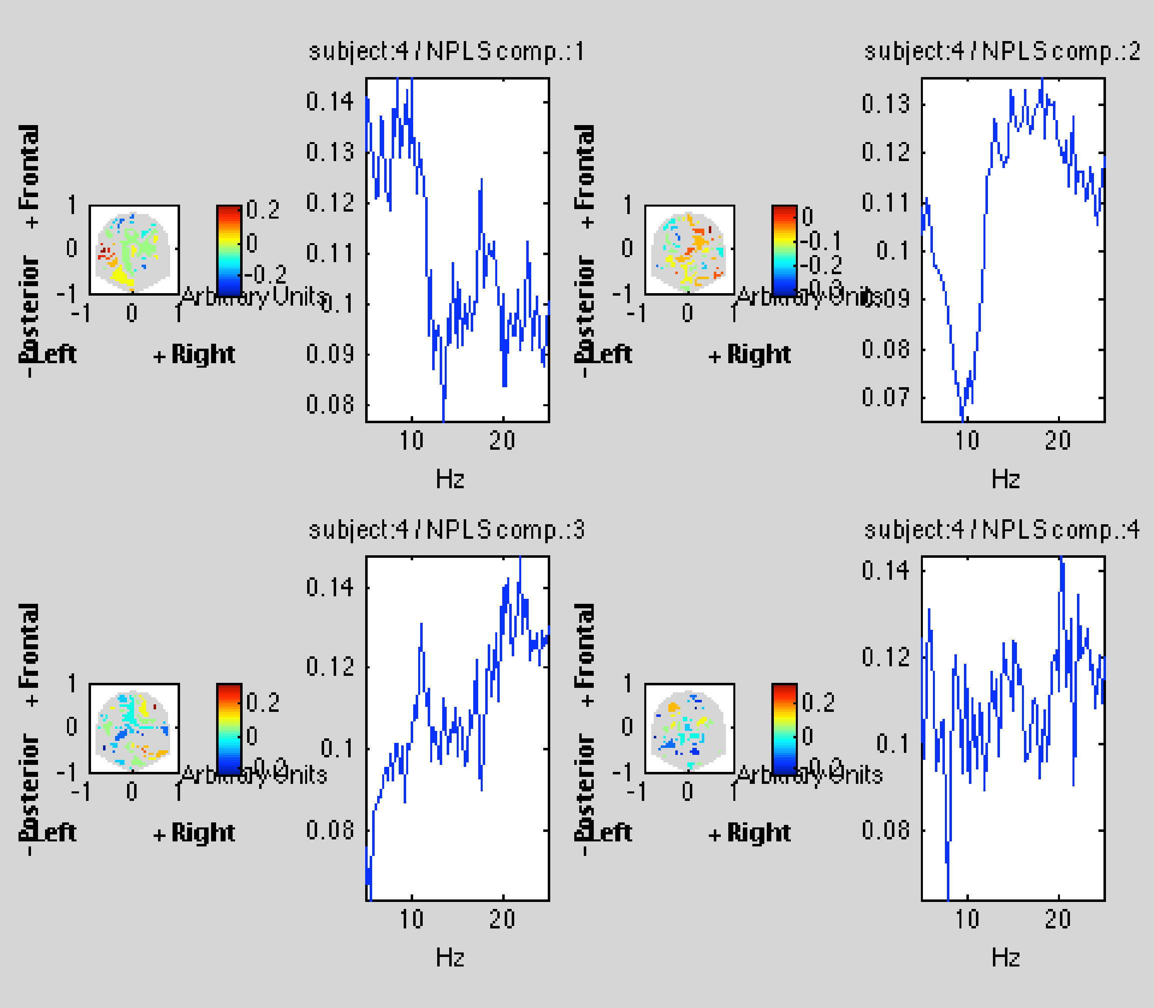

Fig. 13. These are the NPLS atoms for the left column of Fig. 12; that is training using the first and last 5 min of day1 data of subjects 100, 101,102, 105, and 107. Note that atom 1 shows high loadings in the theta band whereas atom 3 shows a focused dip in the loadings in the alpha band.

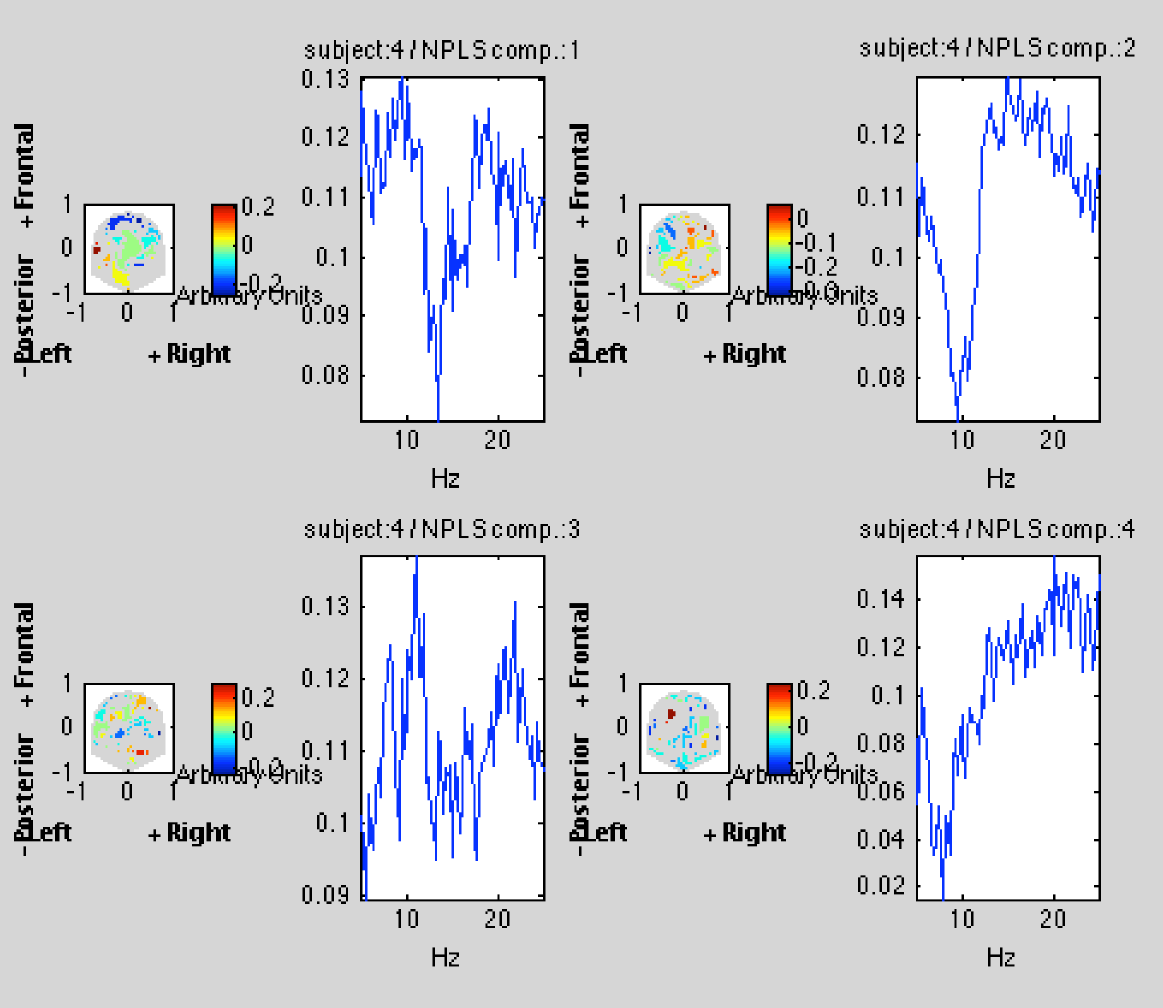

Fig. 14. These are the NPLS atoms for the right column of Fig. 13; that is training using the first and last 5 min of day1 data of subjects 100, 101,102, 105 but not 102. Note that leaving one subject out did not greatly change the spatial and spectra loadings of the atoms in the model. Several atoms show peaks or dips in the loadings in the alpha and theta bands.

Conclusions

These analyses show that using the APECS NPLS algorithm to develop classifiers for fatigue can lead to useful EEG-based models of fatigue. The results generally agree with our findings in mental arithmetic, that most subjects begin to experience fatigue in a s few as 15 minutes on task. In addition, atoms with loadings focused in the alpha and theta bands were important. While the direction of loadings can be peaks or dips in this band, one must keep in mind that in a classifier both peaks and dips are important, as they interact with the sign of the LDA model coefficient to yield an overall classification result.

As we may expect, we observe that training with same-day data in single subjects leads to the most successful models. However, interestingly, models derived from on day's data can successfully predict EEG-based estimates of fatigue on another day.

Perhaps most surprisingly, a model that used several subject's combined data was successful in predicting fatigue in the individual subjects whose data entered the model. And using four subjects' data to predict fatigue in a fifth subject was also moderately successful.

Considerably more analysis, which is beyond the scope of this contract, will be needed to understand the physiological significance of the atoms entering these models. Also we need to survey more subjects and tasks systematically. Nevertheless we may conclude that single-subject and normative NPLS models of mental fatigue for cognitive tasks can be developed successfully and applied generally across time and subjects.

Appendix H.

Analyses of EEG biofeedback effects on LANT performance, EEG SMR atoms, and event-related potentials (Experiment 3, UCLA)

Demonstrating conditioning in individual participants

1. Rationale: three-prong approach
    a. Use clinical and theoretical expertise to determine protocol and evaluate training/conditioning (Barry Sterman)
    b. EEG Monitoring (Len Trejo and Roman Rosipal)
        i. Concurrent EEG monitoring of training and of cognitive assessment (attention networks)
        ii. Automated discovery of EEG atoms (PARAFAC)
    c. Improved site-of-action analysis: Revised LANT (Eran Zaidel)
        i. Four target positions (allows for distinguishing invalid cueing within each hemisphere and between them)
        ii. New Conflict measure (geometric shapes)
2. Redesign
    a. Longer training (number of sessions>10)
    b. Follow-up four individual participants for many sessions (2 C3 and 2 C4)
    c. If C3 and C4 training produces contrasting results, use ABA procedure with the best responder. For example, for Subject 004, A = C3 SMR and B = C4 SMR.
    d. Use a well-established paradigm (Theta down/SMR up)
3. Procedure
    a. Participants
        i. Subject 006: C3 SMR
            01. No Conditioning
        ii. Subject 014: C4 SMR
            01. In progress
        iii. Subject 005: C4 SMR
            01. No conditioning
        iv. Subject 004: C3 SMR
            01. The results and discussion for this subject are described next.
    b. Conditioning with NeuroNavigator 2 (Barry Sterman)
        i. A session consists of ten rounds lasting two minutes each.
        ii. The feedback consists of a display showing if the four conditions are simultaneously satisfied.
        iii. The software produces a record of conditioning by round for each session.
        iv. We developed an algorithmic assessment of (a) conditioned sequence(s) of rounds in each session (see Figure 3.b.2). This procedure incorporates the number of rewards per round, the pattern of SMR bursts, and the absence of muscle noise. The algorithm is currently being programmed as part of the protocol.

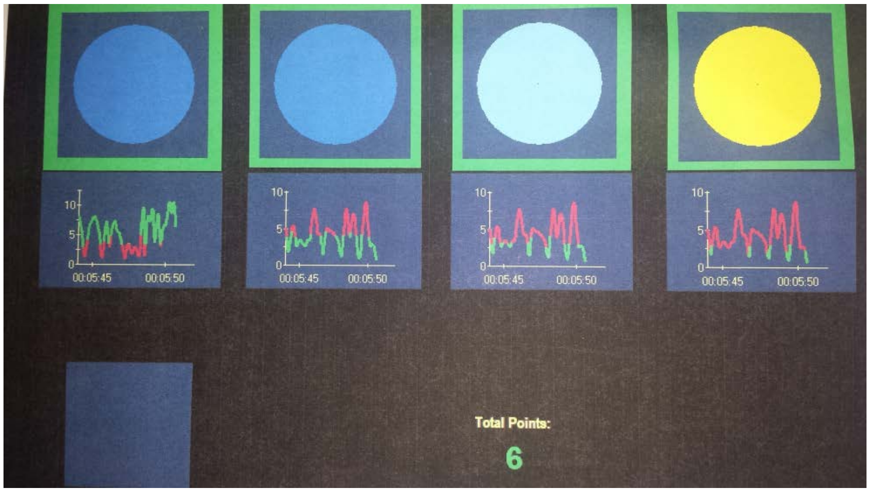

Figure 3.b.1

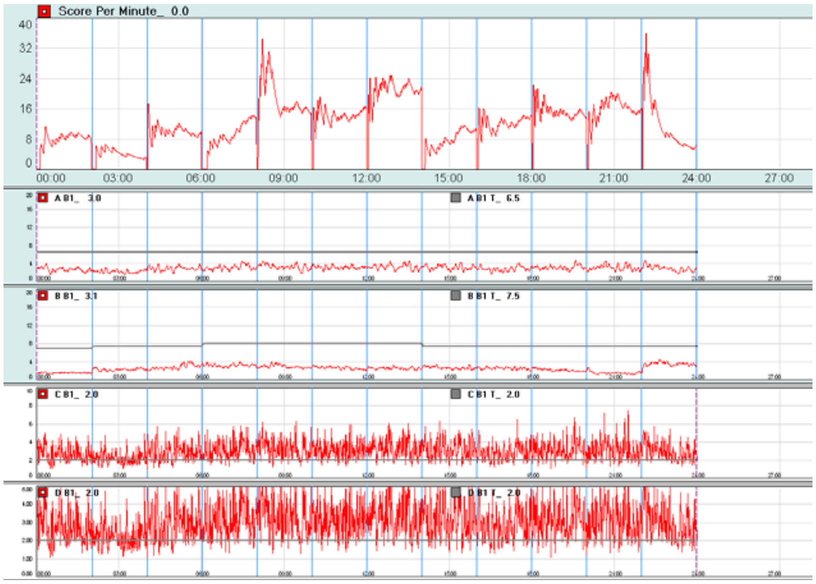

Figure 3.b.2

RESULTS AND DISCUSSION OF SUBJECT 004

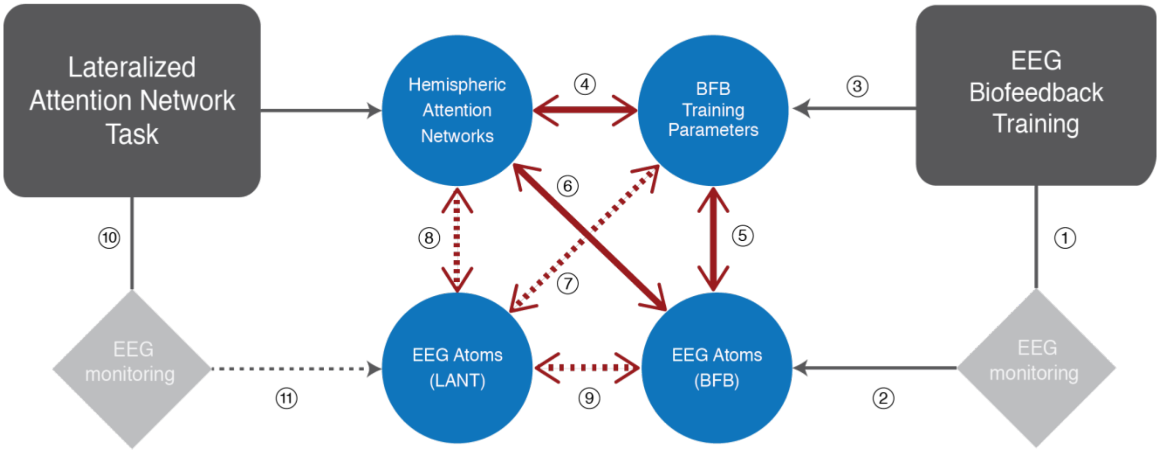

Figure 1: Schematic of the steps taken for analyzing subject 004

1. EEG BF Training vs. Hemispheric Attention Networks

1.1 Results

We correlated the training parameters of the conditioned sequences with the measures of hemispheric attention network across sessions. Significant correlations are summarized in Table 1.1. We further examined whether a significant correlation indicated a monotonically increasing/decreasing function across session (correlation with ordinal session number).

Table 1.1: EEGBF Training Parameters vs. Hemispheric Attention Networks

	Attention Measure	Correlation with Ordinal Session
Current:	Left Hand-RVF-Conflict	+
	Left Hand-LVF-Orienting Within	-
	Block 1-Left Hand-LVF-Orienting Within	-
	Block 1-Right Hand-RVF-Orienting Within	-
	Block 2-Left Hand-RVF-Orienting Within	+
	Block 2-Left Hand-RVF-Conflict	-
	Block 2-Right Hand-RVF-Orienting Between	-
Previous:	Left Hand-LVF-Orienting Between	+
	Right Hand-RVF-Conflict	-
	Block 1-Left Hand-LVF-Orienting Within	-
	Block 1-Right Hand-RVF-Conflict	-
	Block 1-Right Hand-LVF-Orienting Within	-
Next:		

Consider first the correlation between the current EEG Biofeedback training session and the measure of hemispheric attention immediately following it. When combining the first and second block, two measures of hemispheric attention correlated significantly with a training parameter of a conditioned sequence (Left Hand-RVF-Conflict and Left Hand-LVF-Orienting Within). However, only one of them (Left Hand- RVF- Conflict) showed a significant correlation with ordinal session number (See Figures 1.1 and 1.2). When separating the first and second blocks, five measures of hemispheric attention correlated significantly with a training parameter of a conditioned sequence. However, only one of those (Block 2-Left Hand-RVF-Orienting Within) correlated significantly with ordinal session number (See Figures 1.3 and 1.4).

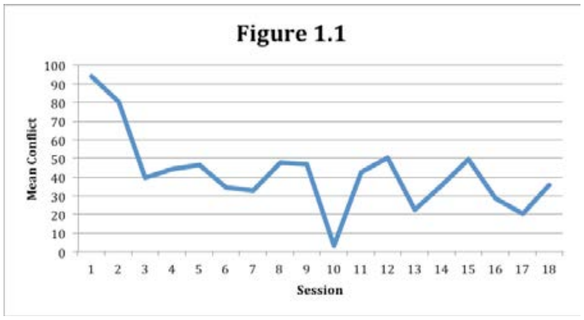
Figure 1.1

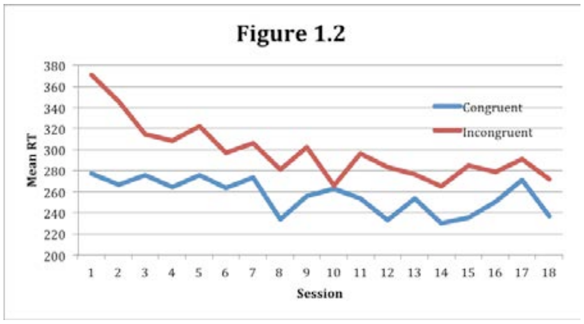
Figure 1.2

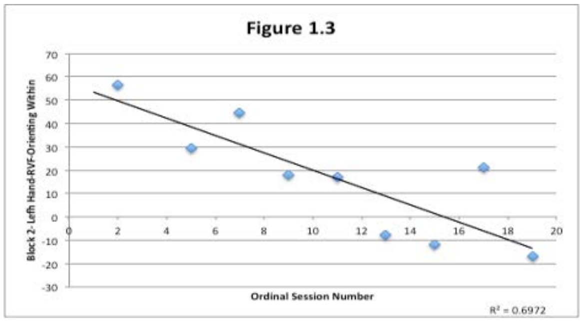
Figure 1.3

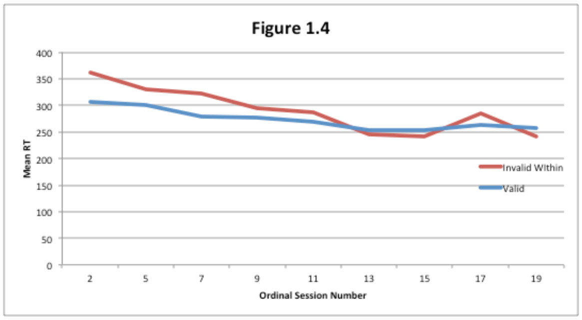
Figure 1.4

Consider next the correlation between the previous EEG Biofeedback training session and the measure of hemispheric attention immediately following the current session. When combining the first and second block, two measures of hemispheric attention correlated significantly with a training parameter of a conditioned sequence of the previous session. However, only one of those (Left Hand-LVF-Orienting Between) showed a significant correlation with ordinal session number (See Figures 1.5 and 1.6). When separating the first and second block, three measures of hemispheric attention correlated significantly with a training parameter of a conditioned sequence of the previous session. However, none of those correlated significantly with ordinal session number.

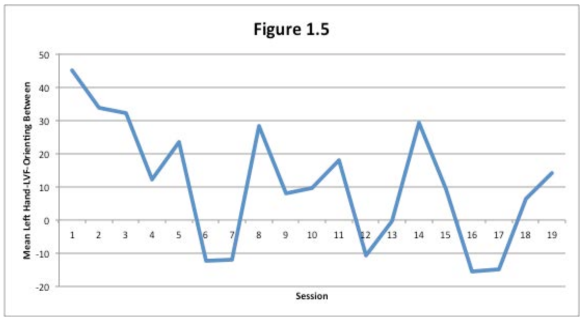
Figure 1.5

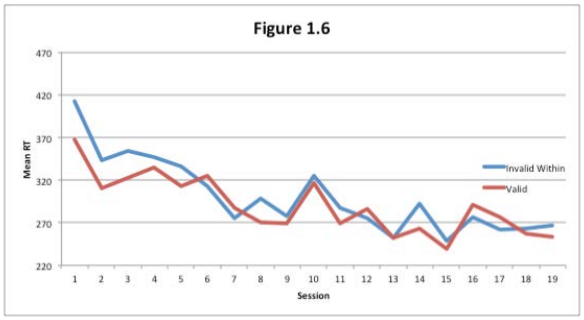
Figure 1.6

1.2 Discussion

The significant correlation between a training parameter and a hemispheric attention network shows that the training had a definite effect on hemispheric attention. In fact, the data suggests that training is selectively effective for pure hemispheric conditions (current trials: 2 out of 4 for intrahemispheric conditions vs. 3 out of 8 for interhemispheric conditions; previous trials: 2 out of 4 for intrahemispheric conditions and 2 out of 8 for interhemispheric conditions). However in only two cases did the correlation indicate a systematic change in hemispheric attention across sessions (see Figures 1.1 and 1.2). The fact that some hemispheric attention measures showed significant correlation with the previous session analysis but not with the current session analysis suggests that the former requires a longer consolidation time.

Significant correlations between the training parameters and some LANT measures indicate that training created a stable change in the cortical networks that underlie hemispheric attention. However, from a clinical point-of-view, the goal is to show a systematic, monotonic change in some measure of hemispheric attention as a function of the number of training sessions. We found this pattern in only one out of twelve unblocked possible correlations involving current trial measures (a ratio of 0.083), in one out of twenty-four blocked possible correlations involving current trial measures (a ratio of 0.042), and one out of twelve unblocked possible correlation involving previous trial measures (a ratio of 0.083). None of those ratios are significantly above chance.

1.3 Conclusion

Our results show that training has definite effects on the hemispheric networks of attention. However, training showed clinically significant (cumulative) effects on attention in only few cases. The reason may be that the critical effects of training are not expressed directly in the measures of our version of the LANT. Another possibility is that there is another critical change in the EEG (e.g. the divergence or convergence of the SMR 1 and the SMR 2 atoms, see below), which is not simply affected by our training protocol.

2. From EEG Monitoring to SMR Atoms of EEG Biofeedback Training

2.1 Results

We applied the PARAFAC discovery procedure to the EEG record during training as well as with eyes open before and after training. We discovered two SMR atoms, both narrowly centered at 13 Hz. The first atoms, SMR 1, showed a scalp distribution with a maximum at C4. SMR 2 showed a bilateral distribution with maximums at FC5 and C4, larger at FC5 (See Figure 2.1).

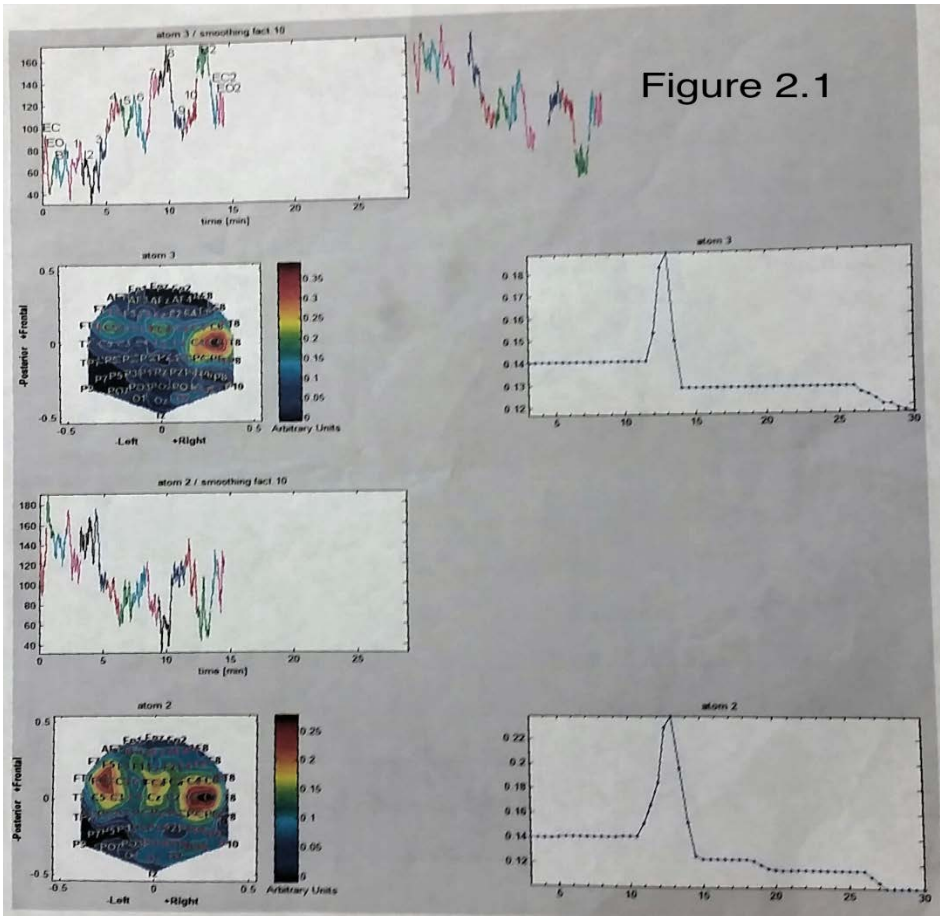
Figure 2.1

The average training session showed little difference between the amplitudes of SMR 1 and SMR 2 with eyes closed either before or after the training. However, there was a substantial difference between the two atoms with eyes open both before and after the training. Before the training session with eyes open, SMR 2 was larger than SMR 1 while, following the training session with eyes open, SMR 1 was larger than SMR 2 (See Figure 2.2). The increase in SMR bursts during conditioning may reflect Post-Reinforcement Synchronization.

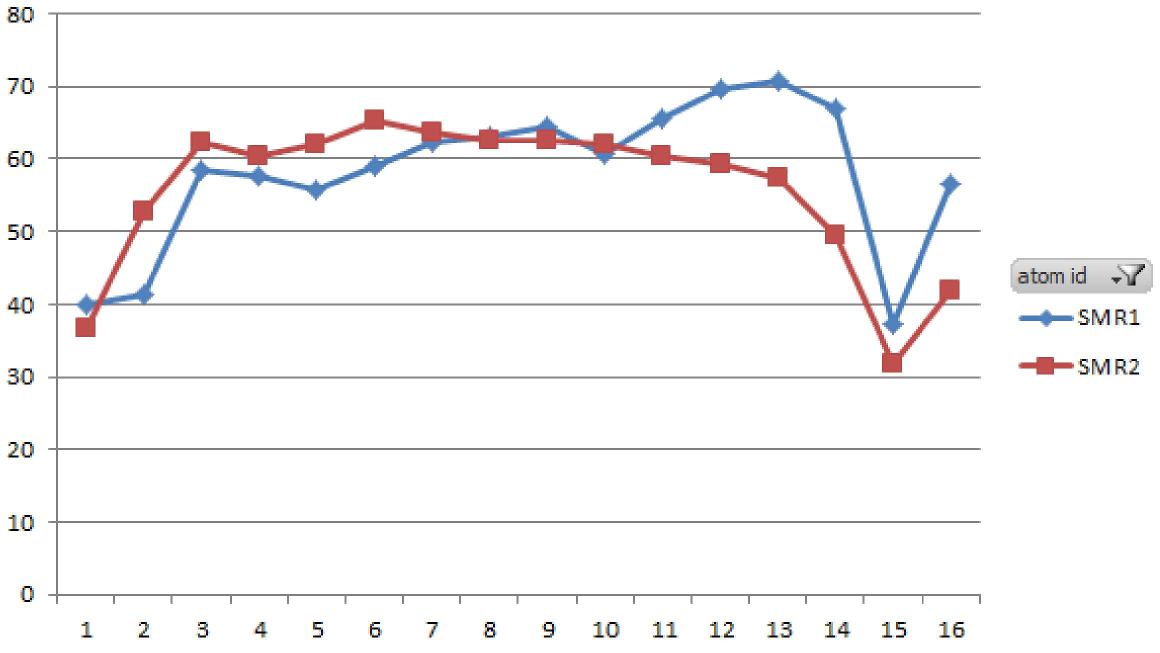

Figure 2.2

2.2 Discussion

The discovery of the two SMR atoms is perhaps the most important discovery of this study thus far. The combination of SMR 1 and SMR 2 allows different degrees of right hemispheric dominance and it provides a natural computational scheme for relating attention in the two hemispheres to each other during the LANT. This is especially remarkable given that the SMR atoms from EEG that was not collected during the LANT. One possible explanation is that EEG BF became sensitive to the hemispheric structure of the LANT because the latter was always administered after the former. In that way, the structure of the EEG during the LANT became associated with the training. This is supported by the finding that there was a significant correlation between the effects of training on SMR factors, on the one hand, with hemispheric networks of attention in the <u>previous</u> training session, on the other.

3. Conditioning the SMR Atoms with EEG Biofeedback Training

3.1 Results

Figures 3.1 illustrates the number of rewards, the amplitude of SMR 1, and the amplitude of SMR 2 during rounds 1-10 for session 14. The background color of the graphs indicates the rounds that were part of a conditioning sequence. Different colors correspond to different conditioning sequences. Inspection of the graphs reveal that SMR 1 and SMR 2 often diverge, such that one increases and the other decreases as a function of the number of rewards. Such divergences tend to occur at a greater rate during the later sessions. However, the number of divergences varies widely from session to session and it seems to be equally likely to be within a conditioning sequence or outside it (See Figure 3.2).

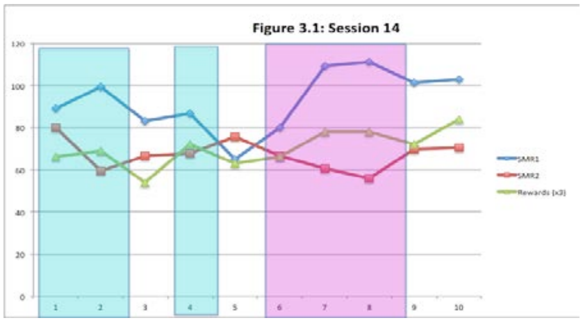

Figure 3.1: Session 14

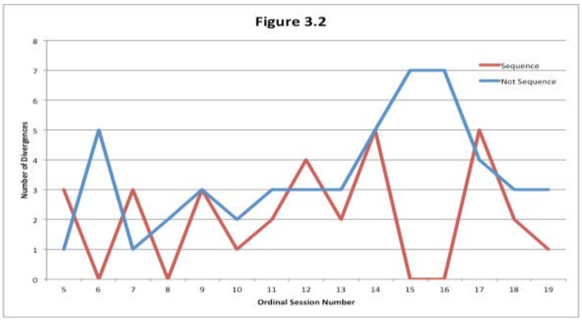

Figure 3.2

3.2 Discussion

Let the amplitude of SMR 1 = a in the right hemisphere and 0 in the left hemisphere. Further, let the amplitude SMR 2 = a+δ in the left hemisphere and a in the right hemisphere, where a is the typical amplitude for SMR and δ is small relative to it. Then, linear combinations of the two atoms allow for degrees of right hemisphere dominance, ranging from - δ to 2a- δ (more or less equal to 0 to 2a). Thus the atom analysis during eyes open following training suggests that C3 SMR training only serves to modulate the degree of right hemisphere dominance without permitting a large left hemisphere dominance. It remains to be found whether (1) this is selectively true for C3 SMR training, (2) this is selectively true for training during LANT, or (3) this is true for other training bands or sites.

4. From SMR Atoms to Hemispheric Attention Networks

4.1 Changes following a training session: eyes open before and after the training session

Results 4.1.1

We correlated the size and the change in size of the SMR 1 and of the SMR 2 atoms during eyes open following training with hemispheric attention networks across sessions. The results are summarized in the table below (Table 4.1.1).

Table 4.1.1: LANT vs. Training Session

	Attention Measure	**Atom**	**Correlation**
Current:	Right Hand-LVF-Conflict	SMR 1-SMR 2	Negative
	Right Hand-RVF-Orienting Between	SMR 2	Positive
	Right Hand-RVF-Orienting Between	SMR 1-SMR 2	Positive
	Block 1-Right Hand-RVF-Orienting Between	SMR 2	Positive
	Block 2-Right Hand-LVF-Orienting Between	SMR 1	Negative
	Block 1-Left Hand-RVF-Orienting Within	SMR 1	Negative
	Block 1-Left Hand-RVF-Orienting Within	SMR 1-SMR 2	Positive
	Block 2-Right Hand-LVF-Orienting Within	SMR 1-SMR 2	Positive
	Block 2-Left Hand-RVF-Orienting Within	SMR 1	Positive
Previous:	Right Hand-LVF-Conflict	SMR 1	Positive
	Right Hand-RVF-Orienting Within	SMR 1-SMR 2	Negative
	Left Hand-LVF-Orienting Between	SMR 1-SMR 2	Negative
	Block 1-Right Hand-RVF-Conflict	SMR 1-SMR 2	Positive
	Block 2-Right Hand-LVF-Conflict	SMR 2	Positive
	Block 1- Left Hand-LVF-Orienting Between	SMR 1-SMR 2	Negative
	Block 1-Right Hand-RVF-Orienting Within	SMR 2	Positive
	Block 1-Right Hand-RVF-Orienting Within	SMR 1-SMR 2	Negative
	Block 2-Left Hand-RVF-Orienting Within	SMR 2	Positive
	Block 2-Left Hand-RVF-Orienting Within	SMR 1-SMR 2	Negative
Next:	Left Hand-RVF-Orienting Between	SMR 2	Negative
	Block 1-Left Hand-RVF-Conflict	SMR 2	Negative
	Block 2- Right Hand-RVF-Orienting Between	SMR 2	Positive
	Block 1- Right Hand-RVF-Orienting Between	SMR 2	Negative

4.1.2 Discussion

The results show that the size and the change of the first SMR atoms with eyes open correlate with reduced scores in hemispheric attention networks and these changes always involve the right hemisphere to some extent (left hand, LVF, or both). By contrast, the size and the change of the second SMR atom with eyes open correlates both positively and negatively with hemispheric attention networks. The atomic decomposition of the SMR atoms during eyes open seem to have “built-in” hemispheric selectivity following training, consistent with their localization.

4.2 Changes within sessions: From training of SMR atoms to hemispheric attention networks

4.2.1 Results

In order to examine the relationship between conditioning of the SMR atoms and the subsequent behavioral measures of attention networks of the LANT, we computed a two-step correlation: first, for each session, we correlated the number of rewards per round with the size of the SMR atoms for that round for all the rounds in the largest conditioning sequence of that session. Second, we correlated the resulting correlation coefficients for each session with the hemispheric attention networks following that session. The significant results are summarized in Table 4.b.1. The second correlation was computed separately between the current training session and (1) the immediately following LANT (Current), (2) the LANT administered following the next training session (Previous), and (3) the LANT administered prior to the current training session (Next). In all cases, the LANT consists of two blocks, each using a different response hand with the order of the leading hand alternating across sessions. If the effects of training are consolidated rapidly (over several minutes), we would expect the LANT immediately following training (Current) to show significant effects. If, however, the effects of consolidation are slower (over several days), we would expect the LANT administered the following training session (Previous) to show significant effects. Finally, if the current training session correlates significantly with the LANT administered prior to it (Next), we would conclude that the experience of the LANT guides the training by increasing the salience of the underlining SMR atoms of the task.

Table 4.2.1: EEGBF Training Parameters vs. Hemispheric Attention Networks

Attention Measure	SMR Atom	Time of Recording (Post, Pre)	Correlation
Right Hand-LVF-Conflict	SMR 1	Post	Negative
Left Hand-LVF-Orienting Within	SMR 1	Post-Pre	Negative
Left Hand-LVF-Orienting Within	SMR 2	Post	Positive
Left Hand-LVF-Orienting Between	SMR 1	Post	Negative
Left Hand-LVF-Orienting Between	SMR 1	Post-Pre	Negative
Left Hand-LVF-Orienting Between	SMR 2	Post-Pre	Positive
Left Hand-RVF-Orienting Between	SMR 2	Post-Pre	Positive
Block 2-Left Hand-LVF-Conflict	SMR 1	Post	Negative
Block 2-Left Hand-LVF-Conflict	SMR 2	Post	Negative
Block 1- Left Hand-LVF-Orienting Between	SMR 1	Post-Pre	Negative
Block 1- Left Hand-LVF-Orienting Between	SMR 2	Post-Pre	Positive
Block 2- Left Hand-LVF-Orienting Between	SMR 1	Post	Negative
Block 2- Left Hand-LVF-Orienting Between	SMR 2	Post	Negative
Block 1- Left Hand-LVF-Orienting Within	SMR 2	Post	Positive
Block 2- Left Hand-LVF-Orienting Within	SMR 2	Post-Pre	Negative

4.2.2 Discussion

The results show a remarkable relationship between changes in the two SMR atoms during training and subsequent changes in hemispheric attention networks. In particular, we found that the relationship was stronger with the previous training session than with the one immediately preceding the administration of the LANT. Most dramatically, there were three correlations that were significant between hemispheric attention networks of the LANT and the following training session (Next). This suggests that the administration of the LANT primes the two SMR atoms and engages their training. This is particularly important because it “solves” one of the mysteries of EEG Biofeedback. Namely how does the brain “know” which behaviors to relate to changes in SMR.

The finial critical step is to determine the degree to whether the same SMR atoms are engaged during the performance of the LANT when it is administered. This could establish the relationship between the SMR atoms during training and the corresponding SMR atoms during performance of the LANT. This analysis is currently being carried out. Alternatively, the changes in the SMR atoms during training may engage different problem-solving networks, characterized by their connectivity as well as their spectra. The PARAFAC discovery procedure can be used to measure both the spectra and the connectivity of the networks changed due to EEG Biofeedback.

5. From resting state atoms to hemispheric attention networks.

5.1. The changes following training

5.1.1 Results

The results are summarized in table 5.1.1. They show significant correlations of changes in alpha 2 and in theta, associated with reduced conflict in the "pure right hemisphere trials" (left visual field, left hand).

Table 5.1.1. Changes following training

L_L_Conflict -> LANT1_Alpha2, r = .544, p = .02
L_L_Conflict -> LANT1_Theta, r = .562, p = .015
L_L_Conflict -> Session, r = -.594, p = .007
R_R_Conflict -> Session, r = -.436, p = .062
rh_LVF_Conflict -> Session, r = -.594, p = .007
lh_RVF_Conflict -> LANT2_Theta, r = .509, p = .031
lh_RVF_Conflict -> Session, r = -.662, p = .002
lh_RVF_OrientWithin -> LANT2_Alpha2, r = .616, p = .006
L_L_OrientBet -> LANT1_Alpha1, r = -.524, p = .026,
L_L_OrientBet -> LANT2_Alpha1, r = -.476, p = .046
L_L_OrientBet -> Session, r = -.500, p = .029

5.2 Discussion

Participant 004 showed a selective ability to benefit from EEG biofeedback training using the C3-SMR protocol. There are three outstanding features in the resulting pattern of data.

1) Participant 004 exhibited successful conditioning but the control participant (006) did not.
2) Conditioning successfully modified the alpha-2 and theta atoms, resulting in improved right hemisphere control of the conflict resolution.
3) Remarkably, there was no evidence in any participant for the SMR atoms during performance of the LANT. It follows that modulating the SMR atoms during EEG-biofeedback resulted in changes in the alpha-2 and theta atoms, which were associated with the reduced conflict resolution in the right hemisphere. This most likely reflects changes introduced by EEG biofeedback training in the activation and connectivity of other atoms.

6. General conclusion

Our results demonstrated that there are large individual differences to EEG-biofeedback training. Successful training can result in changes in atoms other than the ones targeted by the training protocol and centered in locations other than the training electrode. During the SMR protocol, Participant 004 showed evidence for simultaneous changes in two separate SMR atoms whose net effect is a systematic increase in right hemisphere SMR via suppression of the left hemisphere SMR. We call this pattern the “contralateral training effect” and it can serve as a model for recovery of function. Following focal damage to one hemisphere by activating homologous regions in the contralateral hemisphere.

7. ERP Analysis

The EEG records were petitioned into 1 second epochs consisting of 300 ms baseline before the target and 1 second following the target. There was evidence for three independent components, a P100 component, an N160 component, and a P360 component. The dependent variables were the peak amplitude and latency of the peak amplitude for the component. The P100 component showed evidence for early activation in the hemisphere contralateral to the lateralized target, followed by activation in the opposite hemisphere. There was a clear significant asymmetry in the transfer of visual information from left to right and then from right to left. There was no evidence for an effect on conflict resolution or response hand. The N160 component showed a main effect of conflict resolution and an interaction with target visual field, as well as with a recording electrode. The P360 component showed a main effect of conflict resolution and an interaction with response hand, visual field, and the target electrodes. These data support the general conclusion that the LANT paradigm in participant 004 is valid and yields evidence for systematic changes in performance, associated with a specific time period during trial performance.