

BIOMARKER EVALUATION REPORT



**SADAR PSYCHOLOGICAL
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Executive Summary of Results and Recommendations

Name:	Adult Female	Date of birth:	12.17.1990
		Sex:	f
Recording Date:	01.20.2023	Referred by:	Saul Rosenthal
Medication(s)	Wellbutrin, Lexapro, Propranolol (as needed)		
Evaluator	Andrea Meckley Kut yana, PhD, BCN, BCB, QEEG-T		
Reason for evaluation	Anxiety and depression		

SUMMARY OF FINDINGS

Questionnaire	Significant Self-Reported Responses
Amen	The answers indicate a slight level of strain in the cingulate cortex, also a high level of strain in basal ganglia and deep limbic system.
van Deusen	Functions that have been allocated to the left hemisphere are significantly more affected. Functions of the left medial temporal lobe are strongly affected. Functions of the supplementary and premotor cortex are strongly affected.
ADHD	Criteria met for inattention.

VISUAL CONTINUOUS PERFORMANCE TASK

Data	Within Normal Limits	Statistically Significant
Omission	Yes	
Commission	Yes	
Reaction Time	No	Slightly slow reaction time
Reaction Time Variability	Yes	

NEUROLOGIST EEG FINDINGS:

Within Normal Limits: Yes

Description: A posterior dominant rhythm was noted at 8.5-10.5 Hz with only mild to moderate attenuation with eye opening. Brief drowsiness was demonstrated. This EEG is without diagnostic abnormality for age in the awake and drowsy states.

qEEG FINDINGS

Results	Description
---------	-------------

Slower alpha component	Slower 8.06 Hz alpha component is noted, maximal in the left posterior temporal region with eyes closed.
Alpha remains prominent	Alpha remains prominent with eye opening (maximal in the right mid temporal region BA 7) and during the task.
Theta/beta ratios increased	Significantly increased theta/beta ratios in all locations and all conditions.
Arousal index reduced	Significantly reduced arousal in all conditions
ADHD Index	Severe attention issues are predicted largely due to Cingulate dysregulation
Vigilance Decrement	In Go task: steep slope in perception with flat slope during relaxation; overall low variability

EVOKED RESONSE POTENTIALS

Components	Early potentials		Mid potentials		Late potentials	Specific pattern
	Amplitude	Latency	Amplitude	Latency		
Visual Input			high	late	-	N1 Stress Marker No
Auditory Novelty			-	-	-	
Left Association Areas	-	-	-	-	-	
Right Association Areas	-	-	-	-	-	
Left Memory	-	-	-	-	-	
Right Memory	-	-	-	-	-	
Engagement	-	-	-	-	-	N2 Attention Marker No
Inhibition/Suppression	low	-	low	-	-	
Monitoring	low	-	low	-	-	
Working Memory						
Slow Wave Activity						
Readiness Potential						

DISCUSSION:

There are several findings of interest in Adult Female's evaluation. First, she has an alpha rhythm in the healthy range at 9.77 Hz, however, a slower alpha component is noted at 8.06 Hz, maximal in the posterior and temporal regions with LORETA estimating the source to be Brodmann area 7. This activity also remains prominent with eye opening and during the task and contributes to the significant increase in slow wave activity, increased theta/beta ratios, and the reduced arousal index. Alpha is considered the brain's idling rhythm and typically found between 9-11 Hz. Individuals with a slower alpha rhythm may process information slowly (consistent with the late latency of the visual ERP and slower reaction times) and this pattern may have a negative impact on cognitive efficiency and mental sharpness in general. Behaviorally, these patterns may be expressed as a lack of motivation and a lowered willingness towards effort. In unsecure situations, she might express fears and misgivings. A depressive mood modulation, significant unreal perception of everyday life, and loss of focus may also be observed. Second, several patterns in the ERPs and Vigilance suggest a pattern of initial intensity followed by reduced activation. This is evidenced by a high amplitude visual ERP suggesting high processing intensity, high amplitude of the Readiness Potential suggesting intense preparation for stimuli, and steep vigilance slope during the perception/memory phase of the Go task as well as overall reduced vigilance variability suggesting high inner tension when preparing

to respond and overall rigidity. This initial intensity is then followed by low amplitudes of the later ERP components suggesting less control of monitoring processes leading to attentional errors, low activation of the limbic energy during decision making often defined by a state of indifference and perplexity and lack of resources after responding.

SUMMARY OF RECOMMENDATIONS

MEDICATION

Recommended	Comments
No	Adult Female is currently taking medications that maybe impacting the findings; therefore, no recommendations can be made at this time.

RECOMMENDATIONS FOR THERAPEUTIC INTERVENTIONS

Lifestyle	Recommended	Modifications Recommended
Daily Life	Yes	Routine and structure
Sleep	Yes	Review sleep hygiene and biofeedback
Diet	Yes	Review guidelines
Exercise	Yes	Meet daily minimum recommendations.
Drugs/Alcohol	No	
Electronics	Yes	Limit to 2 hours per day

Biofeedback	Recommended	Detailed information can be found in the recommendations section in the report
EEG	Yes	
Heart Rate Variability	Yes	
Pir-HEG	Yes	
EMG	No	
Capnography	Consider evaluation	

Home Training	Recommended	Detailed information can be found in the recommendations section in the report
UNYTE/Mightier	Yes	
BAUD Bio-Acoustical Utilization Device	No	
Alpha-Stim CES	No	
David Audio-Visual Entrainment	No	
Lumosity	No	

Additional	Recommended	Comments
Psychotherapy/Coaching	Yes	
Medical	Possibly	Consider nutritional/metabolic testing

Index of Contents

I. Introduction	5
II. Questionnaires	6
1. Questionnaire: Personal and clinical data	6
2. Questionnaire: Symptoms and Cortical Networks (Amen)	7
3. Questionnaire van Deusen	8
4. ADHD-Questionnaire	9
III. Neuropsychological Measures:	10
1. Performance	10
IV. Evidence-based investigation by measuring neurophysiological brain functions (functional neurophysiology, biomarkers):	12
1. Spontaneous EEG	12
2. Spike Detection	14
3. Evoked Potentials (in continuous performance task)	33
4. Event related potentials – ERPs	38
5. Diagnostic-Algorithms	41
A. ADHD-Diagnose-Index	41
B. Emotion regulation, including mood modulation.	42
V. Recommendations	44
1. Medication	44
2. Everyday Life/Work	44
VI. Appendix	47

I. Introduction

Important notice: qEEG and evoked potential assessment do not replace a medical-clinical checkup. They solely serve to generate comparable physiological data in different cognitive states. No neurologic diagnostic statement will be made. A neurologic assessment must be done by a licensed Neurologist.

Procedure: EEG recording was computed according to the 10-20 placement using 19 scalp electrode caps. Brain electrical activity was digitally recorded on a NeuroAmp x23 System, using a linked ears reference montage. Impedances of less than 5k Ohms were achieved at all sites before recordings were initiated and kept >5k Ohms at all times during recording. The signal was digitally processed by a quantitative topographic analysis system (ERPrec software), band passed from 1-50Hz, and saved on a local disc.

The client was seated 1.5m in front of a display monitor. The EEG was recorded in relaxed condition with eyes closed (EC) and eyes opened (EO) for 10 Minutes each and saved. After a short break, a visual or auditory continuous performance task (ACPT/VCPT) was presented on the monitor and performed during recording (task condition). The data was saved separately.

The digitized data is run through an artifact program where eye blinks, movement and other artifacts are identified and removed. The data is then additionally manually processed for artifacts and important transients are marked.

Corrected digital recording of the client is run through a mathematical program called Fourier-Transformation. This procedure analyzes the recorded brain waves and expresses the recordings as a mathematical function - time as a function of frequency - known as its frequency spectrum. To evaluate the data there are diverse descriptive and statistical repetitions which are performed to provide a spectral analysis, topometric analysis, covariance analysis, and comparisons between the states of data acquisition. The data collected is compared and evaluated against a known FDA approved data base.

This report aims to present the results and conclusion of this analysis. Also, therapeutic recommendations are given, according to dysfunction and cortical organization of the client's brain. Presented results are to be handled with caution, as they represent a momentary picture of a whole complex system.

The graphs represent an approximation of the source generator in the cortex calculated through mathematical procedures. Hence the calculated localization can differ from the real source. Therefore, expert knowledge based on functional neuronal models should ultimately determine the clinical relevance of these findings.

II. Questionnaires

1. Questionnaire: Personal and clinical data

General information

- Name (family name, given name) or code: **Adult Female**
- Date of birth (Day. Month. Year): **17.12.1990**
- Gender (M-male, F-female): **F**
- Handed (L- left, R – right, ambidextrous): **Right**
- Reason of having QEEG/ERP assessment: **Anxiety and depression**
- Medication taken now: **Wellbutrin 300 mg daily, Lexapro 10 mg daily, propranolol 10 mg as needed**

Pre- and post-natal history

- Birth trauma and/or hypoxia: **None**
- Early development, such as started to talk/walk too late: **All WNL**
- Head trauma (with loss of consciousness): **Denied**
- Poor grades in school, poor performance at work: **Did well.**

General Brain Regulation

- Often having headaches and/or migraines: **Denied**
- Feels weak and passive during daytime: **Occasional**
- Sleep-related difficulties: **Denied**
- Abuses alcohol or drugs: **Denied**
- Has history of seizures: **Denied**

Sensory system

- Perceptual difficulties in vision, hearing, touch...such as dyslexia, paresis, neglect...: **Denied**
- Difficulties in social interaction and communication, autistic spectrum: **Denied, but some mild anxiety.**

Motor system

- Motor-related difficulties, such as fine motor, tremor, rigidity, apraxia...: **Denied**

Executive system

- Attention difficulties: **Occasional but can compensate**
- Impulsiveness: **Denied**
- Difficulties in correcting behavior: **Denied**
- Psychosis (hallucinations, delusions...): **Denied**

Affective system

- Occupied by mostly positive thoughts, manic: **Denied**
- Occupied by mostly negative emotions, depressed: **Generally neutral, but mood can be low for weeks to months. Unclear triggers/patterns.**
- Anxious: **Work-related (psychiatric resident). Episodes of panic but well-managed.**

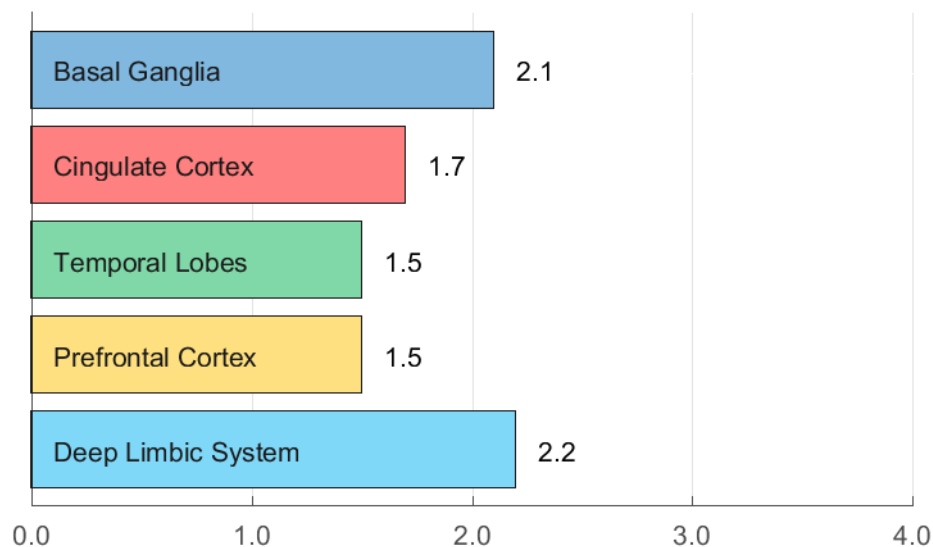
Memory system

- Poor memory for recent events: **Not very good, but writes everything down.**
- Other forms of memory deficit: **Does not remember most of childhood, but otherwise ok.**

2. Questionnaire: Symptoms and Cortical Networks (Amen)

The relations between answers to the questions of the everyday functioning questionnaire and different brain structures have been researched. The figure below shows the weight of stressors on each structure. As answering styles are highly variable between individuals, it cannot be stated if the stressor is significantly impairing everyday functioning or not. Nonetheless it is interesting to observe the differences between various structures.

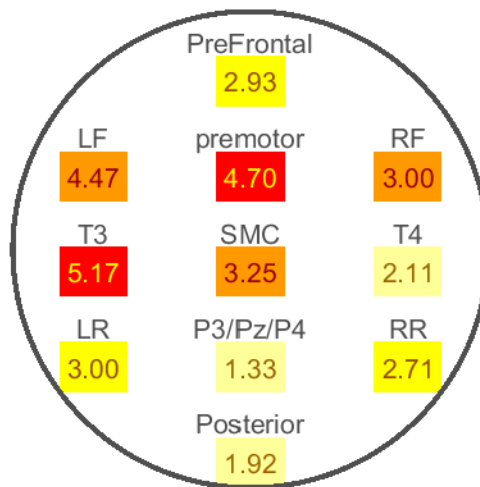
Graphic summary:



The answers indicate a slight level of strain in the cingulate cortex, also a high level of strain in basal ganglia and deep limbic system.

- The strain on the Basal ganglia is defined by the influence of the vegetative nervous system. This includes somatic symptoms like palpitations, sweaty hands, or stomach pain, also anxiety reactions like panic attacks, or fear of negative evaluations of others. These processes are assessed in our measurement by analyzing the experience and feeling of stress.
- The cingulate system goes from the frontal cortex (anterior part) over the medial cingulate cortex and to the posterior cingulate cortex (precuneus). Functions are affected by cognitive and emotional contents. In this context monitoring functions are required, like internal flexibility (vs rigidity). Dysfunctions of the cingulate system influence all other cortical areas. The serotonin system is widespread along the cingulate cortex. The cingulate system receives information from the thalamic anterior nuclei.
- The limbic system is responsible for emotional energy and related functions. In this questionnaire items enquiring about energy level or helplessness are related to this system. Attentional problems may arise indirectly because of high distractibility caused by emotional issues.

3. Questionnaire van Deusen



Summary of results:

- Functions that have been allocated to the left hemisphere are strongly affected.
- Functions of the left medial temporal lobe (difficulties with information processing e.g., reading or orthography) are strongly affected.
- Functions of the supplementary and premotor cortex (fidgety and restless, unable to relax or work quietly, messy handwriting) are strongly affected.

4. ADHD-Questionnaire

Type	Question	Score
Type 1	Combined ADHD-Type → <i>Questions on Attention & Hyperactivity</i> Meets criteria for <i>Inattentiveness</i> questions as well as <i>Hyperactivity/ Impulsivity</i> questions.	5
	Inattentiveness Questions → <i>Questions on Attention</i> 6 (5) or more ratings of 3 or 4 are required to diagnose this type; with more than 4 such ratings suggesting this type of ADD.	5
	Hyperactivity-/Impulsivity Questions → <i>Questions on Hyperactivity</i> 6 (5) or more ratings of 3 or 4 are required to diagnose this type; with more than 4 such ratings suggesting this type of ADD.	0
Type 2	Inattentive ADD → <i>Questions on Attention</i> 6 (5) or more values of 3 or 4 are required to diagnose this type; with more than 4 such ratings suggesting this subtype of ADD; but not 6 or more such ratings for <i>Hyperactivity-/Impulsivity</i> questions.	5
Type 3	Over focused ADD → <i>Questions on Over Focusing</i> Meets criteria for <i>Inattentiveness</i> , as well as 6 or more such ratings in <i>Over Focusing</i> questions.	2
Type 4	Emotion regulation Comorbidity → <i>Questions on Emotion regulation</i> Meets criteria for <i>Inattentiveness</i> , as well as 12 or more such ratings in <i>Emotion regulation</i> questions.	7

Adult Female meets the cut-off (5) for inattention, therefore according to DSM V the diagnosis of ADHD (314.0) can be made. However, the impairment caused by the symptoms must be present in at least two settings (e.g., at work and family) and there must be clear evidence of clinically significant impairment in social or occupational functioning. Additionally, the symptoms do not occur exclusively during the course of a Pervasive Developmental Disorder, Schizophrenia, or other Psychotic Disorder and are not better accounted for by another mental disorder.

III. Neuropsychological Measures:

1. Performance

Performance was recorded during the visual continuous performance task (VCPT). The measures can be interpreted regarding impulsivity (commission errors), attention (omission errors, missed trials), reaction times (msec) and variability of reaction times.

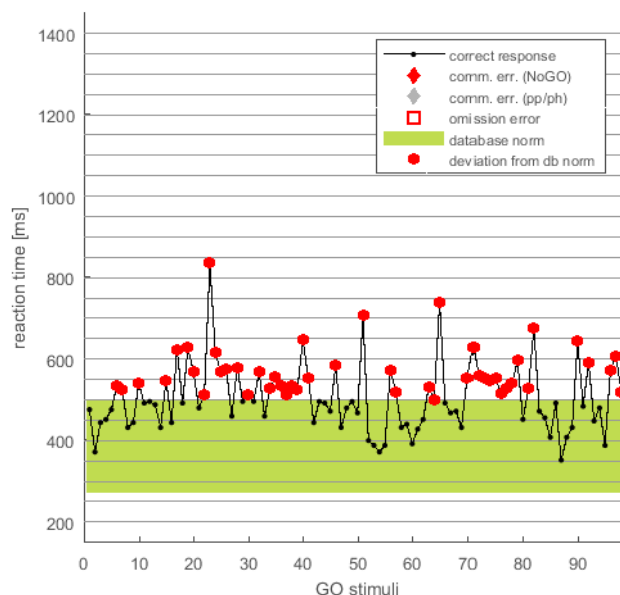
VCPT:

Group name	Correct	Omission	Commission	RT	VR(RT)
a-a GO	100.0 %	0 (0.209)	0	510 (0.071)	8.2 (0.873)
a-p NoGO	100.0 %	0	0 (1.098)	-	-

Number of processed trials: **399** (a-a GO: **99**, a-p NoGO: **100**, p-p: **100**, p-h: **100**)

Overview: The values of Adult Female are within the norm with respect to Attention, Impulsivity and Response consistency, they are slightly conspicuous with respect to Reaction time.

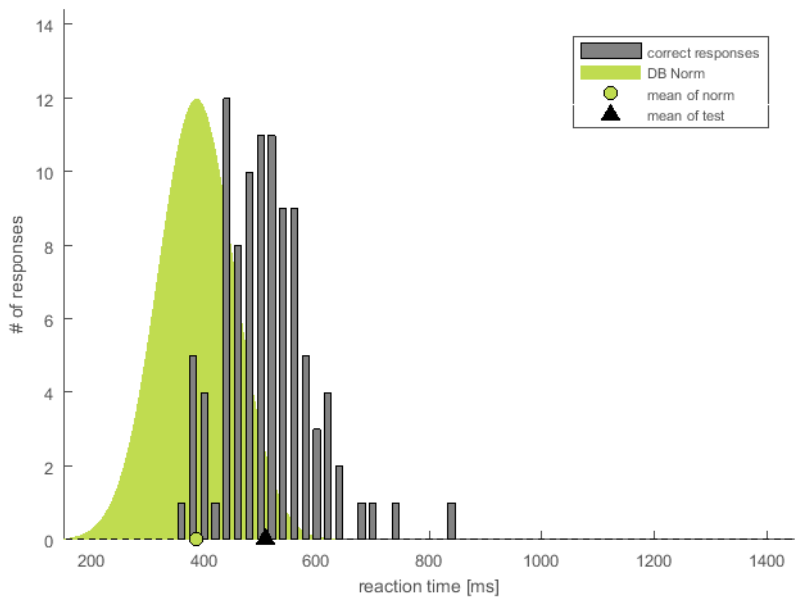
Figure 1: below, reaction times are presented over time. Red dots represent reaction times below or above database (DB) norm levels. Black dots represent correct responses, red squares omission errors (inattentiveness) and red crosses commission errors (impulsivity).



The analysis of Adult Female's reaction times compared to peers (green area) show much longer Reaction times, although good consistency in reaction times.

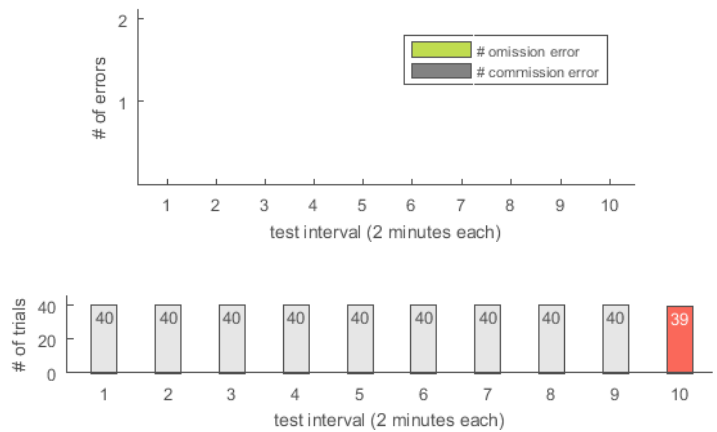
Figure 2: below, reaction times are represented as a function of occurrence. The distribution of grey bars indicates how stable the reaction times were (variability of reaction times). Wide distributions show

unstable performance, while narrow distributions can be interpreted as stable performance. The green area indicates the database norm.



The average reaction time of Adult Female (black triangle) compared with her peers (green dot) is significantly slower.

Figure 3: below, the distribution of errors over time (intervals of 2 min) is illustrated. More errors towards the end of the task indicate growing fatigue in the course of performance.



There are no errors throughout the entire test.

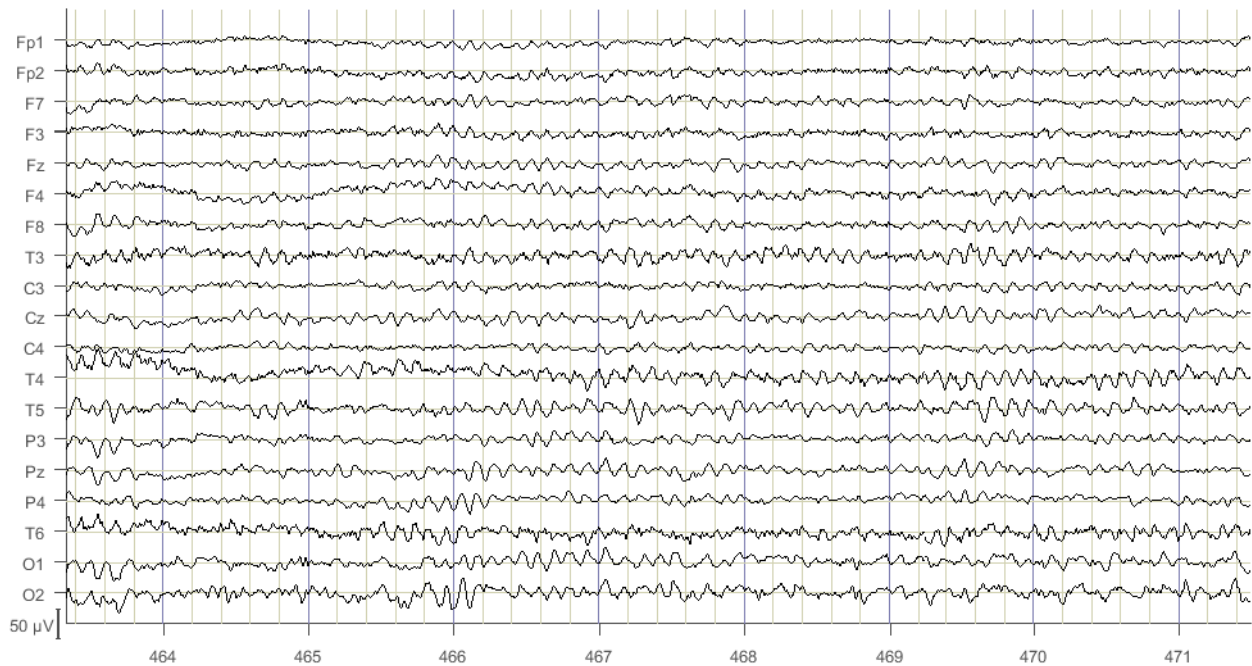
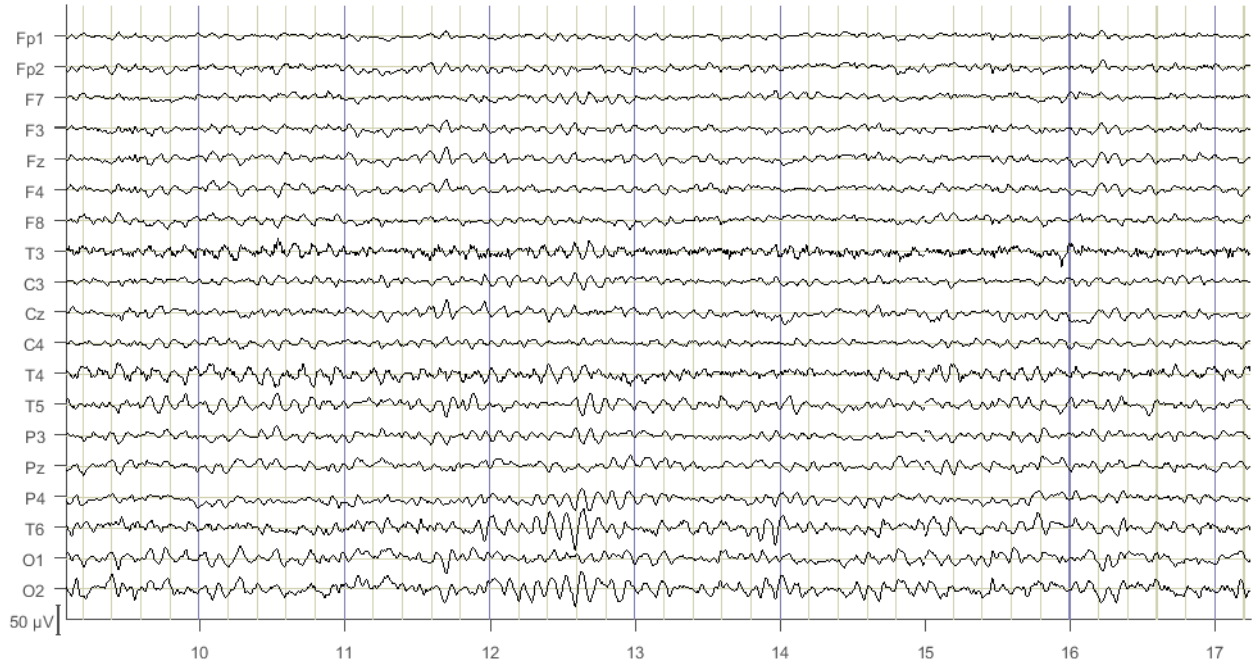
IV. Evidence-based investigation by measuring neurophysiological brain functions (functional neurophysiology, biomarkers):

1. Spontaneous EEG

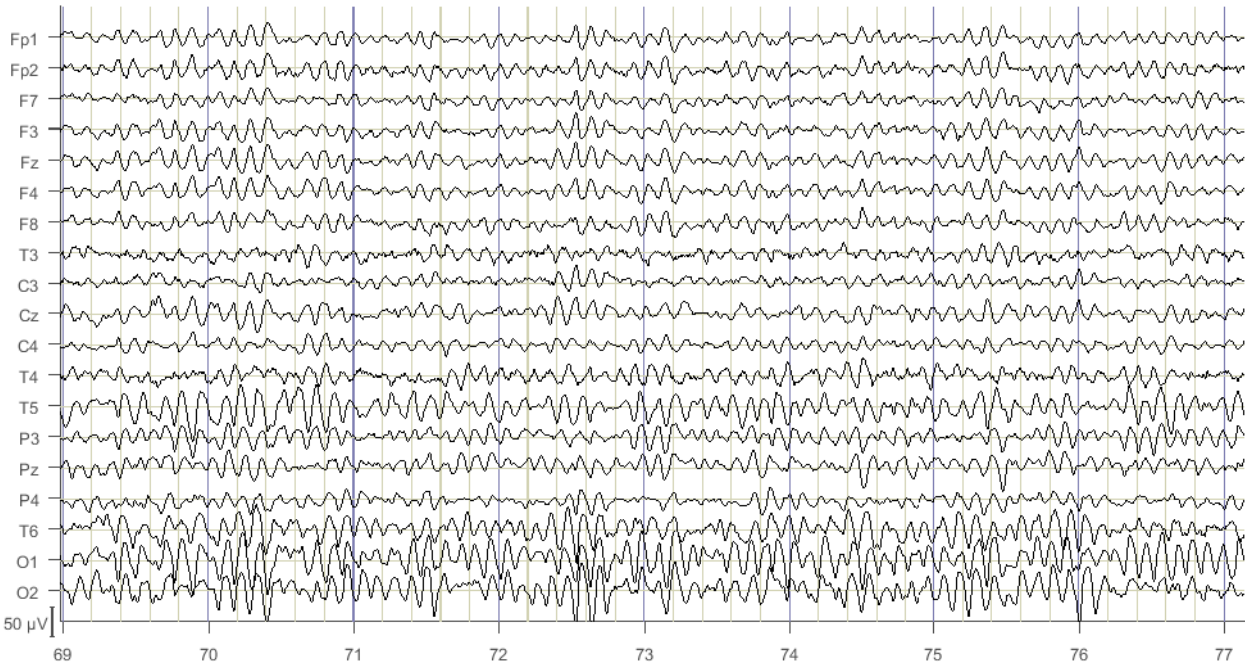
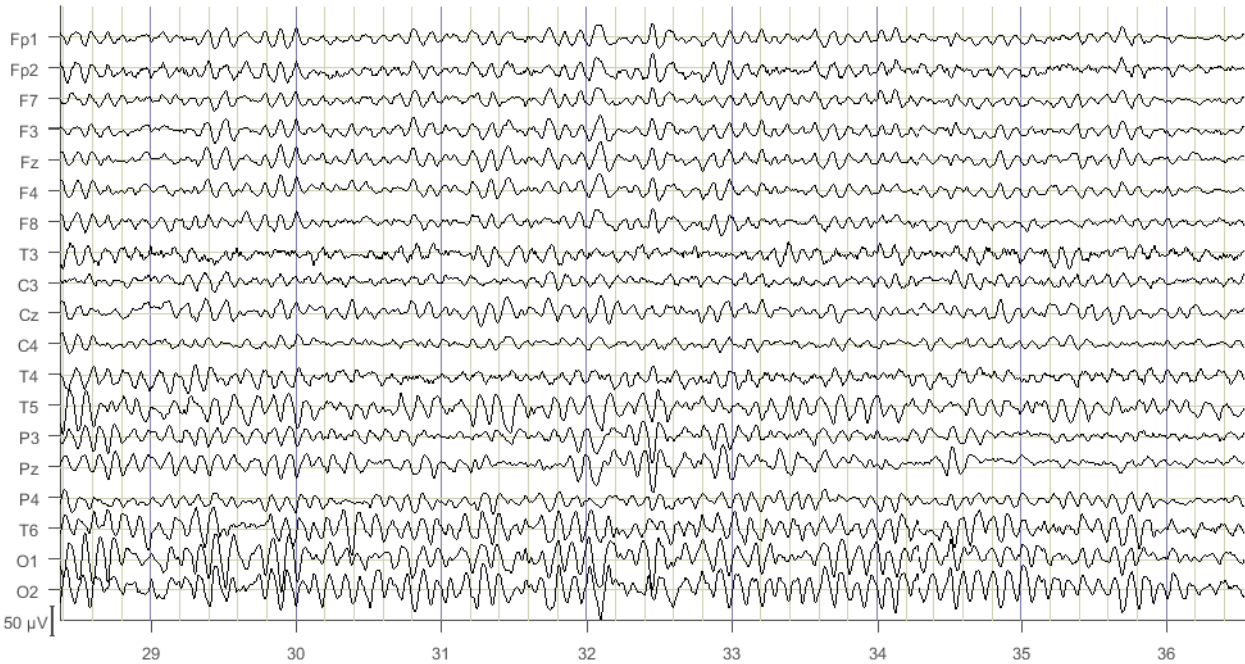
EEG was recorded during relaxation with closed eyes (10 minutes) and opened eyes (10 minutes). From this recording, spectral data was calculated and compared with database population. Database comparison was calculated with weighted montage.

Fragment:

Eyes opened



Eyes closed

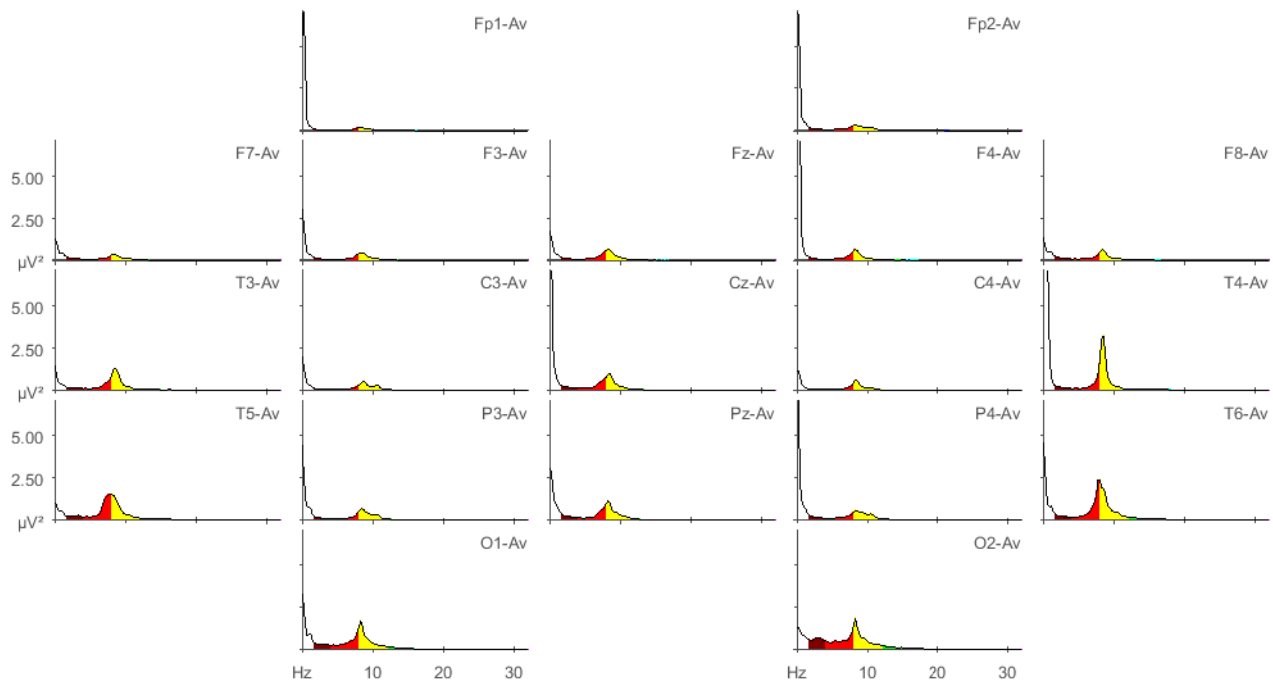


2. Spike Detection

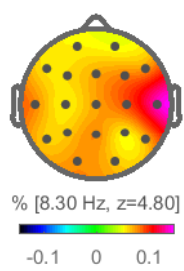
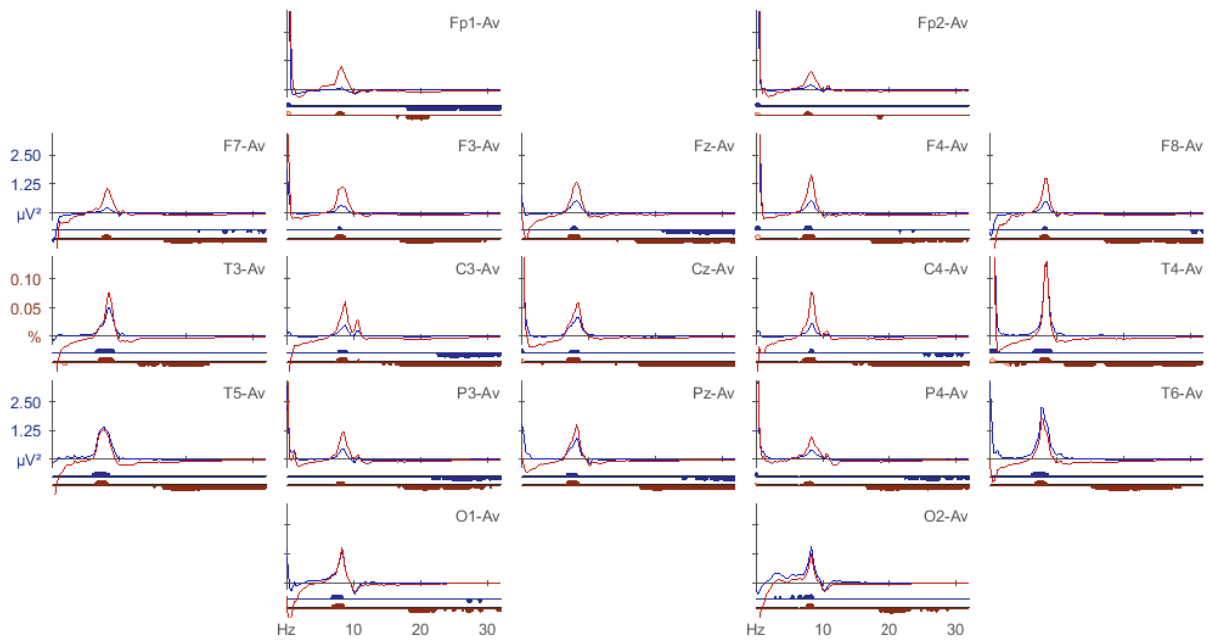
Spikes are sharp transient waves representing interictal epileptiform activity in the brain. The spike detection procedure uses morphological filtering of EEG signals in order to detect such transient activity and separate it from normal background waves.

These recordings were read by a neurologist so this procedure was not applied in this analysis.

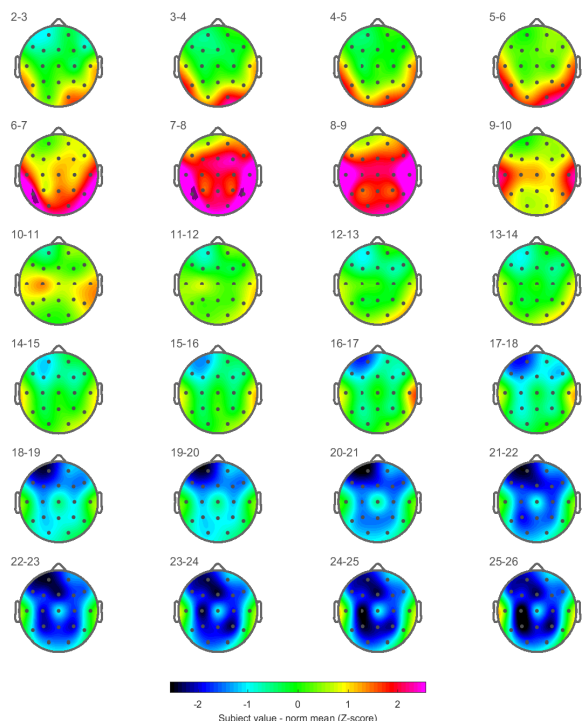
Spectral data: eyes opened (9:41)



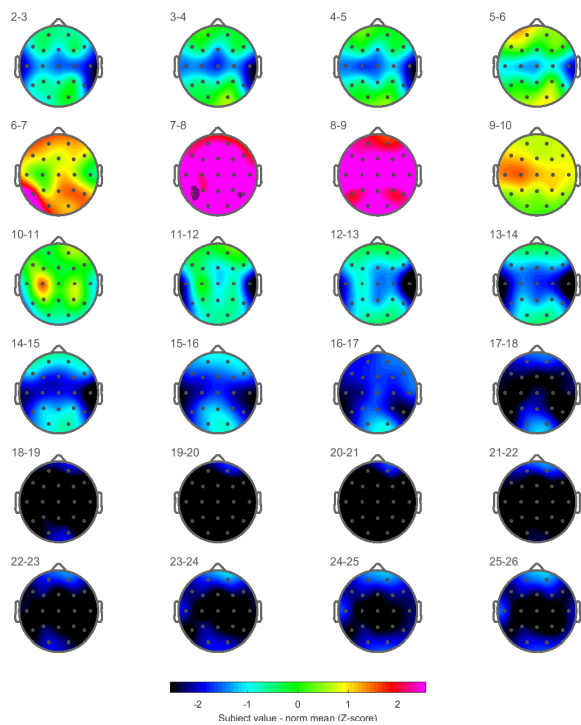
comparison with reference data: Difference (blue: absolute, red: relative). Bars on the bottom line indicate significant deviations from norm.



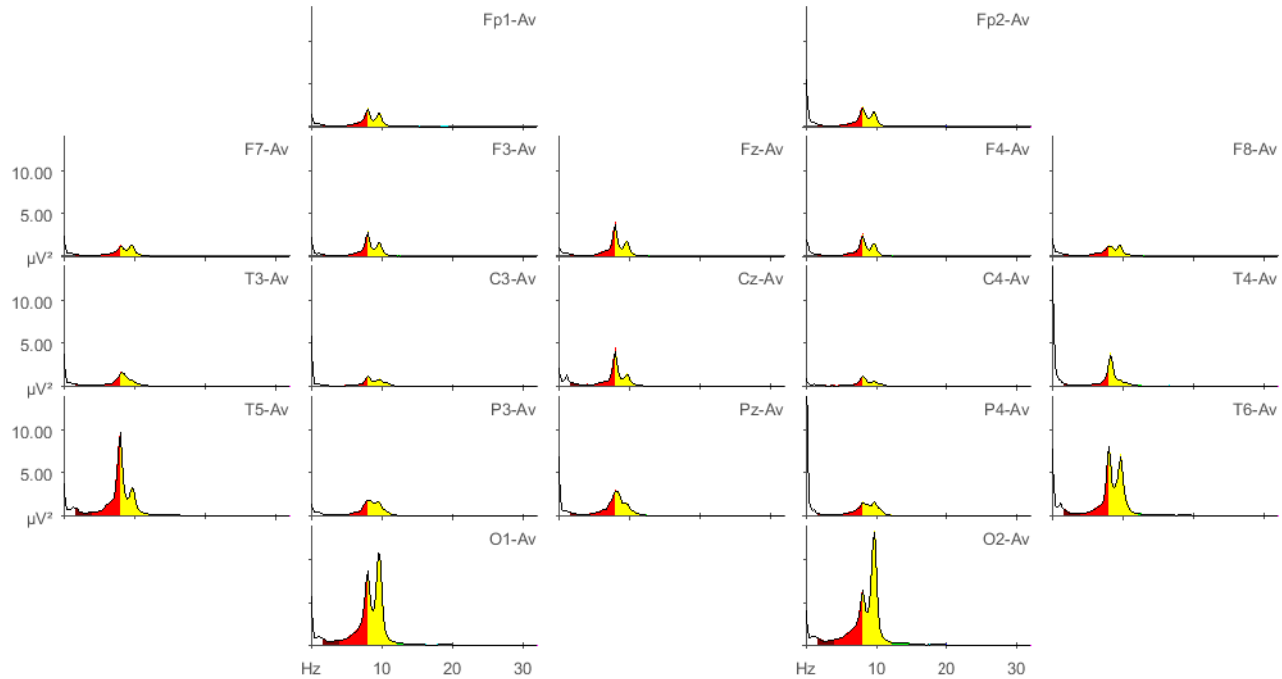
Database - Subject (absolute):



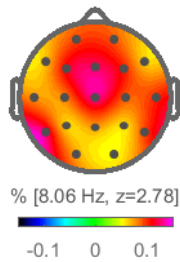
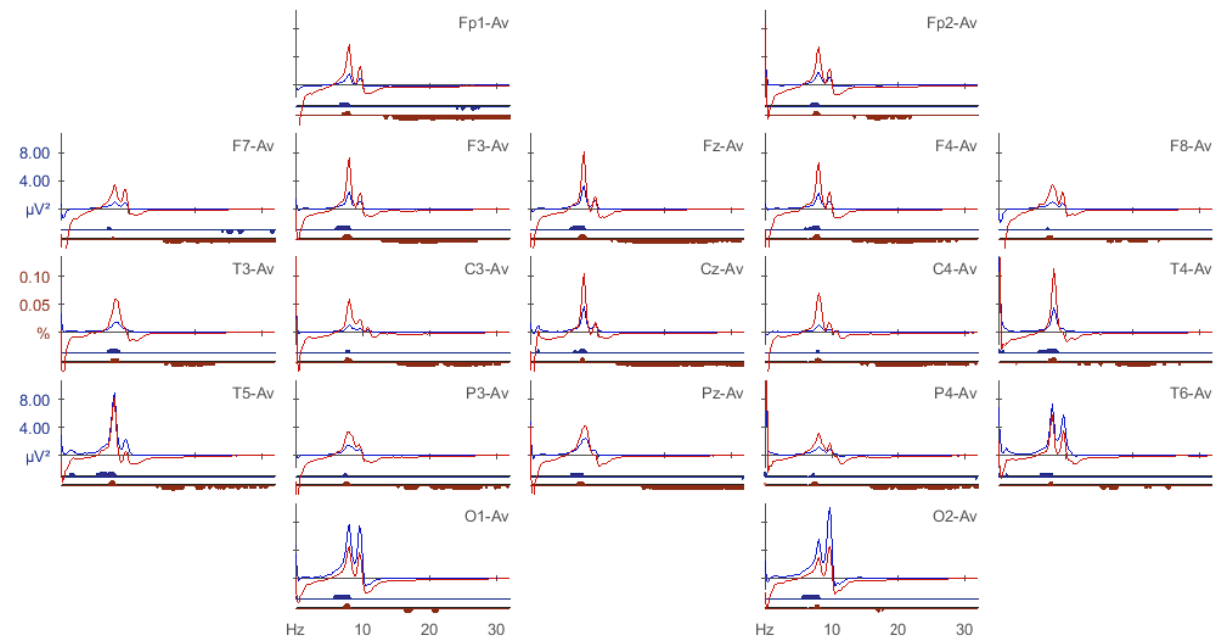
Database - Subject (relative):



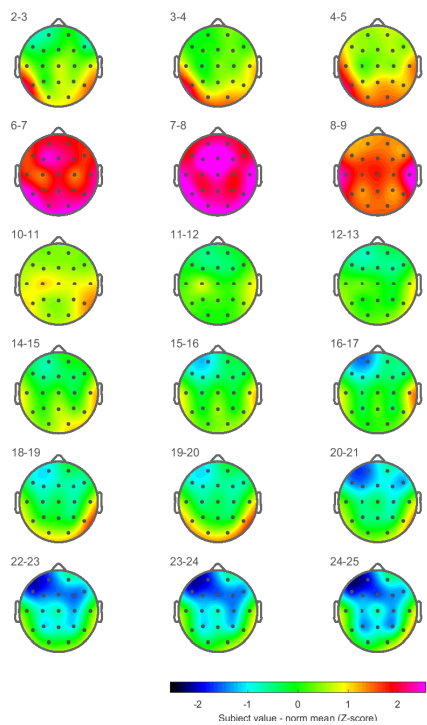
Spectral data: eyes closed (9:36)



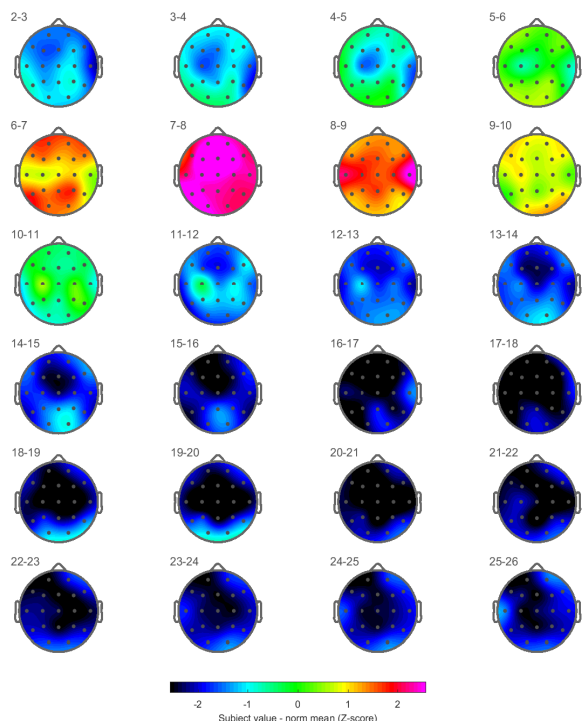
comparison with reference data: Difference (blue: absolute, red: relative). Bars on the bottom line indicate significant deviations from norm.



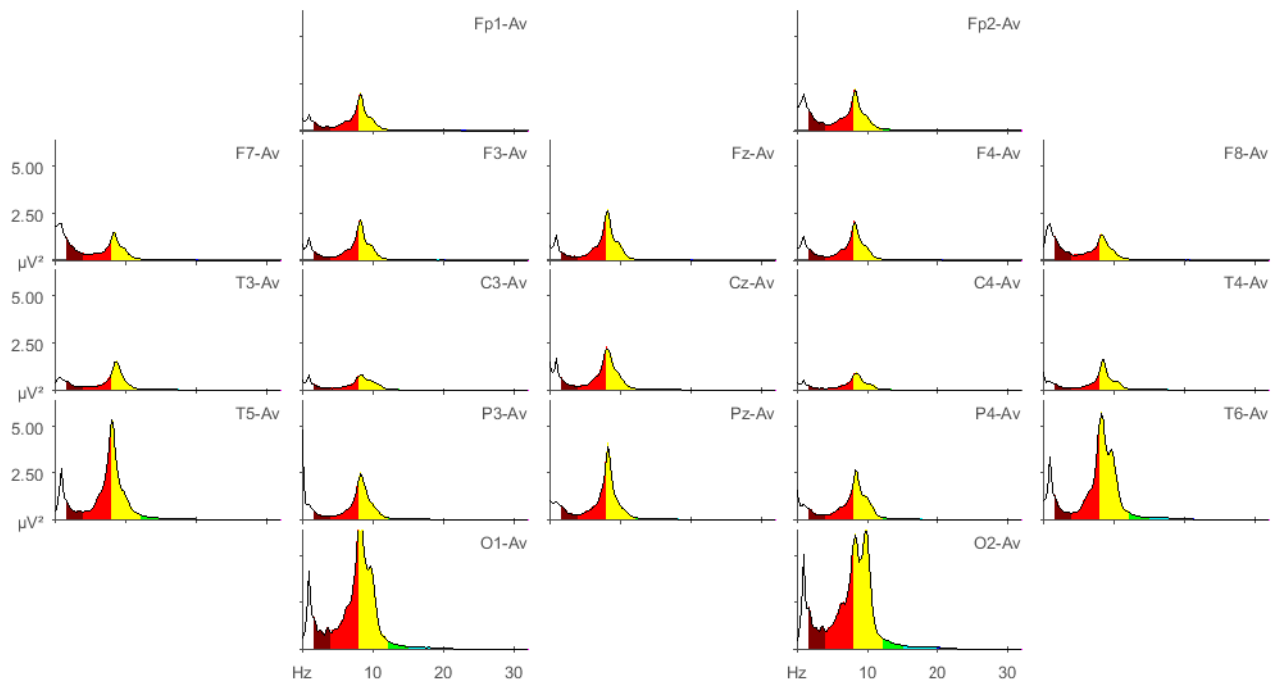
Database - Subject (absolute):



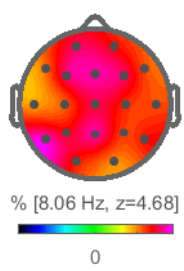
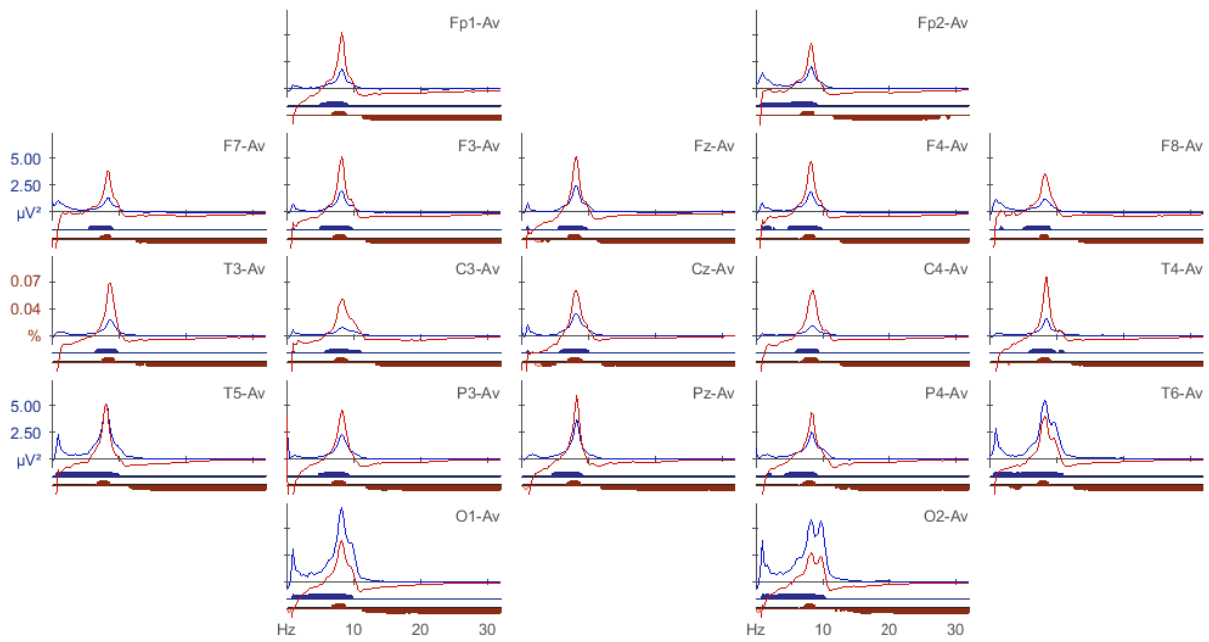
Database - Subject (relative):



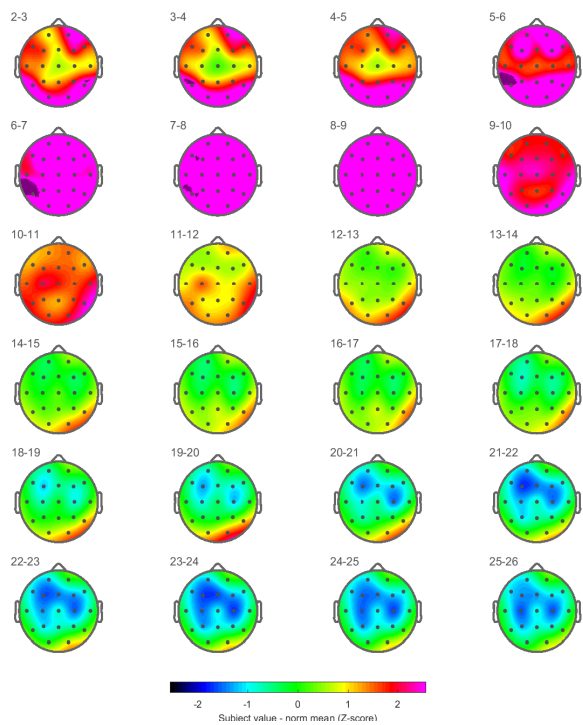
Spectral data: VCPT (20:14)



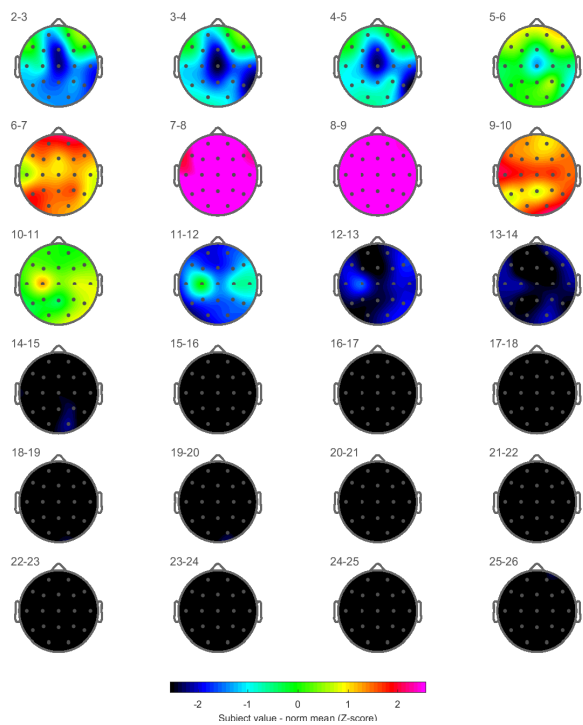
comparison with reference data: Difference (blue: absolute, red: relative). Bars on the bottom line indicate significant deviations from norm.



Database - Subject (absolute):



Database - Subject (relative):

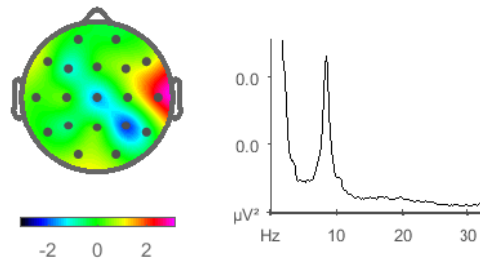


The graphs represent an approximation of the source generator in the cortex calculated through mathematical procedures. Hence the calculated localization can differ from the real source. Therefore, expert knowledge based on functional neuronal models should ultimately determine the clinical relevance of these findings.

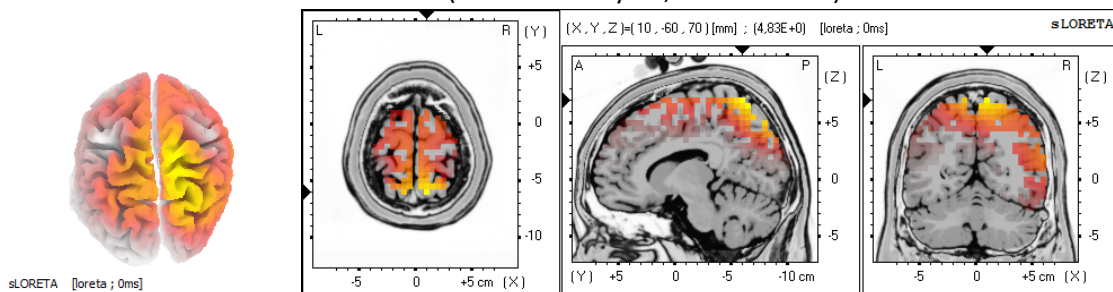
Following deviations were calculated (EO):

1. frequency: 8.30 Hz

Graph of the independent component of this activity:



sLORETA localization Brodman area 7 (Postcentral Gyrus, Parietal Lobe)



Brodman area 7: Precuneus the Precuneus represents the end of the cingulum and has the following functions:

Awareness: the precuneus is essential for conscious information processing.

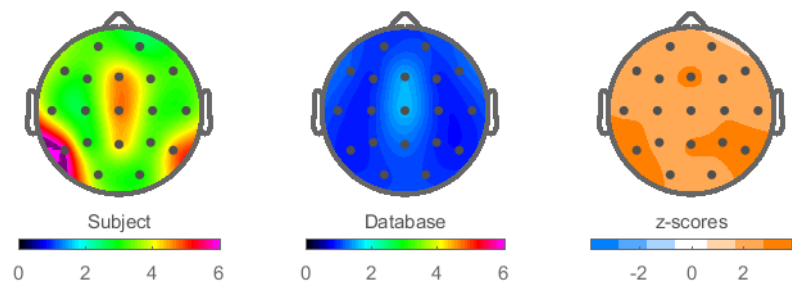
Default-mode network: The default network is responsible for the awake resting state of the brain; the ventral precuneus is part of this network, meaning that self-awareness and self-perception are important components of the default network.

Parietal-prefrontal-central network: The precuneus is part of the fronto-parietal network, which is in charge of activating many cognitive and emotional functions.

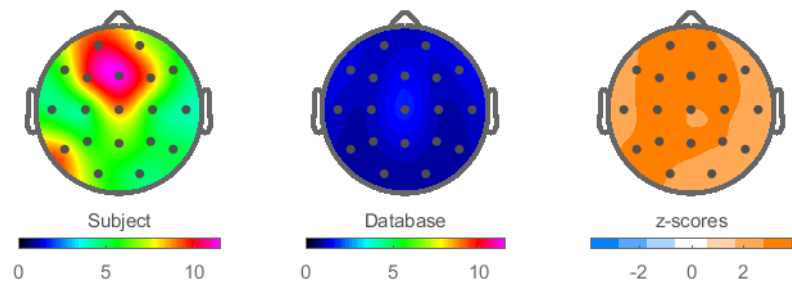
Visual and sensory association area functions. Speech comprehension in the dominant hemisphere. This association cortex integrates somatosensory information with visual, auditory and vestibular information, enabling spatial localization of objects. This spatial perception is the basis for directed eye-, hand- and body movements; it provides sensory information fundamental for complex directed movements.

Theta/Beta-Ratio

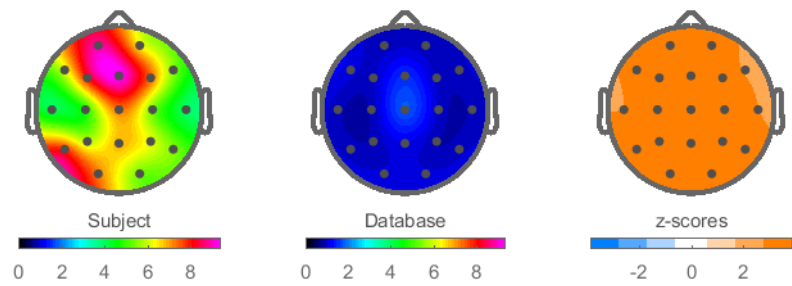
The Theta/Beta ratio gives an index as to the quality of an individual's ability to pay attention. This ratio is negatively correlated with age, as it is expected to be larger in younger children, smaller in adulthood and rises again in later adulthood. This is measured in a GO/NOGO Test where it is expected that a higher ratio will produce more errors. This ratio has been demonstrated in the research of Monastra (Monastra et. al., 1999).



Eyes open



Eyes closed



VCPT

Version	v01	v01	v01
Eyes open	Fz	Cz	Pz
Subject (Stanine)	4.6 (99.9% 9)	4.76 (98.2% 9)	4.38 (99.8% 9)
Eyes closed	Fz	Cz	Pz
subject (Stanine)	11.46 (100% 9)	8.82 (99.7% 9)	6.52 (99.8% 9)

VCPT	Fz	Cz	Pz
Subject (Stanine)	9.34 (100% 9)	7.31 (99.9% 9)	6.83 (100% 9)

Arousal

This index represents the arousal caused by the vegetative nervous system. It is specifically the parietal and occipital branch projected from the insula to the respective regions. The index is calculated separately for each hemisphere. The patient's index is set in bold; the arousal index of the age group is shown in parentheses. Scientific papers on this index are being prepared. Preliminary results show that this index hints at patient's level of apathy, lethargy, unrest, and stress. The higher the value, the higher the inner unrest.

Version	v10	v10
Eyes open	O1 relative Left hemisphere	O2 relative Right hemisphere
Subject (stanine)	0.80 (3.1% 1)	1.17 (3.8% 1)
Eyes closed	O1 relative Left hemisphere	O2 relative Right hemisphere
Subject (stanine)	-1.74 (5.6% 2)	-2.17 (4.2% 2)
VCPT	O1 relative Left hemisphere	O2 relative Right hemisphere
Subject (stanine)	-0.85 (0.2% 1)	-1.16 (0.0% 1)

Arousal in relationship to focusing

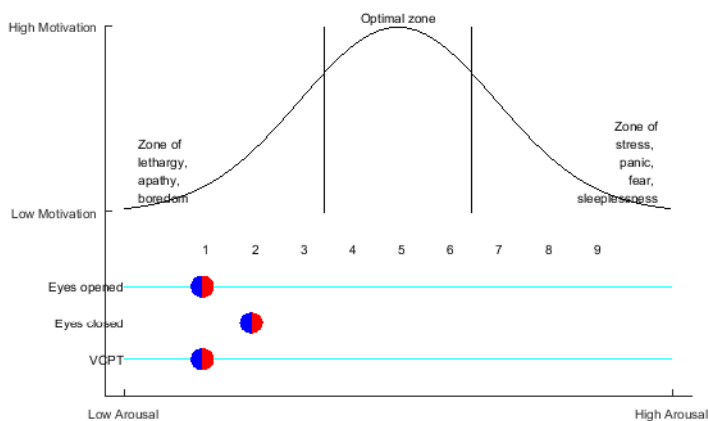
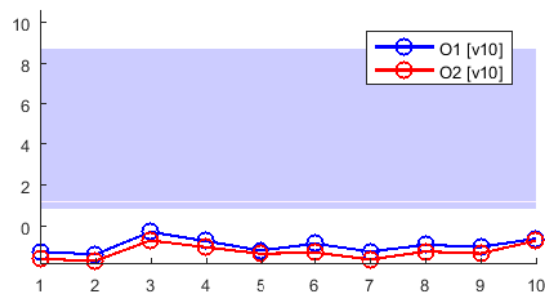


Figure 1: Arousal-Index of the left hemisphere (blue) and the right hemisphere (red) in eyes opened, eyes closed and VCPT.

Compared with peers, Adult Female shows in all conditions significantly reduced values. These values indicate a significantly lower activation. This often leads to a lack of motivation and a lowered willingness towards effort. In unsecure situations, Adult Female might express fears and misgivings. One observes a depressive mood modulation as well as significant unreal perception of everyday life. Often, a compensation is sought through external stimulation (gaming, other excessive behaviors). This behavior yields a bearable internal level of activation. A reduced activation often leads to loss of focus.

Arousal modulation during VCPT

A VCPT recording lasts around 21 minutes. This data was split into 10 equally long epochs, with each epoch lasting for around 125 seconds. Arousal was measured for each epoch. Left hemisphere (O1) and right hemisphere (O2) were recorded separately.

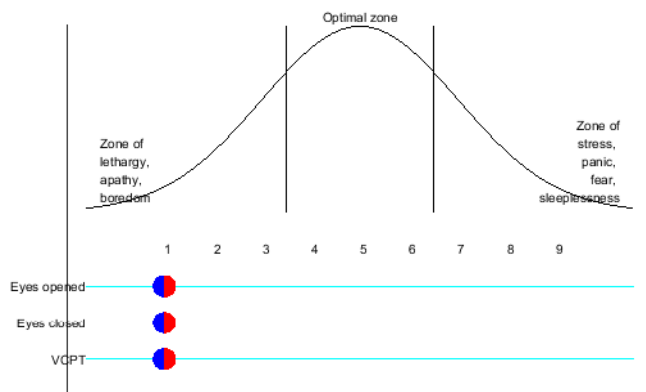


For Adult Female, both hemispheres are synchronized.

Central-sensory Index (relative power, beta-gamma squared); CSI

The central sensory index reflects the organization and functioning of the somatosensory areas. They receive information from many different systems: thalamic nuclei, basal ganglia, limbic system and cingulate system. Functionally, the CSI gives clues to the way of processing: low values are associated with increased introspection/introversion, high values with increased external orientation or extraversion. In children, the CSI provides important information regarding processing in a stimulus-intensive context. In adults, essential indications on the dimension anxiety/internal excitement can be obtained. The scientific publication is still pending.

Version	v01	v01
Eyes open	Left hemisphere	Right hemisphere
Subject (Stanine)	1.5 (0.3% 1)	1.58 (0.5% 1)
Eyes closed	Left hemisphere	Right hemisphere
Subject (Stanine)	1.15 (3% 1)	0.86 (2.4% 1)
During VCPT	Left hemisphere	Right hemisphere
Subject (Stanine)	1.19 (0% 1)	0.86 (0% 1)

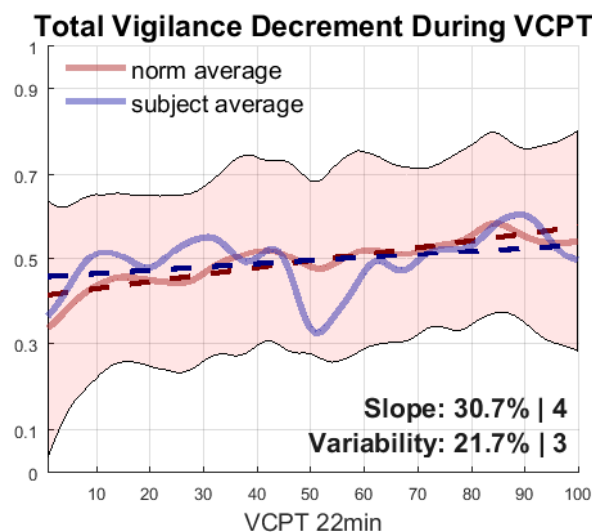


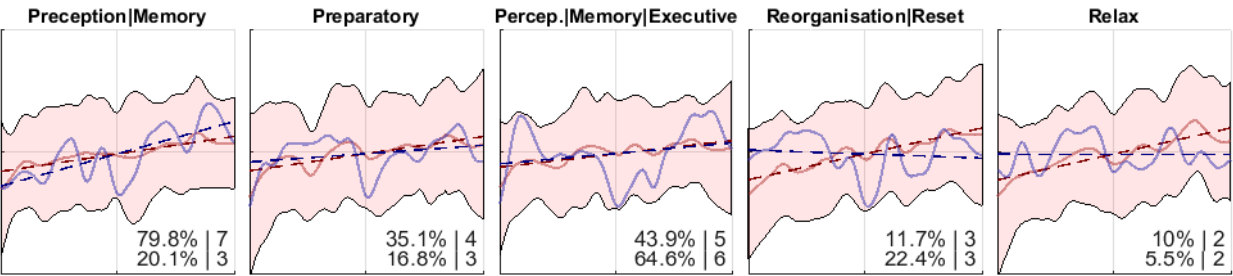
Vigilance and Vigilance decrement

Vigilance refers to the inner, unconscious readiness that enables the solving of tasks: It is the state of increased and permanent readiness to react. It is important to be able to maintain this state over a long period of time. During the concentration course test vigilance means to maintain this readiness to react adaptively over a long period of time according to the requirements. According to the resource model, the readiness to react can only be maintained as long as resources are available. Rising curves therefore indicate that resources can be retrieved, falling curves indicate low resource retrieval. In a detailed analysis it has been shown that the readiness to react does not have to be maintained uniformly during the task. Depending on the demands during task solving, more or less resources are retrieved. For this purpose, the solution process was divided into 5 segments: 1. perception, memory; 2. preparation; 3. perception, memory, action/action; 4 reset/reorganization; 5.relax. The individual data are compared with those of peers in terms of intensity of resource retrieval (slope) and stability of the solution process (variability).

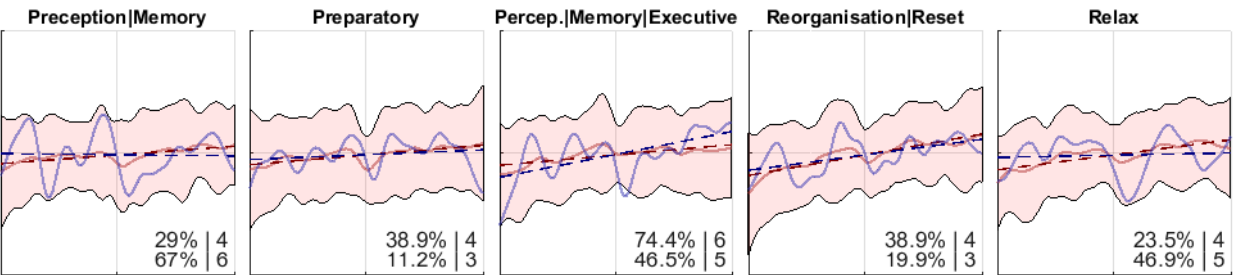
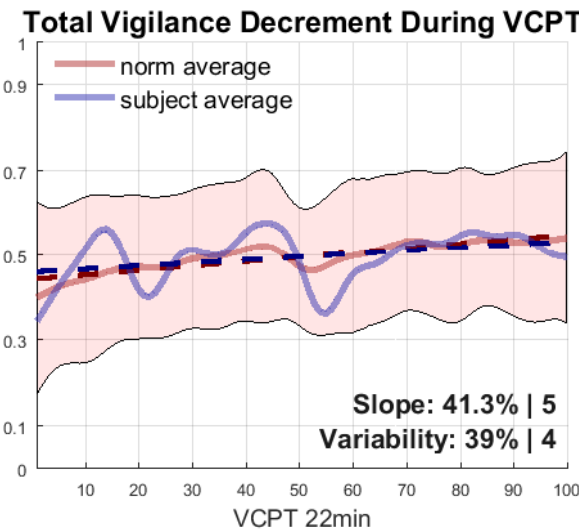
- ❖ **Flat regression curve (Stanine: 1,2,3)** show low resource load, low resources (low inner power) and low inner control (low prediction) (Assumption: ADHD, PTSD)
- ❖ **Steep regression curve (Stanine: 7,8,9)** show high resource load, high resources (high inner tension) and high inner control (high prediction) (Assumption: OCD, high tension, Depression, Anxiety)
- ❖ **Low variability (Stanine: 1,2,3)** means too high inner stability (Assumption: Rigidity, Autism)
- ❖ **High variability (stanine: 7,8,9)** means low inner stability (assumption: ADHD, PTSD, aso)

Go

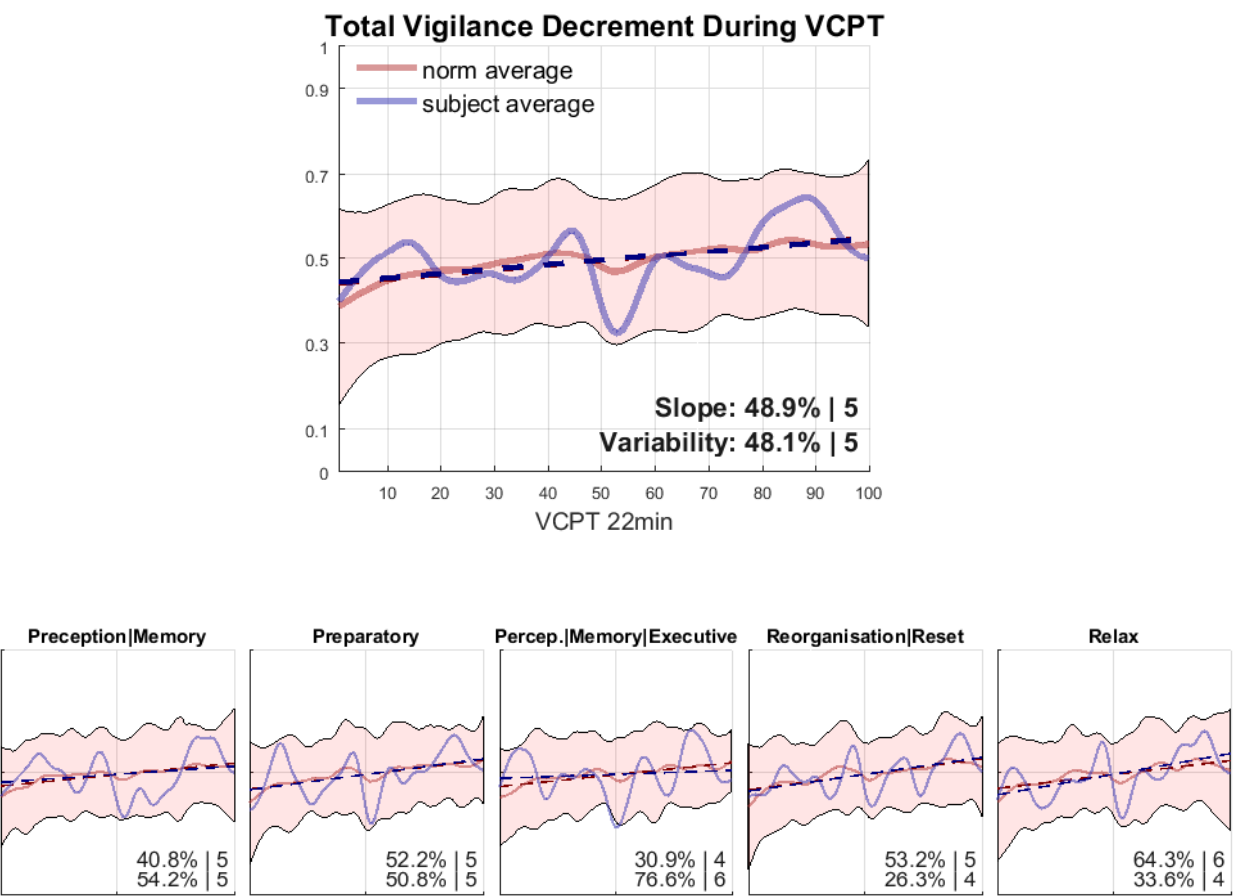




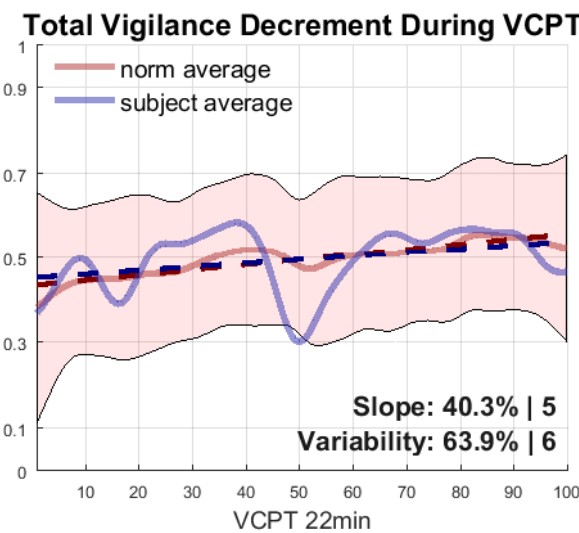
NoGo

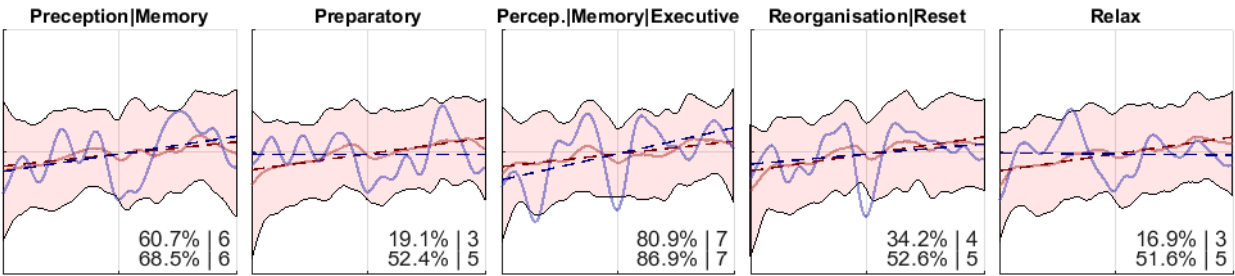


Ignore



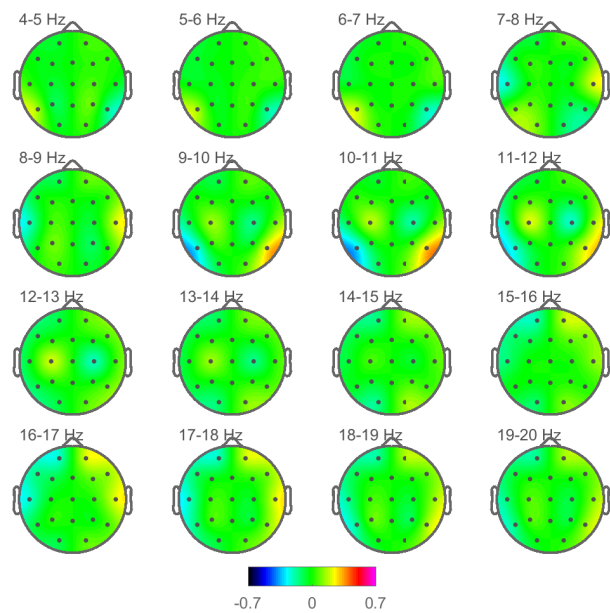
Ignore + Novelty



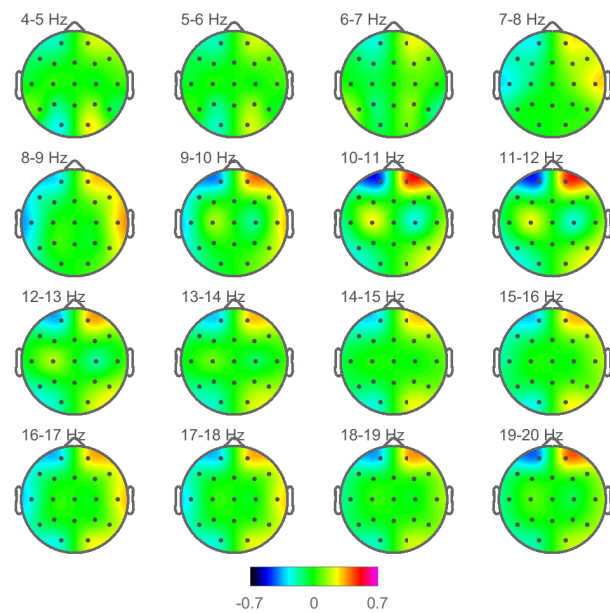


Asymmetry

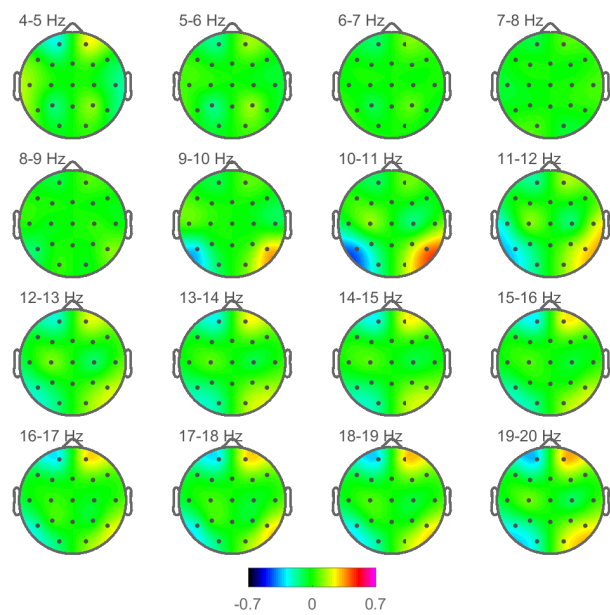
Asymmetry eyes closed:



Asymmetry eyes open:



Asymmetry VCPT:

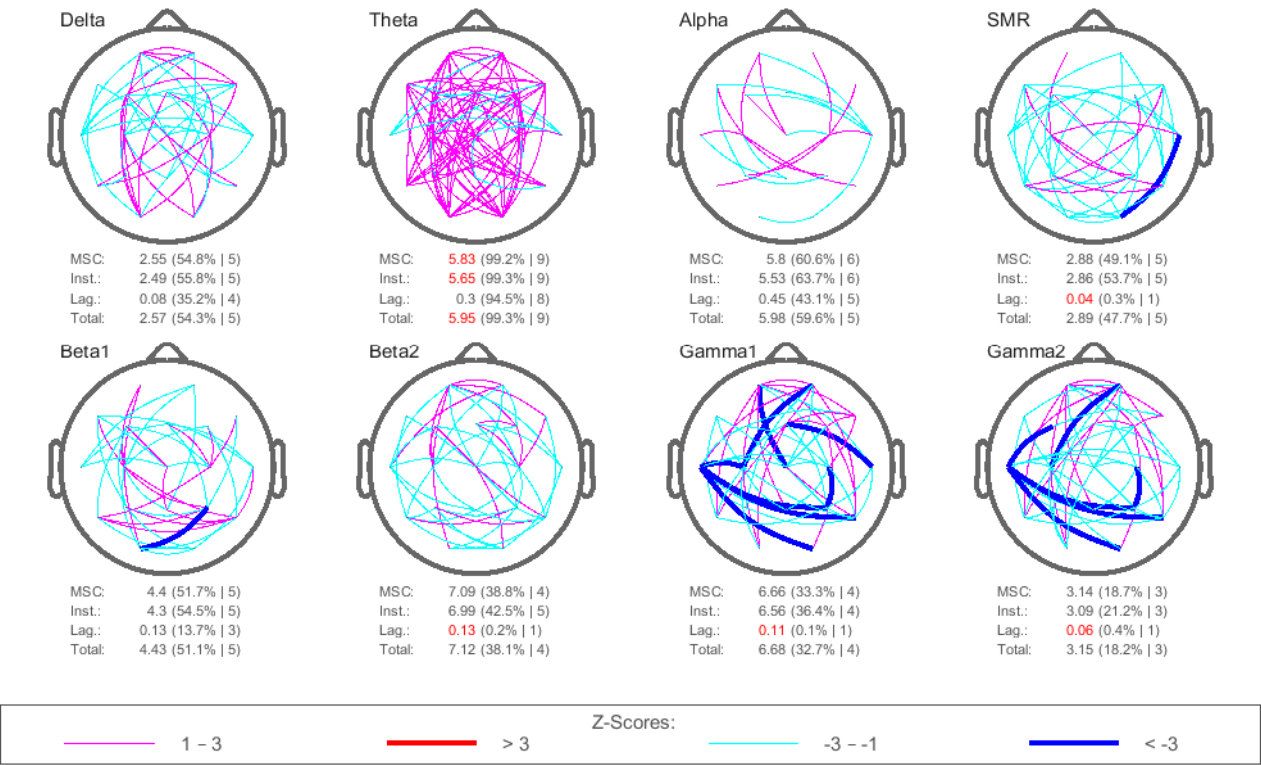


Without significant findings

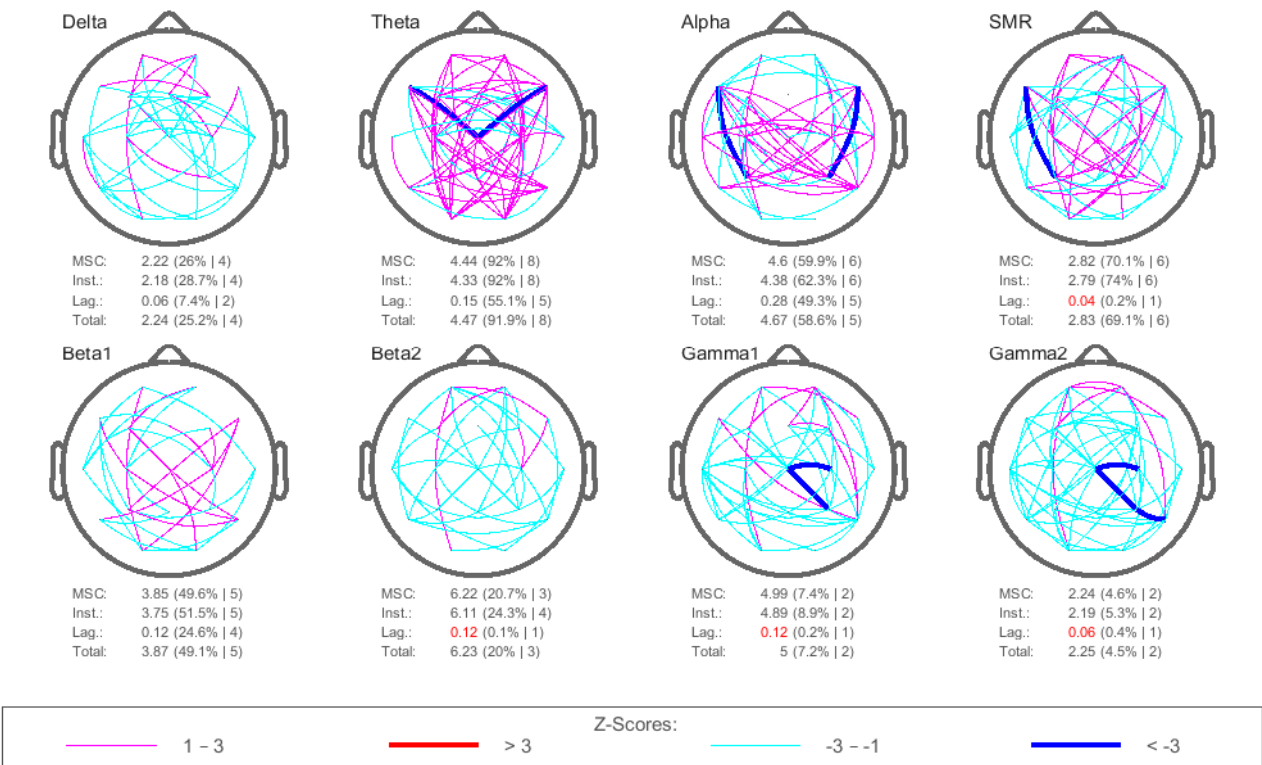
Coherence

The coherence analysis is a measure of the relationship of various structures in the cortex. The coherence analysis provides a ratio of the correlation of a specific frequency range. Violet and red lines represent excessive positive correlations, light blue and dark blue lines represent excessive negative correlations. Excessive positive correlations suggest that there is over-communication between the sites. Excessive negative correlations suggest that there is a lack of communication between the sites.

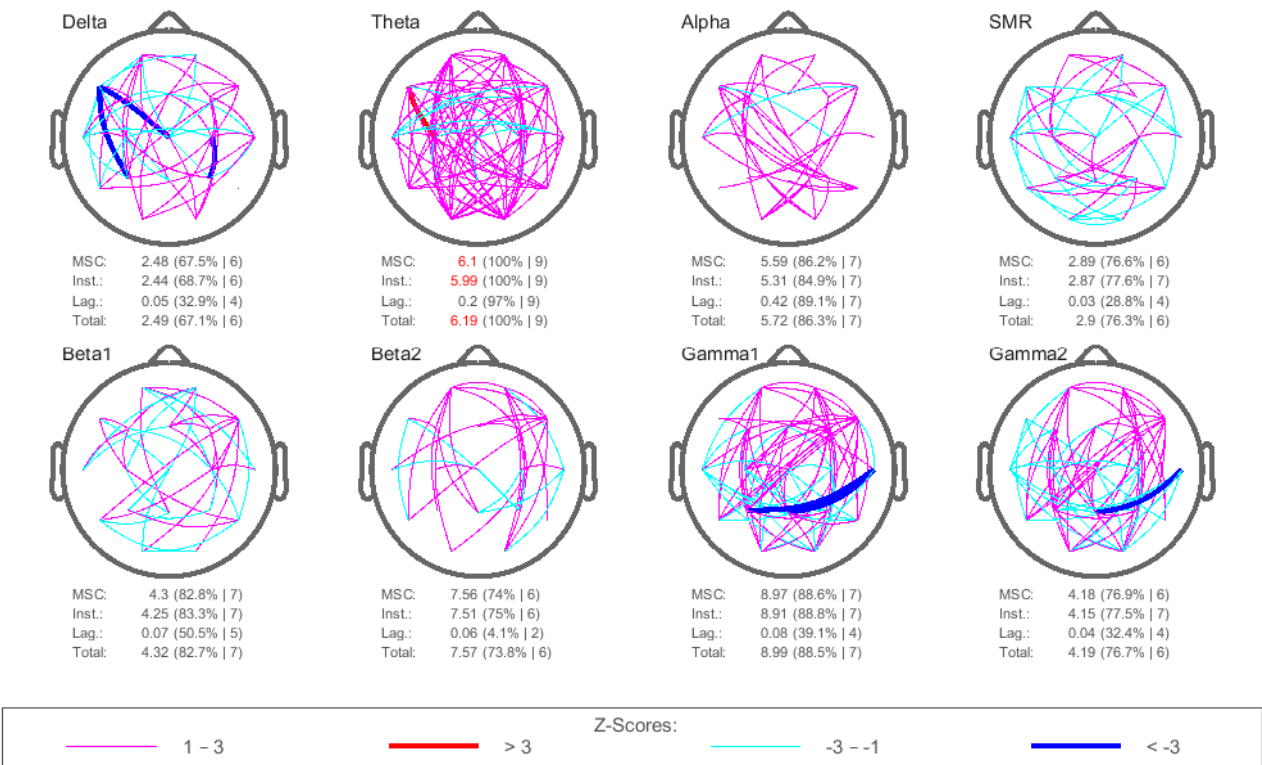
Coherence in eyes closed condition:



Coherence in eyes open condition:



Coherence in VCPT condition:



Without significant findings

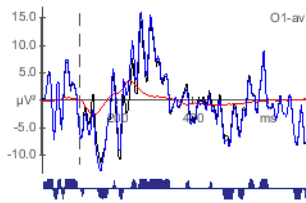
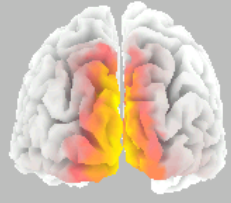
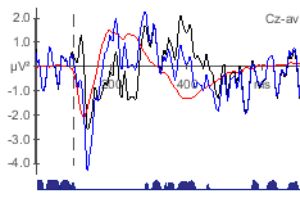
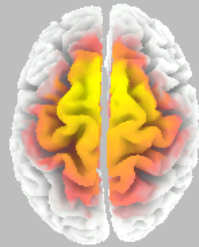
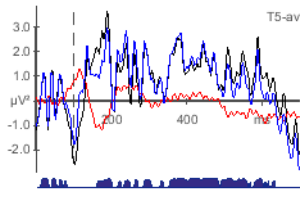
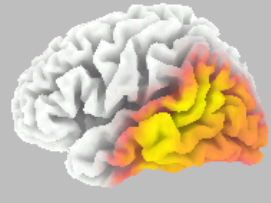
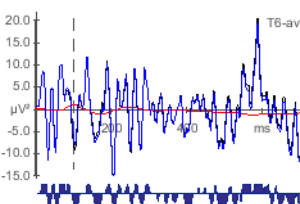
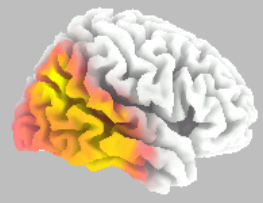
3. Evoked Potentials (in continuous performance task)

The images of the evoked potentials are relevant to information processing in different regions of the brain during the presentation of simple stimuli. In the various potentials, only specific neuronal groups and networks are involved.

Comparison of the components with database:

Input areas:

blue: client/red: database/black: difference (significance)

<p>P1N1</p> <p>Visual Input</p> 	<p>Brodmann area 19 Cuneus Occipital Lobe</p> <p>Best Match at 5mm Brodmann area 18 Cuneus Occipital Lobe</p> 
<p>N1P2</p> <p>Auditory Novelty</p> 	<p>Brodmann area 6 Superior Frontal Gyrus Frontal Lobe</p> <p>Best Match at 17mm Brodmann area 8 Superior Frontal Gyrus Frontal Lobe</p> 
<p>P1N1 vTL</p> <p>left Association areas</p> 	<p>Brodmann area 22 Superior Temporal Gyrus Temporal Lobe</p> <p>Best Match at 7mm Brodmann area 40 Supramarginal Gyrus Temporal Lobe</p> 
<p>P1N1 vTR</p> <p>right Association areas</p> 	<p>Brodmann area 39 Angular Gyrus Parietal Lobe</p> <p>Best Match at 9mm Brodmann area 40 Inferior Parietal Lobule Parietal Lobe</p> 

Memory areas:

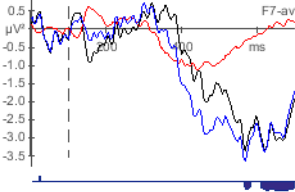
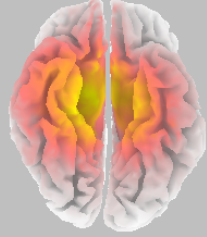
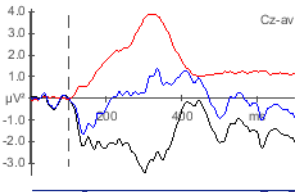
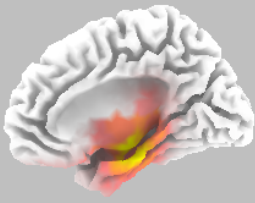
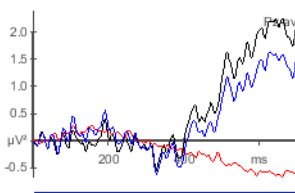
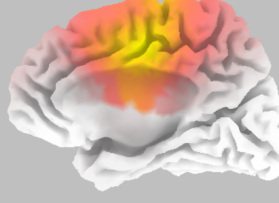
blue: client/red: database/black: difference (significance)

<p>V com TL</p> <p>left</p> <p>Memory areas</p>		<p>Brodmann area 21 Middle Temporal Gyrus Temporal Lobe</p> <p>Best Match at 7mm Brodmann area 22 Middle Temporal Gyrus Temporal Lobe</p>	
<p>V com TR</p> <p>right</p> <p>Memory areas</p>		<p>Brodmann area 21 Middle Temporal Gyrus Temporal Lobe</p> <p>Best Match at 5mm Middle Temporal Gyrus Temporal Lobe</p>	

Executive function areas:

blue: client/red: database/black: difference (significance)

<p>P3b</p> <p>Engagement</p>		<p>Brodmann area 6 Medial Frontal Gyrus Frontal Lobe</p> <p>Best Match at 5mm Brodmann area 5 Paracentral Lobule Frontal Lobe</p>	
<p>P3a</p> <p>Inhibition/Suppression</p>		<p>Brodmann area 6 Superior Frontal Gyrus Frontal Lobe</p> <p>Best Match at 17mm Brodmann area 8 Superior Frontal Gyrus Frontal Lobe</p>	
<p>P4 monCC</p> <p>Monitoring</p>		<p>Brodmann area 25 Anterior Cingulate Limbic Lobe</p> <p>Best Match at 15mm Brodmann area 34 Subcallosal Gyrus Frontal Lobe</p>	

<p>P4wmF</p> <p>Working Memory</p> 	<p>Brodmann area 34 Parahippocampus Gyrus Limbic Lobe</p> <p>Best Match at 5 mm Brodmann area 28 Parahippocampal Gyrus Limbic Lobe</p>	
<p>SW PHC</p> <p>Slow Wave Activity</p> <p>This component reflects a part of limbic system activity</p> 	<p>Brodmann area 28 Parahippocampal Gyrus Limbic Lobe</p> <p>Best Match at 5 mm Brodmann area 34 Parahippocampal Gyrus Limbic Lobe</p>	
<p>CNV</p> <p>Bereitschaftspotenzial</p> <p>Readiness Potential</p> 	<p>Brodmann area 24 Cingulate Gyrus Limbic Lobe</p> <p>Best Match at 7 mm Brodmann area 6 Medial Frontal Gyrus Frontal Lobe</p>	

Shown are various deviations from the norm:

P1N1 - Visual Input:

Mid potentials: Late latency, High amplitude (negative & positive)

P3a - Inhibition/Suppression:

Early potentials: Low amplitude (negative & positive)

Mid potentials: Low amplitude (negative & positive)

P4 monCC - Monitoring:

Early potentials: Low amplitude (negative & positive)

Mid potentials: Low amplitude (negative & positive)

CNV - Readiness Potential

Mid potentials: High amplitude (negative & positive)

P1N1 - Visual input

The activation of primary visual areas informs about the quality of picture decoding into neurophysiological signals.

Mid potentials

Latency provides information about processing speed while amplitude provides information about the intensity of information processing. Adult Female shows late and high activation, what indicates delayed information processing. High amplitudes indicate high processing intensity. This is not so common and is likely associated with internal control processes (executive functions).

P3a - Inhibition/Suppression

Executive functions/inhibition/suppression/selection: This function is highly relevant not only for motor and cognitive (perceptual) control, but also for emotional behavior. Inhibition is a fundamental function of neuronal networks, which regulate the planning, execution and control of different processes. These functions are involved in all processes as inhibition (suppression) of processes represents a fundamental part of neurobiological networks. The **Inhibition** phenomenon works by influencing a neuron through an impulse that prevents the occurrence of an action potential, meaning that it impedes the firing of the neuron. Synaptic inhibition can occur be either pre- or postsynaptic inhibition. This inhibition function is localized in the fronto striatal loop (cortex-basal ganglia-thalamus-cortex).

Early potentials

Early potentials of inhibition/suppression are related to sensory processing functions that are not under cognitive control. The inhibition function of early potentials pertains mainly the monitoring of sensory assimilation and processing modalities.

Low amplitudes of early potentials in inhibition/suppression are usually related to dysfunctional control of diverse sensory processes.

Mid potentials

Mid potentials of inhibition/suppression are a complex interplay that involves control processes of the aforementioned functions. Cognitive and sensory parts are involved. Monitoring, planning and control of different functions like attention, executive system tasks, and general control of activity are defined by mid potentials of inhibition and suppression.

Low amplitudes of mid potentials in inhibition processes result in less intense and less incisive control and monitoring of processes. Often distinct situations are not differentially structured, which leads to attentional errors and difficulties in impulse control.

p4 monCC - Conflict monitoring

Executive functions/Monitoring: Like all executive functions, this function is essential for everyday functioning as it enables assessing one's performance and processes. The anterior cingulate cortex occupies about 2/3 of the medial surface in frontal lobes, located ventral, rostral and dorsal to the corpus callosum: a fiber tract that connects both hemispheres. The anterior cingulate cortex corresponds to the Brodmann areas 24, 25 and 32. In the context of executive functions the anterior cingulate cortex is involved in conflict solving between competing responses and arbitrary selection of action alternatives. Furthermore, this structure is involved in learning processes together with basal ganglia, assessing different action alternatives according to relevance. Within the anterior cingulate cortex two parts can be further differentiated: a rostral-ventral area that becomes activated in response to emotional conflicts, and a dorsal area that is more related to controlling cognitive functions. Even if this function is not entirely clear yet, it can be said that through this network a comparison operation takes place: by comparing one's actual behavior (emotional, cognitive, behavioral performance) with the expected outcomes.

Early potentials

Early potentials of conflict monitoring influence preparatory functions of sensory assimilation. Hereby emotional constitution and strain exert an important impact on several sensory functions.

In Adult Female, low amplitudes in early potentials of conflict monitoring are observed. Low potentials occur in correlation with minor discharges of electric potentials indicating in this context that sensory input is marginally influenced by the limbic system. This means that no clear monitoring of different action alternatives takes place.

Mid potentials

Mid potentials of conflict monitoring are influenced by different functions of the limbic system and vegetative nervous system. The limbic system proceeds over the amygdala/insula to the hippocampus, and

from here to anterior nuclei of the thalamus, influencing the anterior cingulate cortex. According to the definition of the anterior cingulate cortex the functions of mid potentials of this component are defined by the monitoring of different action alternatives.

In Adult Female, low amplitudes in mid potentials of conflict monitoring are observed. Low amplitudes in mid potentials indicate low activation of limbic energy during appraisal of action alternatives. Psychologically this state is defined by indifference and perplexity.

CNV - readiness potential

The readiness potential is an indicator of the activation and preparation processes for the next stimulus. Here, the initiation of a motor movement is significant. It is measured in the central parietal cortex. See Walter, Cooper, et al (1964); Gaillard, A.W.; Näätänen, R. 1976); Thigpen, N.N., Keil, A. (2017). the readiness potential has an early component modulated by noradrenergic systems and a late component thought to be related to motor readiness and under dopaminergic control (cf Rohrbaugh, et al 1986; Birbaumer, et al, 1990).

Mid potentials

High amplitudes mean that the brain prepares more intensively for the next stimulus.

4. Event related potentials - ERPs

Total number of trials: **399** (a-a GO: **99**, a-p NoGO: **100**, p-p: **100**, p-h: **100**, +: **199**, -: **200**, a-p-a-a: **0**)

Number of processed trials: **395** (a-a GO: **97**, a-p NoGO: **100**, p-p: **98**, p-h: **100**, +: **197**, -: **198**, a-p-a-a: **100**)

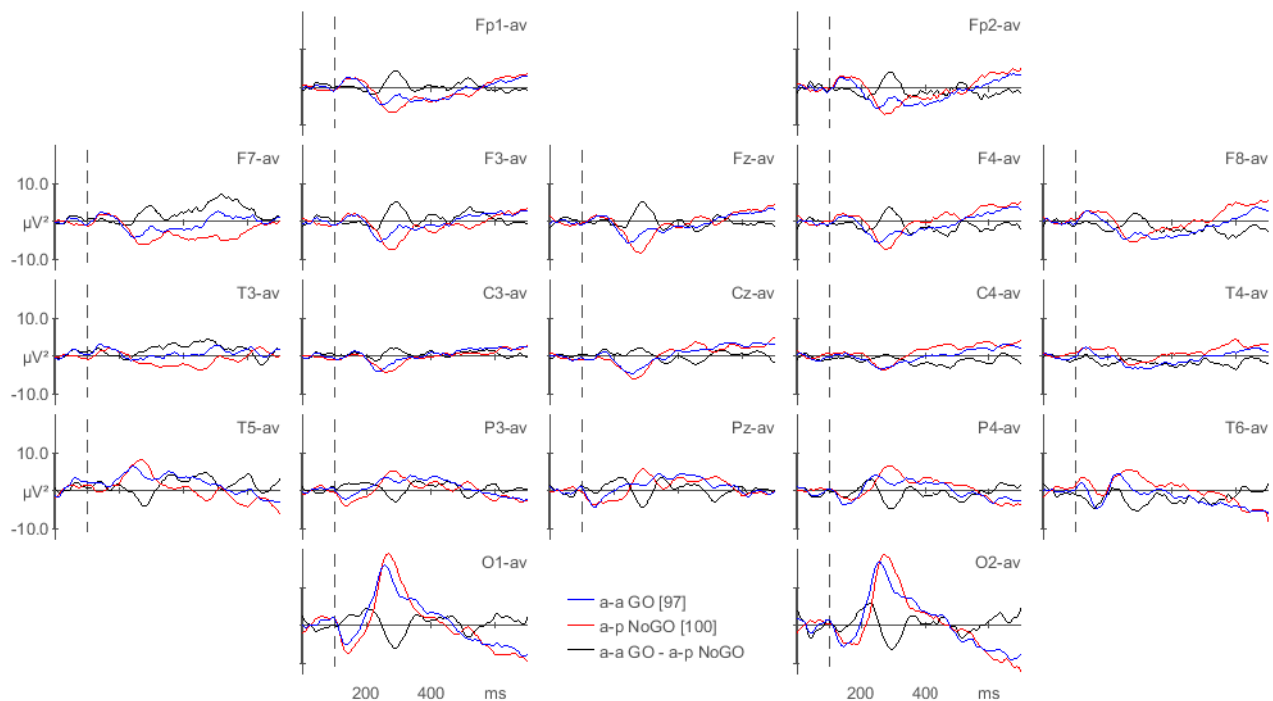
ERP Components

Comparison of the client's GO and NoGO ERPs computed for the second stimulus.

ERPs in the GO-NoGO task computed for GO, NoGO stimuli and ERP differences (GO- NoGO) are presented below.

blue: GO/red: NoGO data/black: difference curve (GO-NoGO)

GO-NoGO:



Differences between GO-condition and NOGO-condition are observed in central cortex and superior temporal cortex. This indicates an ability to perceptually discriminate different situations.

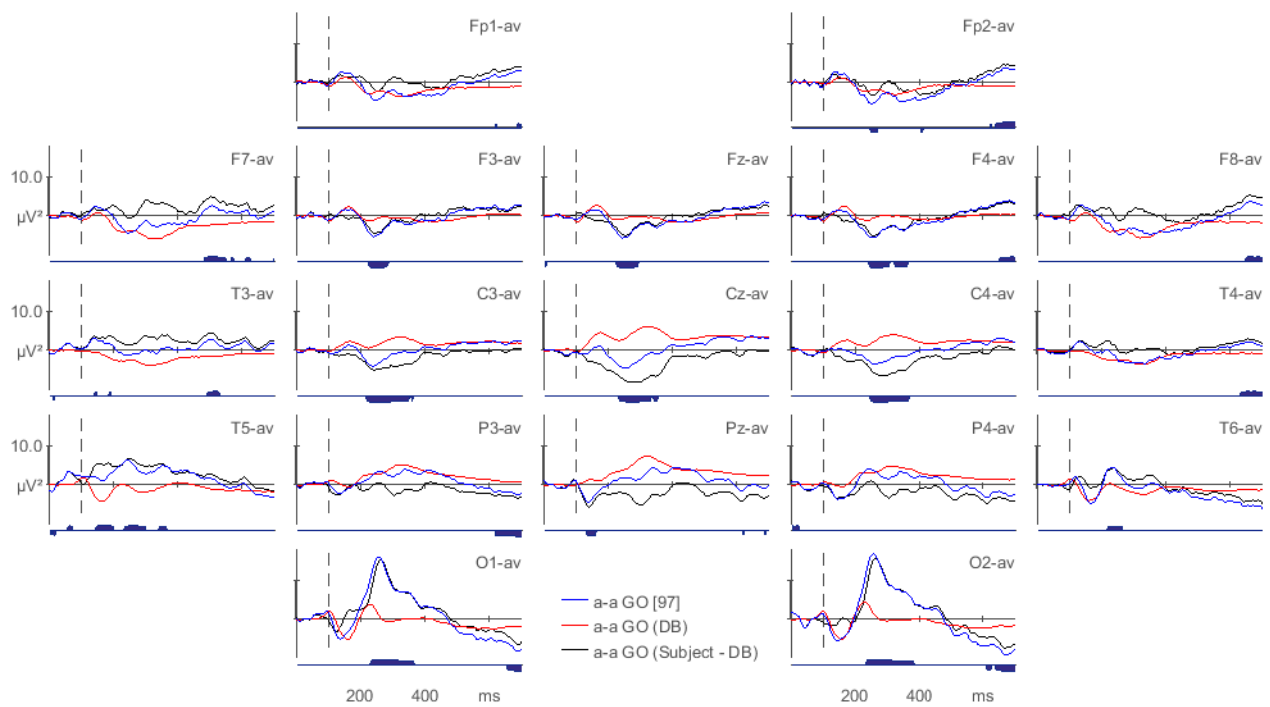
Simple ERPs

Comparison with the normative ERPs computed for the second stimulus.

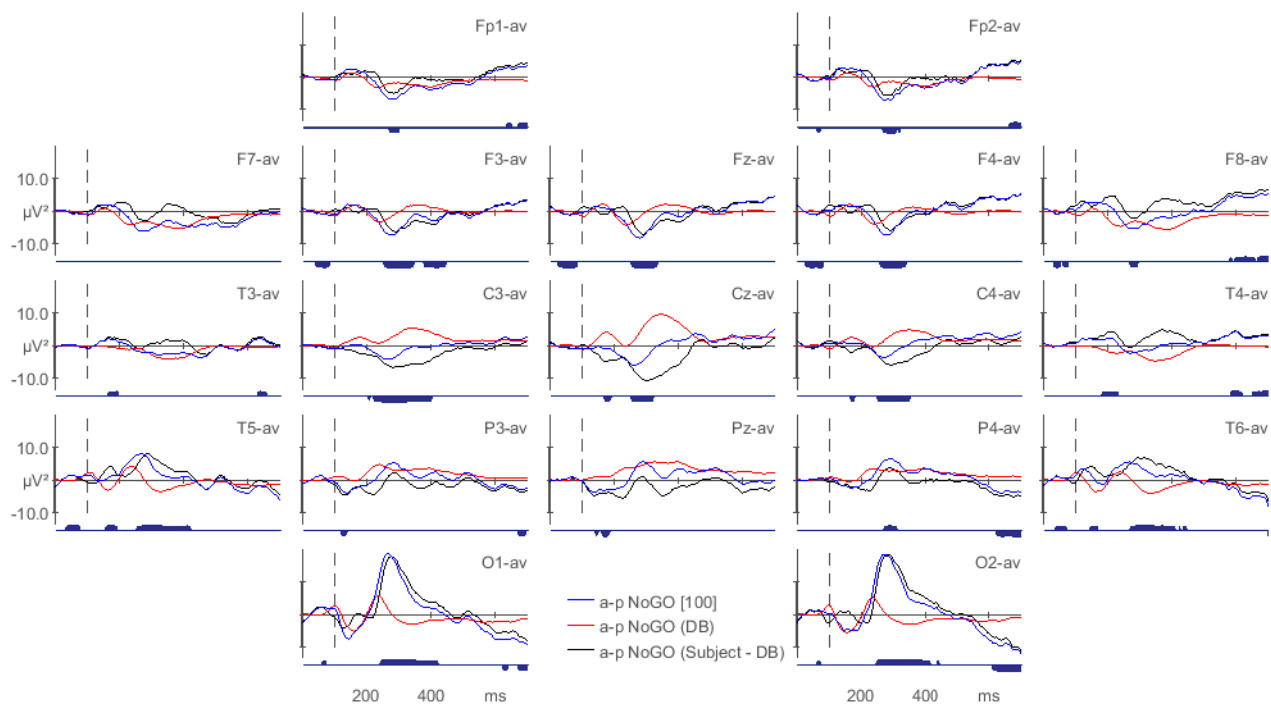
ERPs in the GO-NoGO task computed for GO, NoGO and Novelty (p-h) stimuli are presented on the next pages.

blue: subject/red: reference data/black: difference curve (significance)

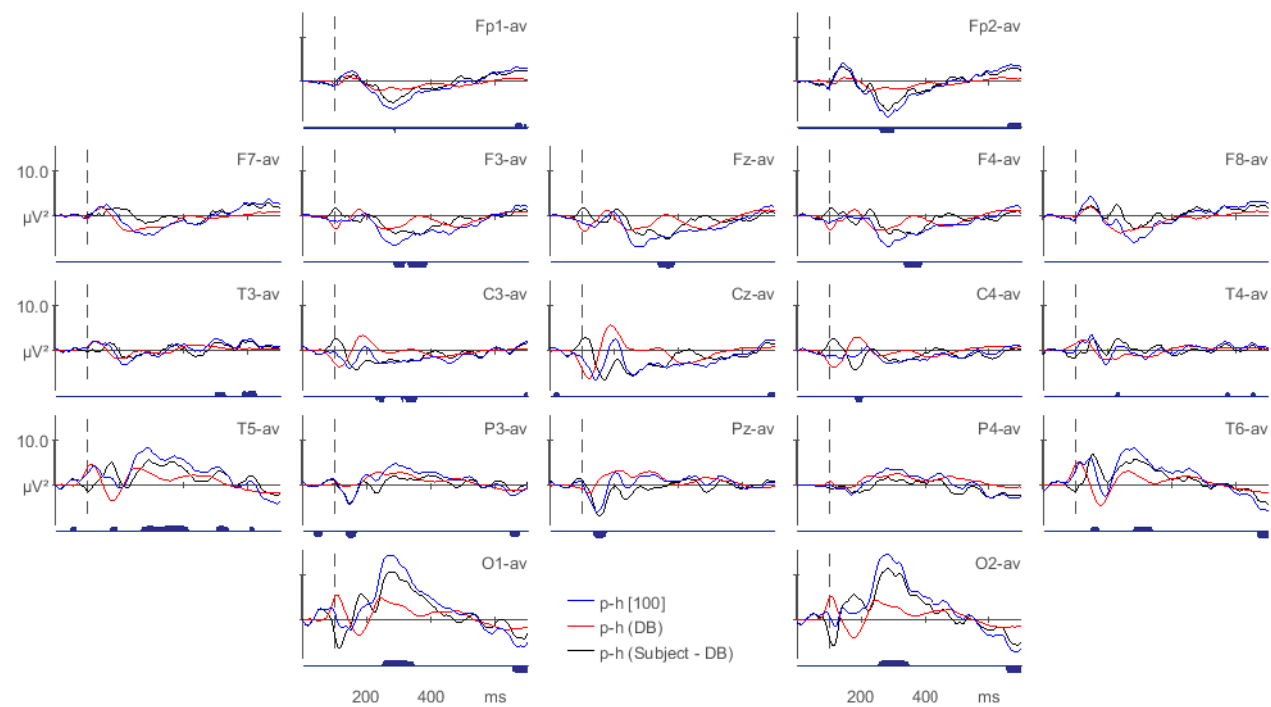
GO condition:



NoGO condition:



Novelty condition (p-h):



5. Diagnostic-Algorithms

According to the medical tradition, a diagnosis is to be made on the one hand by the reported suffering of the patients and, on the other hand, by evidence-based, objective diagnostic procedures. Focusing on neurophysiological characteristics implies that norms have been defined by a meticulous method according to scientifically recognized criteria and compared with patient groups. The patients included in the patient groups were all diagnosed by the usual criteria of the diagnostic and statistical manual (gold standard) as well as by experts. This allows a reliable definition of the patient group and its subtypes.

Psychopathology varies according to age and shows different characteristics depending on age group. Therefore, the patient groups must be divided into age groups. For each age group, the corresponding biomarkers are calculated and validated within the age group. This is done according to the following procedure: several hundred patients from several patient groups were subjected to standardized scientific examinations. This affects patient groups to attention disorders, learning disabilities, autism, depression, schizophrenia, obsessive-compulsive disorder, slight traumatic brain injury and stress disorders (patients after heart attack). For each of these patient groups, algorithms are developed for various age groups using complex statistical methods (big data, learning machines). For each individual patient, the probability of matching to the different patient groups can therefore be calculated using the algorithms. So far, there are algorithms for attention disorders as well as stress disturbances. Further algorithms follow 2017/2018.

Such an extended approach can provide support for diagnostics and statements regarding sensitivity and specificity. The probability of the diagnosis being accepted in percentages is calculated and output in the individual case. It is recommended that these markers be clinically validated in individual cases. However, the result of the algorithm comparison is not the clinical diagnosis!

It is clinically evident that diagnoses are a generalization and thus always an approximation to the actual, individually very different processes and circumstances of the individual humans. This is currently the best possible representation of a membership of a patient group. Our data, which are not yet used in clinical studies so far, help to better characterize the characteristics and to differentiate between the subtypes with consequences for prognosis and therapeutic measures, which is a step closer to the individual as a matter of fact. To this extent, it must also be emphasized once again that the information of the neurophysiological constellations represents a complementary mosaic piece of the findings which extends the previous diagnostics. It is also clear that the demarcation to other patient groups is necessary. This will be all the more possible, the more algorithms of other patient groups are present and the patient's affiliation to existing patient groups can be defined as precisely as possible. It is also clear that the quality of the algorithms is closely linked to patient numbers and patients in general. The higher the number of patients, the clearer the patient's diagnosis, the better the algorithms. Since the present algorithms are dynamic variables, they will be constantly updated over time.

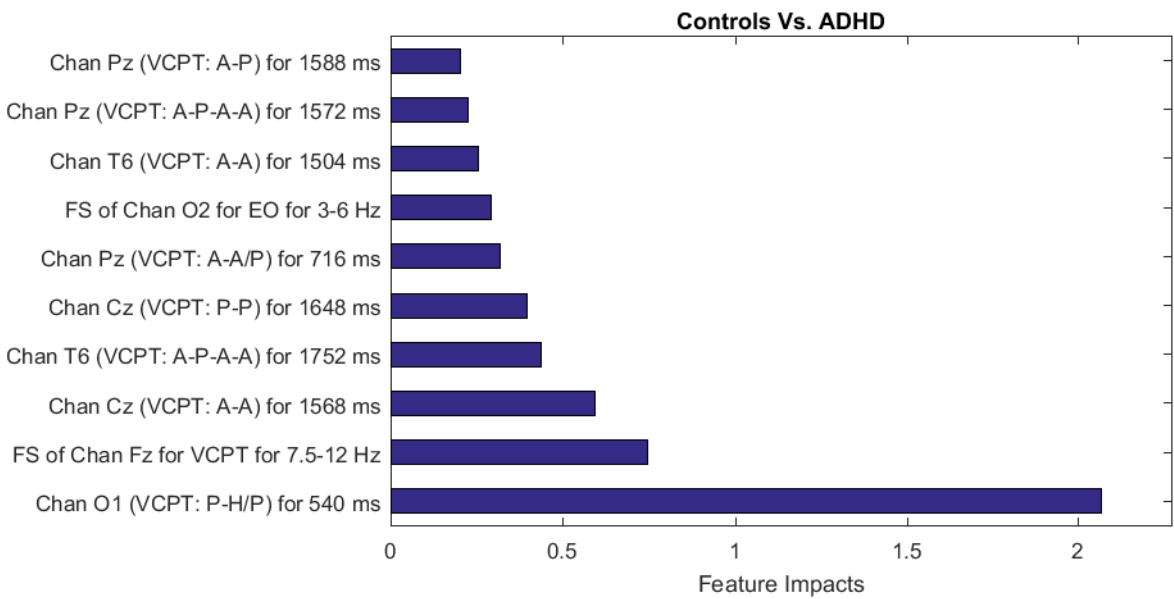
A. ADHD-Diagnose-Index

The ADHD algorithm or ADHD index was realized in the context of the CH-ADHS project on three different samples. The following algorithm was used: Regularized Logistic Regression.

Adult Female belongs to the age group 18 - 67.

For Adult Female the following probability of belonging to this group is shown:

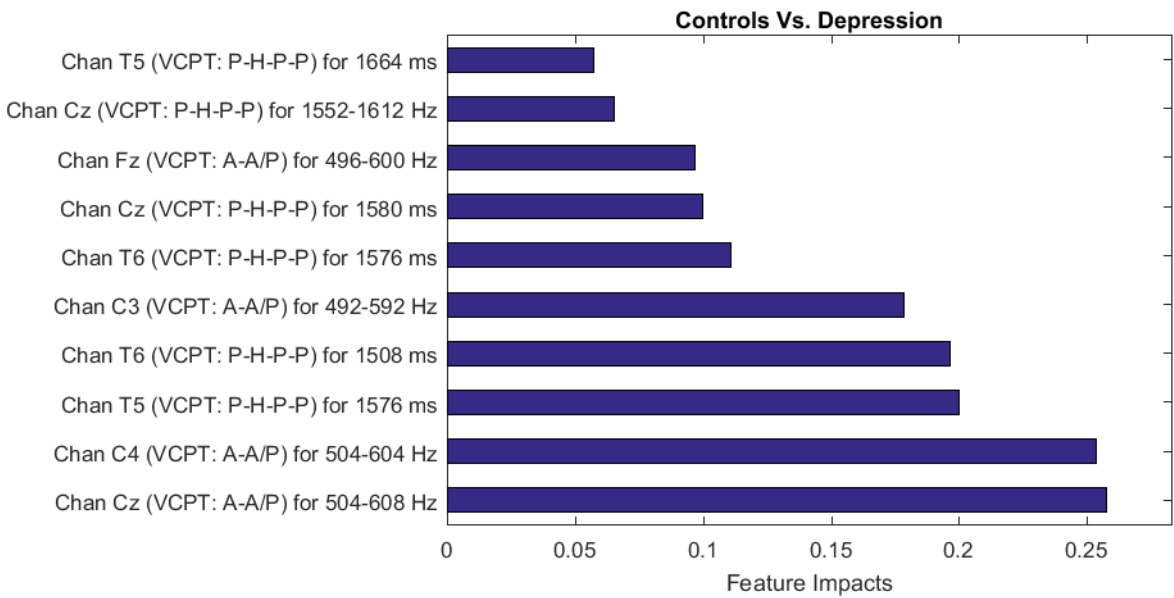
ADHD: 83%



B. Emotion regulation, including mood modulation.

For Adult Female the following probability for the presence of deviance in Emotional regulation is calculated: Depression: 56%

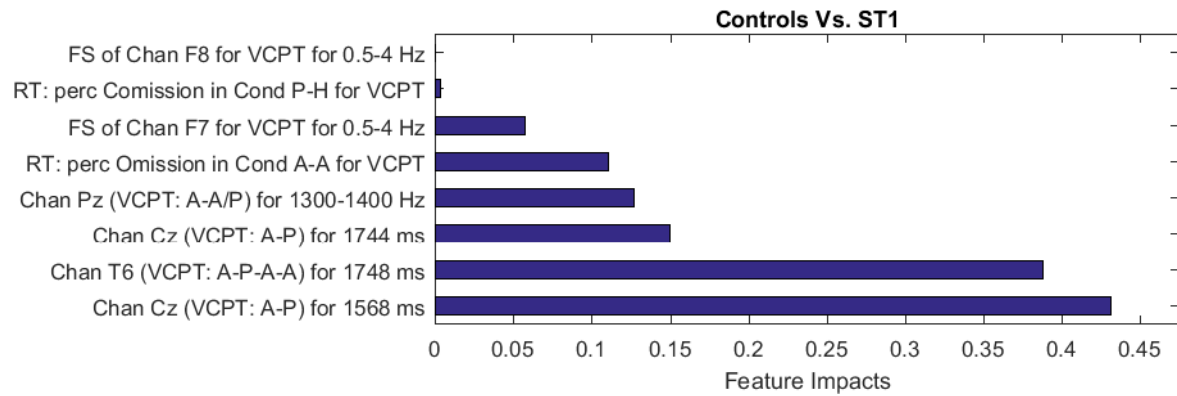
The following features are particularly significant:



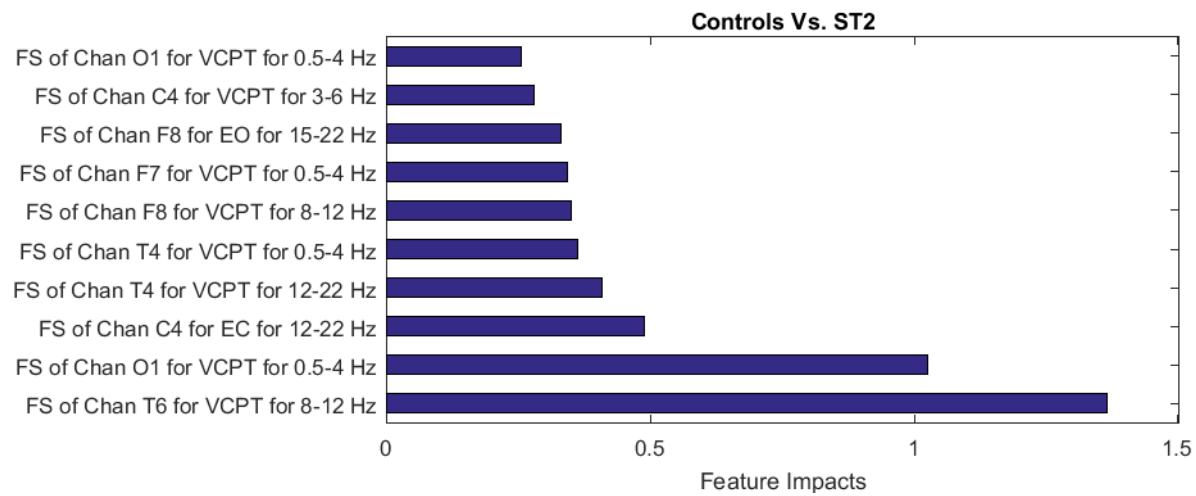
Subtypes

[description]

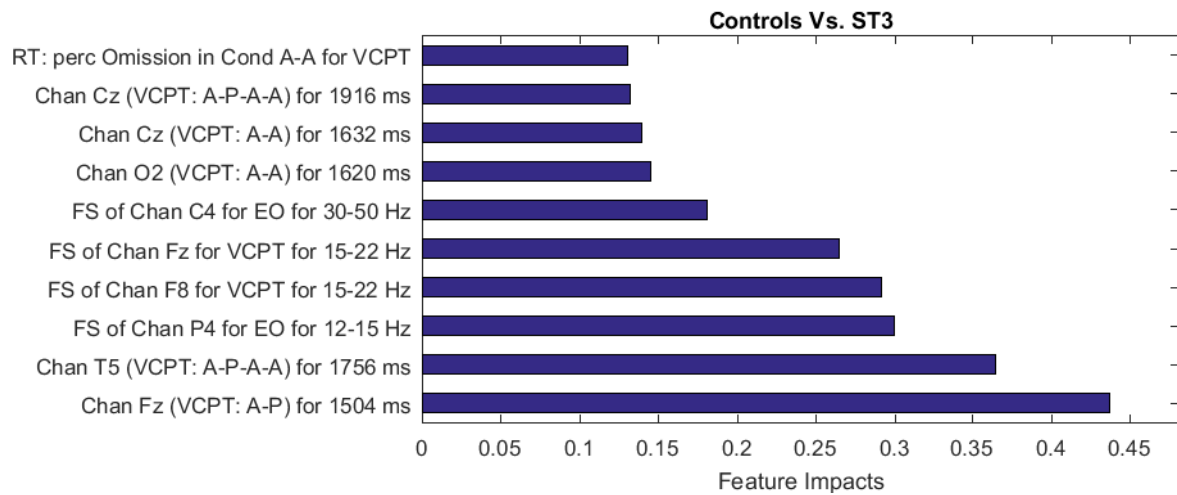
ST1: 43%



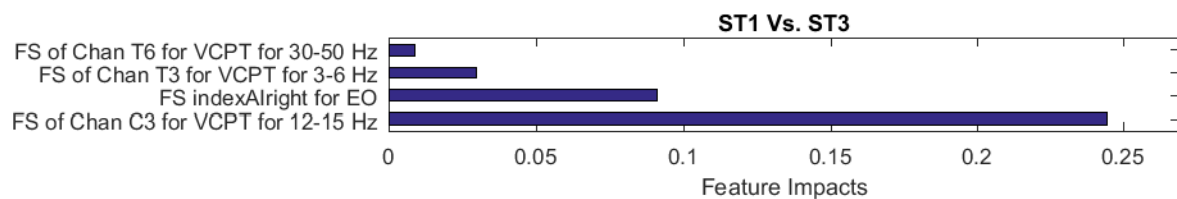
ST2: 63%



ST3: 32%



ST3 (ST1vsST3): 46%



V. Recommendations

We would like to point out that the therapeutic approach must be holistic and include various aspects of life. This means that in addition to cognitive, behavioral and emotional aspects, a person's physiology must also be considered. An all-inclusive change strategy is beyond the scope of this report. However, we believe that difficulties must be addressed in a multi-modal approach that takes into consideration a variety of aspects involved in the individual. The recommendations that follow seek to do that within the scope of the information provided by the results of this evaluation.

1. Medication

These medication recommendations are based merely on the reported neurobiological parameters. Different people react differently to medication. Side effects are especially hard to predict. The responsibility for any given medication lies in the hands of the prescribing medical doctor.

Adult Female is currently taking medications that maybe impacting the findings; therefore, no recommendations can be made at this time.

2. Everyday Life/Work

General statement: Our basic principle is that a high degree of neurobiological change is possible. Thanks to worldwide, intensive research in the field of neuroplasticity, we know that new neuronal connections can be formed in every area if the right information is given. Personalized interventions are listed which are based on research and rated highly as potential facilitators of change.

Daily Life: Adult Female will benefit from incorporating as much routine and structure into her day as she can. For example, routines can be instituted for waking in the AM, around meals, times for work, pre-sleep routines, household chores, etc. It may take discipline to follow the routines initially, but once they become actual routines, life will become easier, better organized and more efficient. It will also put less strain on her brain.

Sleep: Not reported to be an issue. It may be helpful to discuss good sleep hygiene practices such as establishing a bedtime routine that includes relaxing activities (warm shower, reading, etc.) to ensure sleep is optimized. More information can be found on the Sadar Psychological Services website (<https://sadarpsych.com/take-care-of-your-brain/sleep/>).

Diet: No information provided. The following guidelines are offered for consideration. There is considerable science suggesting that a diet higher in protein (leaner meat, eggs, fish and dairy products) and lower in simple carbohydrates (sugar, rice, pasta, potatoes, flour and bread) improves concentration and general brain function. Meals that are primarily simple carbohydrates (breakfast cereal, pastry, pasta, French fries, etc.) cause an initial rapid surge in blood sugar making the individual more hyperactive. Soon thereafter, there is a rapid fall in blood sugar leading to mental fatigue. Meals with more protein and complex carbohydrates (vegetables, fruits and whole grains) keep blood sugar more stable, give steady energy and reduce chances of storing excess fat.

There is significant evidence that increasing Omega-3 oil benefits learning, helps stabilize mood and helps overall wellness. A good source of this is oily fish such as salmon and tuna, although there is significant controversy regarding mercury contamination of ocean raised, farm raised and even canned fish. An alternative is fish oil capsules and/or fish oil liquid supplements. These can be found in most health food sections and are not expensive. Our research review shows that fish oils produced in triglyceride form are the best source of Omega-3, when taken as recommended on the bottle. Vitamin D3 is also being recommended by the scientific community as being important for efficient brain functioning. For example, it is being recommended at the Amen Clinics in addition to Omega-3 fatty acids. It is important to have one's D3 level checked before beginning such supplementation.

Exercise: No information provided. Our recommendation is to reach a point where you engage in moderate or greater physical activity/exercise for thirty minutes or more at least five days a week. For Adult Female focusing on cardiovascular activity is recommended.

Drugs/Alcohol: No information provided.

Electronic Screen Use: No information provided. The general recommendation is to limit screen time to 2 hours a day.

3. Other Recommendations

Psychotherapy/Coaching: Making several lifestyle changes can feel stressful if an individual is already experiencing over arousal and anxiety. Working with a therapist who can break down these changes into manageable pieces and encourage these efforts may be beneficial in the long term.

Biofeedback:

Heart Rate Variability (HRV) is a measure of the beat-to-beat variations in heart rate. HRV is an important indicator of both physiological resiliency and behavioral flexibility, reflecting the individual's capacity to adapt effectively to stress and environmental demands. It is a skill that can be learned and practiced to improve health, performance, and overall well-being. This technique, once learned and practiced, can give Adult Female a way to regulate arousal. The more balance in the autonomic nervous system, the easier it is to concentrate and to control one's emotions and behaviors.

Capnography measures exhaled carbon dioxide (CO₂) levels through the use of a nasal canula. Through changing aspects of breathing (such as tidal volume or breathing rate) an individual can learn to increase CO₂ levels. This is important as maintaining adequate CO₂ is essential for maintaining pH, delivering oxygen to cells and many other cellular functions. An evaluation maybe helpful to rule out or address over breathing as it relates to anxiety/panic.

Neurofeedback: EEG Biofeedback (also called neurofeedback, neurotherapy, or neurobiofeedback) is a type of biofeedback that uses real-time measurements of brainwaves (EEG) to provide a signal that can be used by a person to receive feedback about brain activity, often with a goal of controlling and enhancing central nervous system activity.

During training, sensors are placed on the scalp and then connected to sensitive electronics and computer software that detect, amplify, and display specific brain activity. Resulting information is fed back to the trainee virtually instantaneously with the conceptual understanding that changes in the feedback signal indicate whether or not the trainee's brain activity is within the designated range.

Based on this feedback, changes in brain patterns occur and are associated with positive changes in physical, emotional, and cognitive states. Often the trainee is not consciously aware of the mechanisms by which such changes are accomplished although people routinely acquire a "felt sense" of these positive changes and often are able to access these states outside the feedback session. Generally, trainees do not experience adverse effects.

If EEG-bf is pursued, the following protocols are recommended:

1. Pz-A2 inhibit 2-8 Hz.
2. T5-T6 inhibit 2-9 Hz and 22-36 Hz, reward 12-15 Hz (depending on response)
3. Fz-A1 inhibit 2-9 Hz and 22-36 Hz, reward 12-15 Hz (depending on response)

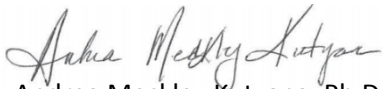
pirHEG (passive infrared Hemoencephalography): pirHEG involves wearing an infra-red sensor over one's forehead. This allows for the reading and the feeding back of the amount of blood flow occurring in the regions of the prefrontal and frontal lobes. Blood flow is an indication of the amount of metabolic activity. When the metabolic activity in the frontal and prefrontal areas increases, executive brain functioning

occurs. Outcomes include improved attention, improved mental flexibility, improved emotional/behavioral control, improved planning and organization, etc. This type of training has been referred to as a type of neurofeedback as it impacts the functioning of the brain. Its' strength, relative to forms of EEG biofeedback, is its focus on frontal lobe functioning.

Home Training Options:

Unyte is a computer software program that you control with your heart rate variability. The program - developed by a team of doctors and spiritual leaders - artfully combines state of the art technology with beautiful visuals, soothing sounds and effective meditation and breathing techniques to help you master your body's natural ability to counter the effects of stressful situations and live a happier, more balanced life. <https://unyte.com/>. There are also several apps available for smart phones which can be explored by searching: HRV telephone apps. Two of the better known are Inner Balance and Elite, but there are many others available. These options can be considered if Adult Female seems to need ways to facilitate regular practice of the HRV breathing technique. This is something that needs to be practiced on a regular basis to enjoy the maximum benefits it has to offer.

All decisions regarding the implementation of these suggestions are the responsibility of the individual practitioner. I recognize the utility of ongoing consultation and welcome discussion of the clinical progress of individual patients, or related questions and suggestions.



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Dr. Andreas Müller

VI. Appendix

Amen Questionnaire:

Symptoms rated 'frequently' (3) and 'very frequently' (4):

- Frequent feelings of nervousness or anxiety (4)
- Conflict avoidance (4)
- Quick to startle (4)
- Tendency to freeze (4)
- Panic attacks (3)
- Symptoms of heightened muscle tension (headaches, sore muscles, hand tremor) (3)
- Period of heart pounding, rapid heart rate or chest pain (3)
- Period of trouble breathing or feeling short of breath (3)
- Period of sweating, hot or cold flashes (3)
- Excessive fear of being judged or scrutinized by others (3)
- Shy or timid (3)
- Easily embarrassed (3)
- Upset when things do not go your way (3)
- Upset when things are out of place (3)
- Intense dislike for change (3)
- Trouble shifting from one task to another (3)
- Tend to say no without thinking about the question first (3)
- Period of spaciness or confusion (4)
- Periods of panic and/or fear for no specific reason (4)
- Frequent periods of déjà vu (feelings of being somewhere you have never been) (3)
- Periods of forgetfulness or memory problems (3)
- Difficulties with memory (3)
- Difficulty playing quietly (4)
- Forgetful (3)
- Difficulty expressing feelings (3)
- Feeling bored (3)
- Feeling apathetic or unmotivated (3)
- Feeling spacey or "in a fog" (3)
- Decreased interest in things that are usually fun or pleasurable (4)
- Frequent feelings of sadness (3)
- Moodiness (3)
- Decreased interest in others (3)
- Feelings of hopelessness about the future (3)
- Feelings of helplessness or powerlessness (3)
- Feeling of dissatisfied or bored (3)
- Forgetful (3)
- Difficulties with concentration (3)

van Deusen Questionnaire:

Symptom intensity rating:

Symptoms rated 'frequently' (6) and 'very frequently' (7):

- Dislikes new situations (7)
- Does not get angry when others would (7)
- Has lost periods of time from childhood (7)
- Difficulty following spoken instructions (7)
- Hard time following discussions (7)

- Quickly forgets heard information (7)
- Loses/misplaces things (6)
- Negative and unhappy (6)
- Uncomfortable socially (6)
- Low energy (6)
- Eats little or overeats (6)
- Flat or unhappy (6)
- Finds life boring (6)
- Unmotivated (6)
- Doesn't participate (6)
- Greatly disturbed by disorder (6)
- Stubborn (6)
- Annoyed by small things (6)
- Can't stay on task to completion (6)
- Afraid in situations where others are not (6)
- Does not feel pain when others would (6)
- Talks excessively or very little (6)
- Can't relax or work/play quietly (6)
- Can't find the energy to get things started (6)
- Feels shame inappropriately (6)
- Never satisfied with performance (6)
- Extreme or very little sensitivity to touch (6)
- Easily frightened (6)
- Easily forgets faces (6)
- Grinds teeth at night (6)
- Restless sleeper (6)

ADHD-Questionnaire:

Summary of high and very high rated behaviors (● Attention, ● Hyperactivity/Impulsivity, ● Emotion regulation und ● Over Focusing):

- has trouble to maintaining attention during tasks or play activities for a long time (e.g. difficulty sustaining attention during lessons, lectures and conversations or reading longer texts) (4)
- avoids or is reluctant or unwilling to do work that requires prolonged mental effort (such as schoolwork or homework or for teenagers and adults: report writing, filling out forms, checking of longer reports) (4)
- does not listen when others speak to him (seems absent even if no obvious distractions are present) (3)
- has difficulty with time, is often too late or in a hurry, tasks take longer than expected, projects or assignments are done in the last moment / too late (3)
- is forgetful in daily activities (for teenagers and adults: Callbacks are forgotten, bills are not paid, deadlines not met) (3)
- has periods of withdrawal and in this episode lacks emotion (4)
- has periods of panic and / or fear for no particular reason (4)
- often acts sad, often has feelings of hopelessness, helplessness or extreme guilt (4)
- seems anxious or fearful (3)
- often has experiences of déjà vu (feelings of having been somewhere, even if she / he has never been in this place) (3)
- has periods of forgetfulness or memory problems (3)
- sensitive to noise, light, clothing, or contact (3)
- has a strong tendency to fall into negative thoughts, has the same thoughts repetitively (3)
- likes absolutely no changes (3)

10-20 Head Review Example with GO-NOGO

