The influence of retinal preprocessing in visual cortex oscillations in humans

Bachelor of Science Thesis in Psychology

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Abstract

The present report addresses the reliability of non-invasive retinal recordings in humans using two different recording techniques for retinal activity – skin and DTL electrodes. As skin refers to a common disc electrode on the skin surface and DTL to a contact-electrode with a silver-silver chloride coated fibre. Although the literature suggests that the DTL electrode provides stronger signal amplitudes, in this study, it is demonstrated that the two electrode types are similar in terms of signal-to-noise ratio, a more practical measure of signal quality. These results suggest that skin electrodes are equally valuable than DTL electrodes. In addition, they show that skin electrode records high-frequency oscillations, similar to those observed in the human visual cortex, effectively.. In summary present results confirm the feasibility of skin electrodes in measurement and quantification of retinal activity, which in turn might provide a new insight into the dynamics of scalp recordings.

Der vorliegende Bericht untersucht die Reliabilität von nicht-invasiven und minimalinvasiven Messmethoden für retinale Aktivität beim Menschen, indem skin und DTL-Elektroden verglichen werden (herkömmliche Disk-Elektroden, bezeichnet als skin-Elektroden, und Kontakt-Elektroden mit Silber-Silberchlorid-Faser, bezeichnet als DTL-Elektroden). Obwohl die Literatur DTL-Elektroden einen Vorteil in Bezug auf Stärke eines gemessenen Signals zuspricht, zeigt dieser Bericht, dass die verglichenen Elektroden im Signal-Rausch-Verhältnis vergleichbar sind. Die Signal-Rausch-Analyse stellt sich dabei als die geeignetere Vergleichsstrategie im Hinblick auf die Signalqualität heraus. Die vorliegenden Ergebnisse lassen vermuten, dass skin-Elektroden und DTL-Elektroden gleichwertig sind. Zudem zeigen die vorliegenden Ergebnisse, dass skin-Elektroden in der Messung im Bereich hochfrequenter Oszillationen, vergleichbar mit Oszillationen, die im menschlichen visuellen Cortex beobachtet wurden, gute Ergebnisse erzielen.

Zusammenfassend, bestätigen die vorliegenden Ergebnisse, die Einsetzbarkeit von skin-Elektroden in der Messung und Quantifizierung von retinaler Aktivität, welche ihrerseits zu einem neuen grundlegenden Verständnis der Dynamiken in der Skalpmessung beitragen könnten.

Introduction

> *"When the eye is stimulated, a chain of vegetative and neural biochemical and electrical events are activated in the retinal neural cells, glial cells, and retinal pigment epithelium. The electrical voltages reflecting these events are volume conducted through the ocular media and tissues and recorded at the cornea as the ERG*[1]*. […] The era of clinical electroretinography, the measurement of the retinas electric potentials elicited by visual stimulation, began with the introduction of the contact electrode in the 1950s"* (Odom, Bach, Brigell, 2009).

Vision provides essential information of our surroundings, enables us to act purposefully, puts us in the comfortable position to detect and avoid danger and equips us with countless impressions of our environment. Miraculously, we are able to filter all that quintillion of inputs that flood our visual system, transfer it into something meaningful and achieve a reliable grounding for our behavior and cognition. Vision is thus one of mind's window to the world and allows us to interpret it.

Understanding the organization of the vertebrate retina has been and is still the goal of many scientists (Kolb, Fernandez, Nelson, 1995). In the Western world, scientists intensely started to investigate the components of our visual system and its functions since the start of the 20th century. Since the retinal signal is itself a powerful signal, relative to signal power measured in the EEG-scalp-recording, of several hundred microvolts (μV) it does not require much effort and sophisticated apparatus to record it. The first comprehensive anatomic descriptions of the neural cell types that constitute the retina in a number of vertebrate species has already been shown by Ramon y Cajal in the 19th century. Yet, the relationship between retinal and cortical activity, although seemingly of symmetric nature, is still a matter of debate. The agreement of which strongly depends on reliability of methods

1 Electroretinogram (ERG)

available to the researcher (i.e., invasive vs. non-invasive).

The measurement of retinal activity allows for observing deviations in electrical responses and thus the diagnosis of eye diseases. Yet, the contribution of intact retinal responses to vision in general is poorly understood.

The ERG recordings have already been routinely used in ophthalmology, but did not find broad usage in the scientific field so far. Despite the wide usage of ERG in the clinic, a common agreement on standardized protocols assuring data comparability across researchers is lacking. At least, the International Society for Clinical Electrophysiology of Vision (ISCEV) compiled some of the basic principles in ERG recording in several instruction-papers (M. F. Marmor et al., 2009).

The measurement of the ERG is a prerequisite for understanding retino-cortical interactions. Combining Electrooculography (EOG) with scalp recording such as Magnetoencephalography (MEG) the methodical effort is substantial, promises however a detailed insight into the mechanisms of retino-cortical interactions.

Hence, the scope of the present report is first to explore and determine the feasibility of non-invasive recording of retinal activity.

Different electrode types have been invented to measure the VEP[2] directly on or very close to the eyeball. From the Burian Allen electrode[3] to the DTL fibre, to skin electrodes on one eyelid. Literature suggest however, several issues to be considered. This includes mainly signal quality (often rated by amplitude), as well as wearing-comfort electrodes and electrode-handling (McCulloch, Boemel, & Borchert, 1997). Following McCulloch et al. the one electrode should be chosen, that gives the best quality-signal, meanwhile the shortest recording time and the utmost safety and comfort to the participants.

Whereas the Burian Allen electrode provides recording with strong signal, it

2 VEP: Visually Evoked Potential

3 Burian Allen Contact-lens-electrode: one of the first developed contact electrodes.

is considered as the noisiest of all common electrodes and it's use is escorted by low wearing comfort and risk of corneal abrasion and conjunctive infection (McCulloch et al., 1997, p.332). The DTL fibre, one of most recently developed contact-electrodes, increases aspects of comfort compared to the Burian Allen electrode by far, but does not provide enhanced signal quality and also carries at least some risk of infection despite its minimally invasive nature (McCulloch et al., 1997).

The issue with skin electrodes is different. The skin electrodes have been ignored often disqualified by scientists because of weaker recorded signal strength or higher impedance. McCulloch et al., for instance used Signal-to-noise ratio analysis for comparison between different kinds of contact electrodes, but did not include the skin electrode into their comparisons (McCulloch et al., 1997). Its use is health-wise safe, quicker, easier, and is therefore equipped with desirable properties for clinical as well as scientific use given that skin electrodes do not lose too much of the precious contents of retinal signal recording. With ophthalmologists, for instance, dealing with children and scientists dealing with different types of clinical populations, the skin electrodes seem superior to others (Kriss, 1994).

Because of the limitation of contact electrodes outlined above in clinical and scientific environments, that is mainly the high risk of infection due to its invasive nature, the present study examines the handling, signal quality and feasibility of skin electrodes as compared to DTL electrodes.

Methods

Ethics Statement

The research trial, the study protocol, and the recruitment procedure were approved by the ethics committee of the University of Konstanz, in accordance with the Declaration of Helsinki.

Participant Recruiting

This inquiry headed for some basic knowledge about retinal processing and included therefore no clinical participants but unrelated university employees and students of the University of Konstanz, respectively Center of Psychiatry Reichenau (ZfP), who took part in an exploratory study. The data was collected from 13 participants, that have been recruited in the surroundings of the experimenters (i.e., their colleagues and friends). Two participants were later rejected from the data due to bad signal quality. contact lens wearers were preferred, because they were less sensitive to both the presence of the electrode, and to the experimenters working near their eyes.

Informed Consent

The participants have been welcomed in the MEG-Laboratory in the ZfP, associated with the University of Konstanz. They have been instructed in all necessary information, concerning the experiment (i.e., devices, sequences, duration, etc.). Afterward they signed the informed consent form (see Appendix). Participants have been asked for epilepsy and any kinds of ocular disorders. This was of particular interest for the present study because the stimuli presented might be of a seizure triggering nature, due to its flickering lights. “Photosensitive epilepsy is a type of epilepsy, in which all, or almost all, seizures are triggered by flashing or flickering light. Both natural and artificial light may trigger seizures”

(EpilepsyAction, called 19.10.2013).

In this study, technique to measure retinal signal (DTL) that may cause discomfort to participants had been used. Participants have been informed in respect of risk of corneal abrasion and conjunctive infection. According to Dawson, Trick & Litzkow it might happen, that there is some infection due to the use of an electrode touching the eyeball, although the risk is very marginal. “In the past, different types of electrodes contained higher risk of infection”(Dawson, Trick, & Litzkow, 1979).

Any danger of infection has been minimized by using a disposable DTL fibre electrode (described in detail in chapter 'ERG-Electrode and skin electrode') and all means of hygiene, namely disposable gloves, disposable components and satisfaction of of common standards in hygiene have been taken.

After the experiment participants were informed about the rationale of the experiment.

Participants

The 11 included participants were aged between 20 and 34, among which 8 were female. As discomfort due to use of the DTL contact electrode in this experiment was possible, the recruitment of participants focused experienced carriers of contact-lenses. The visual impairment of the participants was thus not necessary or essential for this study, moreover the participants lower sensitivity in respect of having a foreign body near seemed to enhance data set quality and improve participants comfort. Two participants had no experience contact lenses. In consequence one of them reported about high discomfort but pulled through the complete experiment voluntarily. No other subjects reported any discomfort from the recordings.

On the other side, the visual impairment of the participants urged the experimenters to check the ability of each participant to clearly observe the

presented stimuli, although complexity of stimuli was very low. In two subjects MEG glasses have been provided in the right diopter value, to ensure that the participant is optimally refracted, this mainly refers to the grating stimuli.

For their participation in the experiment, subjects were compensated with 30€. The possibility to discontinue participation for any reason has been emphasized.

Electrooculogram (EOG) and Electrocardiogram (ECG)

The electrical potentials of neurons can be measured by placing skin electrodes around the eye. Thus several electrodes have been placed in close distance to the eyes to enable the experimenters to record retinal activity. Yet, a selection of what is the desired retinal activity has to be made, because electrodes measure muscular activity in this area as well. For artifact control, eye movements (EOG) have been recorded from four electrodes attached to the left and right temple and above and below the right eye. In addition two electrodes, one on each forearm, have been applied to measure cardiac activity (ECG). A Nihon Kohden Neurofax EEG- 1100G amplifier (Nihon Kohden Europe, Rosbach v.d.H., Germany) has been used for the recording of EOG, ERG and ECG.

Magnetoencephalogram (MEG)

The ZfP uses a MEG for research purposes. Cerebral activity following the presented stimuli was recorded with a 148-channel magnetometer with superconductor quality (4D Neuroimaging Inc., San Diego, CA, USA), the MEG dewar chamber. The 148 channels are arranged in a cooling appliance formed like a huge helmet, called a Dewar, that needs to be shielded from outside electromagnetic fields due to measurement of incredibly low magnetism, few femto-tesla in magnitude. The channels itself are thinly dispersed in equal. The Dewar covers the whole head excluding the participants face. The signal was recorded with the

highest possible sample rate that matches the EEG amplifier. We used high-pass filter of 0.1 Hz. The stimuli were presented with a projector outside the MEG-chamber which projected through a port in the shielded wall to a screen in about one meter distance to the participant (slightly varying from one participant to the next) via a system of mirrors inside.

ERG-Electrode (DTL) and skin electrode

The DTL electrode is a low-impedance electrode made of medical grade silver and nylon. It is developed for use in ERG testing. It is a ready-to-use disposable corneal eye electrode that does not need anesthesia (Diagnosys LLC).

In comparison to other corneal electrodes, the DTL delivers analogous data, but at the same time allows higher level of comfort to the patients taking part in ophtalmological measurements. In 1995 Hebért, Lachapelle and Dumont already showed, that the signal quality of the DTL fibre electrode is sufficient and it produces reproducible electroretinographic recordings (Hébert, Lachapelle, & Dumont, 1995). Nonetheless it can cause discomfort in sensitive populations and should thus be compared to other non-invasive methods to measure the ERG signal, in order to replace risk-carrying apparatus.

As skin electrodes, common disc electrodes (these electrodes are general-purpose, i.e., could also be used for EKG, EOG, etc.) have been used (Easycap, Herrsching, Germany). These are Ag/AgCl sintered extra-flat electrodes with 8mm sensor, 150 cm heavy-duty-cable and 1.5mm socket. They have been placed in accordance to ISCEV standard protocol on the lower eyelid. (Kriss, 1994, p.140), where it should produce best results. The disc-electrode was thus used as EOG.

Preparation

As soon as the participants changed into MEG clothes, that is clothes without any piece of metal or magnetic material, several electrodes have been applied following the scheme attached below for the skin electrodes as well as the MEG-coils.

With this, skin-parts that later carried electrodes have been cleaned with alcohol and some electrolyte paste has been placed onto the skin to minimize impedance and secure skin electrode contact as good as possible. The ERG-Electrode has been applied later in the MEG-chamber to avoid unnecessary discomfort to the participants.

The present report relied on exact placing of the electrodes. Signal contamination had to be analyzed in order to ensure that only desired retinal activity proceeds into the data-analysis.

Therefore, the vertical EOG (VEOG) electrodes should measure the activation of vertical eye-movements, the horizontal EOG (HEOG) electrodes the activation of horizontal eye-movement. This is why they have been set in horizontal respectively vertical axis to each counterpart as shown in Figure 1. The right HEOG electrode was additionally used as reference.

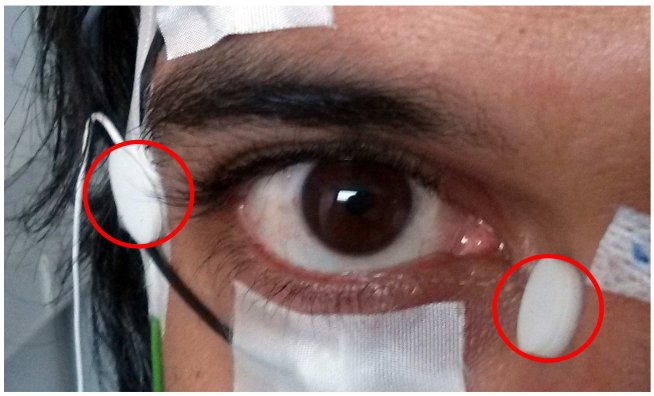
On the right and left forearm electrocardiogram electrodes (ECG) have been applied to measure the participants heart-beat. This was done to identify any heart-beat artifacts in the recorded signal.

The MEG coils have been placed in a standardized manner. The Nasion-Coil was placed right below the hairline on the upper forehead. Inion- and Cz-Coil were placed in non-isosceles-triangle on the the forehead. LPA- and RPA-coil were placed at the temple, so that no muscular activity from jawbone could be measured.

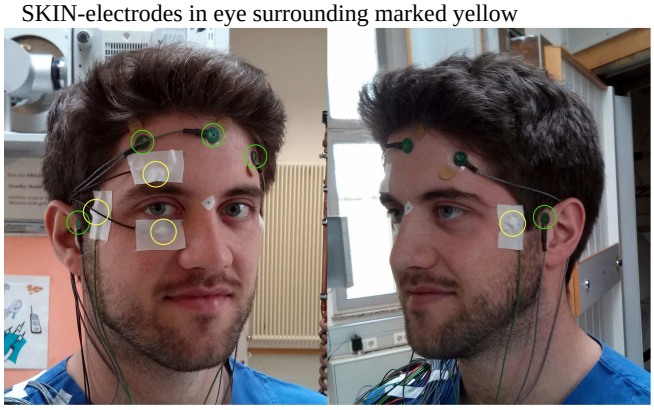
An overview regarding the electrode placement is shown in Figure 1.

Figure 1: Placement of electrodes

The DTL-fibre is located on the lower eyelid, fixed with two gluepads marked in red and almost invisible



MEG-coils located on the forehead and temple marked green, SKIN-electrodes in eye surrounding marked yellow



After completing the set-up, preparations in the MEG have been started. Therefore the head-shape of every participant has been digitalized. Before the experiment could finally start, the DTL electrode was placed carefully on the lower eye-lid. As shown in Figure 1 at the top the DTL electrode uses two points of fixation. One aside the bridge of the nose, second on the temple. It is crucial that the DTL fibre has got the right amount of tension. If the fibre is too loose it might produce segments of flat signal. If the fibres' tension is too strong, it might either rip or irritate the participants eyeball. Thus, it took some time to carefully adjust the fibre, so that both, data quality and comfort of the participants is adequate. This amount of time decreased after the experimenters achieved some routine. After implementing the DTL electrode in the participants right eye the electrode has been dosed with additional paste to comfort wearing the electrode some more.

Inside the MEG-chamber participants have been exactly positioned into the Dewar of the MEG. After the coil measurements the recording of the trial sequence has been started, given that the standard error-value for sensor-position-coil-calculation of one had been undercut.

Experimental design

All participants had been informed about the trial-sequences explained outright. Other data was collected but has been outside the scope of this report.

Participants have been instructed to remain their eyes above distal from the horizon upwards. Anyway, the DTL electrode limited the field of vision of participants due to discomfort by looking downwards from the midline. Following ISCEV standards the scale of the eyes movement from the horizon is important for data-quality. (Kriss, 1994) Michael Marmor and colleagues explain, that signal might be lost if participants rolled their eyes upwards in a too extreme manner, what is actually the case with anesthetized or sleeping participants (M. Marmor, Brigell, McCulloch, Westall, & Bach, 2011).

Flashes

The experimenters placed a screen into the participants field of vision, where the stimuli of the next trials were presented. The visual angle[4] has been set around 30°, following ICSEV standards recommending at least 20° with little variance due to individual differences in participant-stature ((M. F. Marmor et al., 2009).

In addition, one eye has been covered with an eye-patch that shielded the eye from outside light at the best possible way while staying open. Participants response has been used to modify the patch. Lights have been switched off and dark adaptation of the eye has occurred for some 7 minutes until the recording started. First, the participants left eye has been covered. Then the trial sequence started which took 2 minutes for the first 9 participants, and 3 minutes 30 seconds for two participants running through 80 flashes instead of 40. Same procedure took place in the next trial sequence, now with the right eye covered. Change of the eye-patch happened between trials manually by the experimenters. All following analyses made in this report refer to this condition.

4 Visual angle calculated with help from jumk.de

Gratings

The next trial sequence has been composed of different stimuli but stayed the same apart from that. Lights have been switched off. First the right eye has been covered, then the left eye. Participants now had to watch a stimuli consisting of concentric circles seeming to move away from the middle. The duration of the trial was 3 minutes and 30 seconds with 40 trials. This condition was mainly designed for gamma frequency spectrum analysis. The analyses of these blocks is outside the scope of this thesis.

Stimuli

Why flashes?!

> *"The stimulus may vary in intensity, duration, wavelength, rise time, fall time, spatial extent, and spatial location. A diffuse light stimulus varies in time but is uniform across a relatively large area of visual space. A diffuse light stimulus that appears and disappears suddenly and is of brief duration is termed a light flash or simply a flash* (Odom, 2013)*."*

Light flashes are relatively easy to generate in a way that others may reproduce them equally and have several other advantages in respect of our study targets. In order to make separation of desired and undesired signals feasible, yet well explored stimuli have been needed. In addition, the clear onset and offset of the flashlight stimuli facilitates data processing.

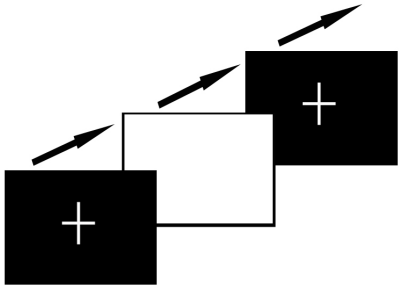
Stimulus Properties

In accordance with ISCEV standards some stimuli properties were set as following

Properties of flashes

```
crosshairs;
font_size = 4;
font ="Arial";
background_color  = 255,255,255;
font_color =  0, 0, 0;
pblank
background_color = 0, 0, 0
visual angle: 30°
duration: 16 ms
```

Figure 2: Exemplary condition 'Flashes'



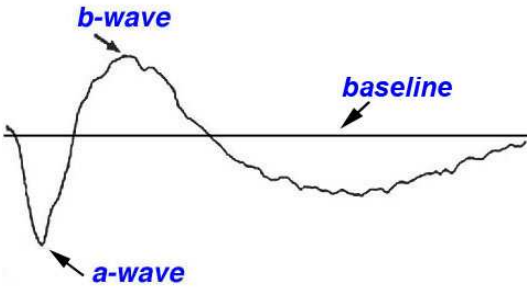
ISCEV standards and desired retinal signal

ISCEV standard.

"The basic method of recording the electrical response known as the global or full-field ERG is by stimulating the eye with a bright light source such as a flash produced by a LED or a strobe lamp"(Creel, 2013). Following ISCEV standard protocol, a full-field ERG is required in order to ensure consistent stimulation of the whole retina. (M. F. Marmor et al., 2009) The flash of light elicits a biphasic waveform recordable at the cornea or nearby. According to Donnell J. Creel, the typical waveform of a true retinal signal evoked by flashlight stimulation should therefore look like this.

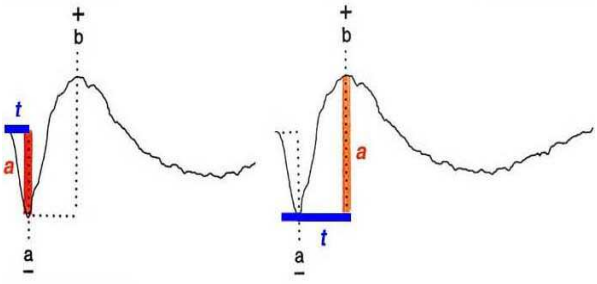
"Two principal measures of the ERG waveform are taken: 1) The amplitude (a) from the baseline to the negative trough of the a-wave, and the amplitude of the b-wave measured from the trough of the a-wave to the following peak of the b-wave; and 2) the time (t) from flash onset to the trough of the a-wave and the time (t) from flash onset to the peak of the b-wave. These times, reflecting peak latency, are referred to as "implicit times" in the jargon of electroretinography (Creel, 2013).

Figure 3: biphasic a and b wave



http://webvision.med.utah.edu/book/electrophysiology/the-electroretinogram-clinical-applications/

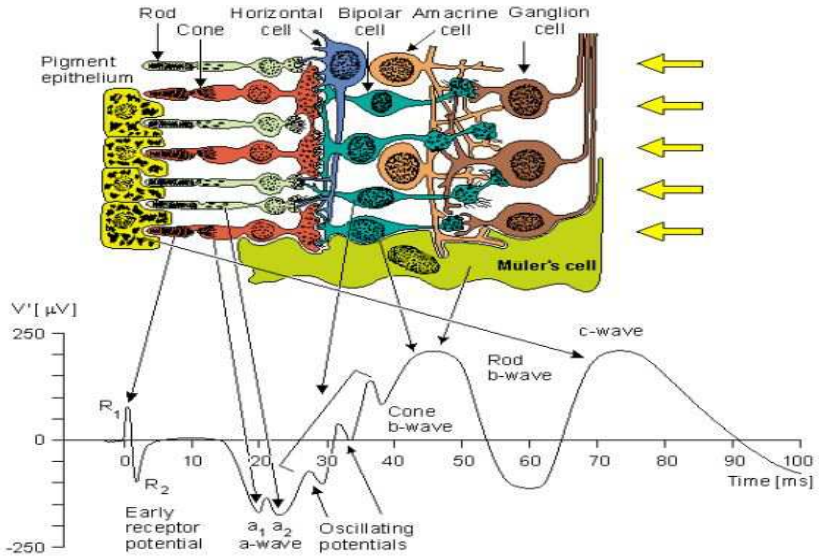
Figure 4: measurement of amplitude and implicit time of a and b wave



http://webvision.med.utah.edu/book/electrophysiology/the-electroretinogram-clinical-applications/

In a clinical respect the a and b-wave provide different information to the examiner. The a wave named the "late receptor potential, reflects the general physiological health of the photoreceptor in the outer retina, in contrast, the b wave reflects the health of the inner layers of the retina […]"(Creel, 2013). The present report did not refer to that functional analysis of the retinal signal in that deepness, yet the complexity of the retina is depicted in Figure 5 below.

Figure 5: Inner and outer retinal layer. Different localization of cells generating a and b wave potentials



http://www.bem.fi/book/28/28.htm

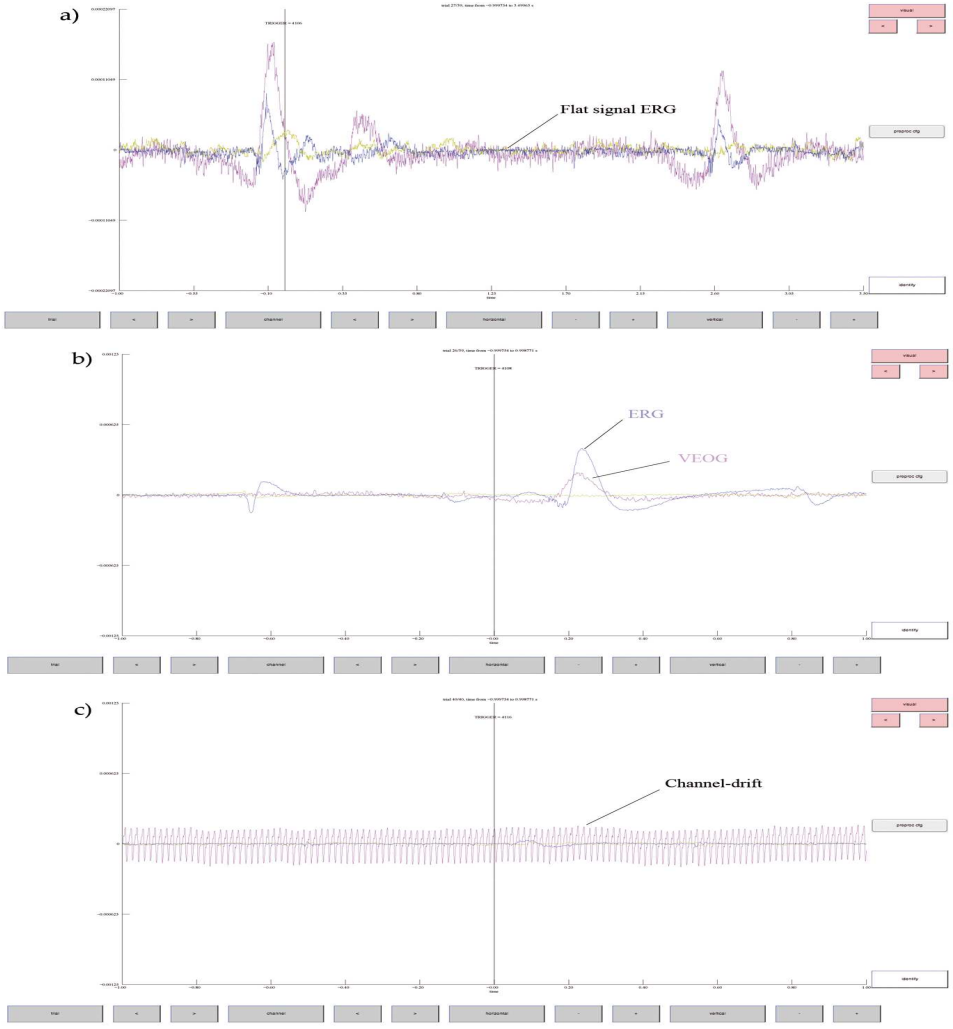
Although the two components that are mostly referred to are the a- and b-waves, there are several other waveforms. The present report focused on a and b waves.

As already mentioned, retinal potential is said to be especially strong, but as well susceptible to artifacts, scientists have to make sure, that they are actually recording retinal signal. "Factors such as the recording position, electrode derivation, upward rotation of the eye, eyelid closure and markedly constricted pupils can degrade the skin ERG,[…]." (Kriss, 1994) Most of these artifacts go along with the corneal ERG. Therefore it is vital to know about the pattern of retinal activity and how to ensure recording of retinal signal with high fidelity.

Desired retinal signal.

Looking at different channels at a time, namely ERG, VEOG and HEOG, the experimenters seemingly have been able to separate desired retinal activity from artifacts. Trials where retinal signal seemed to be corrupted by muscular activity or other artifacts of different origins have been rejected after visual inspection. Still, the data contains a certain amount of noise. The present study used a specific strategy to deal with noise, explained later. Figure 6 shows exemplary data that has been rejected due to artifact contamination.

Figure 6. Artifact-rejection in data preprocessing mode



Plot a in Figure 6 depicts a phase of very flat recorded signal. This might have happened due to saturation of the amplifier from strong signal or noise. Assuming that there has been no meaningful signal recording at that time this trial has been rejected from the data.

Plot b in Figure 6 shows seemingly muscular activity. There is a deduction made in different channels, assuming that there was a saccade[5] recorded right after the stimulus-onset. One crucial part of the artifact rejection was the identification of eye-movement, referred to as saccades, because these artifacts apparently happen frequently in the measurement of retinal potential. This trial has been rejected from the data.

Plot c in Figure 6 shows a bad signal due to channel activity not intended. This bad signal occurred throughout the whole trial and could therefore not been used. The recording has been rejected from the data.

5 Quick eye-movement from one fixation point to the other followed by polarity changes in the eyeball

Data preprocessing

Right after acquisition of data some automatic noise correction has been routinely applied for the data-set. That is a Notch Filter over 50 Hz and its harmonic multiple of 100 Hz to erase artifacts from power supply sources. In addition, a 16 ²/3 Hz filter that is able to erase noise from a train track that passes the Center of Psychiatry Reichenau in a distance of about 500 m has been used.

After that the data has been processed with Matlab, version 2012b and the FieldTrip toolbox (Donders Centre for Cognitive Neuroimaging).

The continuous data has been sequenced with triggers that have been set during the acquisition. To make sure that baseline-correction works properly a time interval of 16 ms previous and subsequent to the stimulus-onset was set, respectively the trigger, and trials with irregular signal near the edges of the interval have been excluded. Along with this, trials that had been either too noisy or had at least some drifts[6] recorded were specified and excluded from the data. Afterward each trial has been checked visually in respect of artifacts already described. Trials containing artifacts were thus removed after visual inspection.

Each participant data-set consisted at least of 33 artifact-free epochs, which have been averaged.

Data of two participants had to be rejected due to bad signal, assuming that wrong montage in that specific participants has been the cause for this.

6 Channel-drift: relocation of channel signal from baseline

Statistical approach

Parametric and Non-parametric testing.

The comparison between the two electrodes skin and DTL has been focused on computing several two-tailed students-t tests for paired samples to investigate differences between the two samples. Therefore the Matlab t test function has been used on the one hand. The *p-value* describes the level of significance reached. The significance value (alpha-level) has been set to .05. Due to the non-normal distribution of most samples and the small number of participants a non-parametric approach has been added. The distribution has been tested for normality with Shapiro-Wilk's Test for Normality (α=0.10). As non-parametric approach, a Wilcoxon Matched-Pairs Signed-Rank test has been used. This test is known as alternative to students t-test in case that the examined data is not normally distributed.

Signal-to-Noise-Ratio (SNR).

In addition, the comparison of both electrodes should provide a fair and meaningful comparison by computing a Signal-to-Noise-Ratio of the recorded signals. The concept of this SNR is to relate the strength of VEP relative to the average of the background noise as baseline. Given that the recorded signal contains noise, the SNR compares the signal in a way that the proportion of amplitudes and signal form a meaningful ratio. Thus, not only the magnitude of an amplitude, but the ratio of signal strength to noise actually gives the scientist a real impression of the data quality.

In this respect it was necessary to apply additional bandpass-filter of 5-45 Hz to the VEOG channel (skin electrode) in order to exclude collateral high frequency oscillations contained in skin electrode signal that would have corrupted the ratio itself. Assuming that these high frequency oscillations likely contain higher muscular activity.

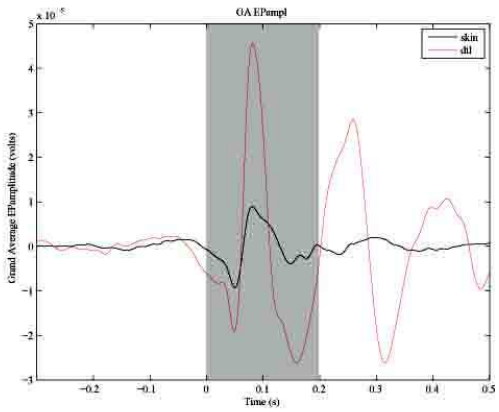
Results

Comparison of skin electrode and DTL electrode

To further analyze the present data, an average across all participants has been computed. This was a necessary first step to check the visual impression, that signal power of the DTL electrode outlines signal power of the noninvasive skin electrode on the lower eyelid by far, based on what literature predicts. To initially get the reader a visual impression of that claim and of the recorded data in general both averaged signals from ERG and skin electrode have been plotted in a 2D plot with time in seconds on the x-axis and signal strength or amplitude in microvolts (μV) on the y-axis which is depicted below in Figure 7.

Inspecting Figure 7 visually there seems to be high synchronicity between both recorded signals. Table1 quantifies Figure 7 to get a deeper impression of the data. Hence, the trial average of each participant is depicted in Figure 8 and Figure 9.

Figure 7: Amplitude – grand average

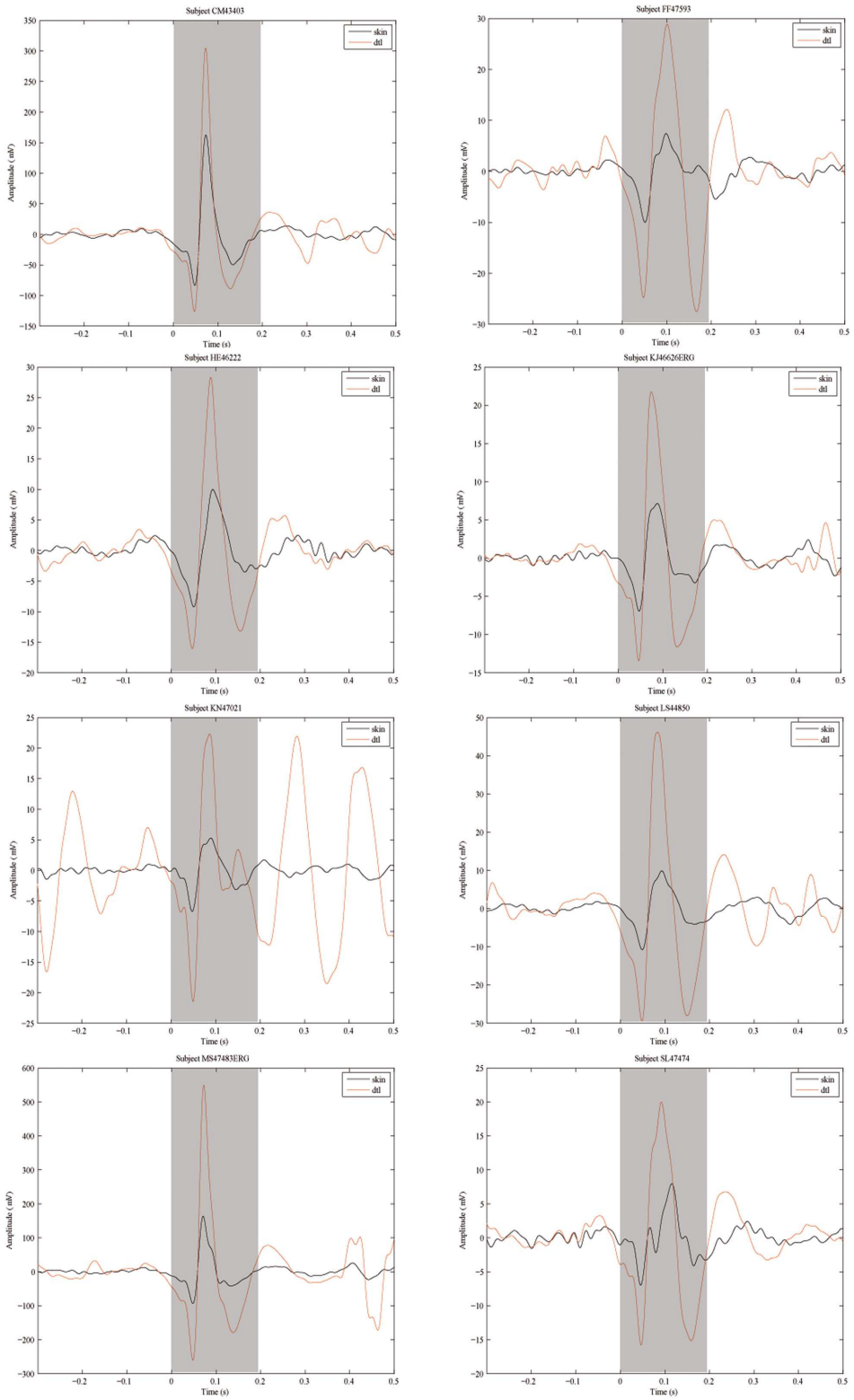


x-axis time (s), y-axis amplitude microvolts (μV); black curve skin electrode, red curve DTL electrode, Time of interest shaded from zero sec. to 0.2 sec.DTL electrode outperforming the skin electrode in respect of amplitude in the grand average.

	Extremes			
	a-wave		b-wave	
Quantification of	amplitude skin	amplitude dtl	amplitude skin	amplitude dtl
VEP amplitude grand average in μVolt	-9,243	-1,911	8,875	4,563

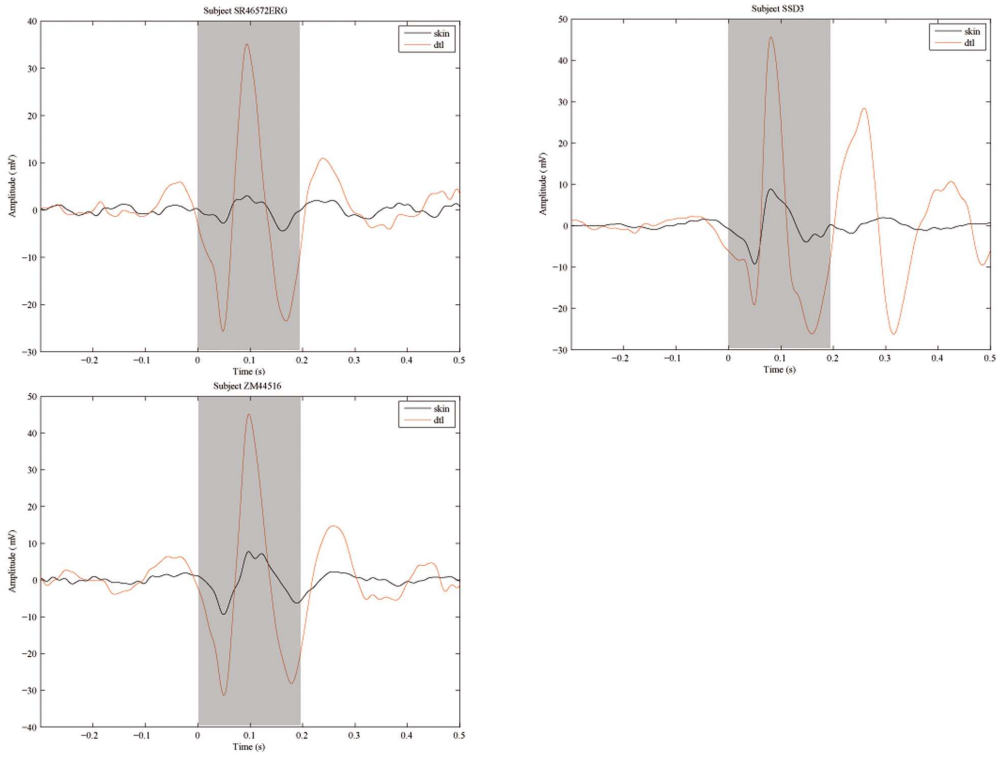
Table1: Grand average – VEP amplitude of skin electrode and DTL electrode in μV sorted by a wave left column and b wave right column

Figure 8: Amplitudes – all participants depicted, each window shows one participant trial average



x-axis time (s), y-axis amplitude in μV; black curve skin electrode, red curve DTL electrode, Time of interest shaded from zero sec. to 0.2 sec.

Figure 9: Continuation of Figure 8 - all participants depicted, each window shows one participant trial average



x-axis time (s), y-axis amplitude microvolts (µV); black curve skin electrode, red curve DTL electrode, Time of interest shaded from zero sec. to 0.2 sec.

Table 2 quantifies the data on individual level shown in Figure 8 and Figure 9.

	Extremes			
	a-wave		b-wave	
	amplitude skin	**amplitude dtl**	**amplitude skin**	**amplitude dtl**
Subject	in µVolt	in µVolt	in µVolt	in µVolt
1	-83.63	-126.30	131.90	231.30
2	-9.99	-24.80	7.40	28.90
3	-9.21	-16.00	10.00	28.30
4	-6.93	-13.40	7.20	20.80
5	-6.72	-21.40	5.30	22.30
6	-10.76	-29.40	9.90	46.20
7	-93.43	-260.60	104.20	406.90
8	-6.96	-15.80	7.20	20.00
9	-2.75	-25.60	3.00	35.10
10	-9.24	-19.10	8.90	45.60
11	-9.37	-31.40	7.80	45.10

Table2: VEP amplitudes - quantified for each participant listed in the shaded column on the left
To achieve comparable data, we extracted the extremes in both, the a and b wave, for DTL and skin electrode.
The values represent extremes in µV between 0 and 0.2 sec of averaged participant data.

A two-tailed students-t test for paired samples and a Wilcoxon Matched-Pairs Signed-Rank test have been computed to compare DTL electrode and the skin electrode. The Matlab students-t test has been used in that respect and compared the extremes of a-wave and b-wave statistically. The Wilcoxon Matched-Pairs Signed-Rank test has been computed with Aabel (Gigawiz Ltd. Co.). The Shapiro-Wilk's Test depicted in Figure 10 shows that a-wave and b-wave sample in respect of amplitude are not normally distributed.

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
a-wave amp skin	-0,0226355	0,032726	-1,92232	1,60944	0,56211	< 0,0001	No

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
a-wave amp dtl	-0,0530727	0,0758346	-2,52995	5,80396	0,565386	< 0,0001	No

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
b-wave amp skin	0,0275273	0,0452256	1,99784	2,08921	0,550346	< 0,0001	No

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
b-wave amp dtl	0,0845909	0,122801	2,32449	4,44446	0,578905	< 0,0001	No

Figure 10: Shapiro Wilk's Test for Normality – distribution amplitudes samples

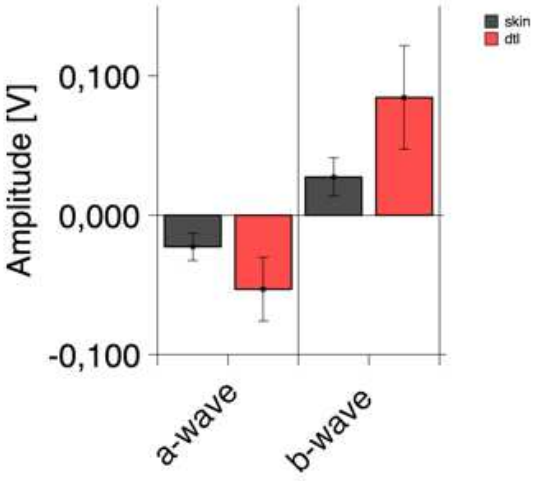
As shown in table 3, the parametric t-test did barely not reach significance for both a-wave amplitudes (t=2.17063, p=0.0551) and b-wave amplitudes (t=2.22719, p=0.0500), giving at least a tendency. In contrast, the Wilcoxon Matched-Pairs Signed-Ranks test shows highly significant results in a-wave amplitude (z=-2.93406, corrected for continuity z=2.8896, p=0.003, corrected for continuity p=0.004) and b-wave amplitude (z=--2.93406, corrected for continuity z=2.8896, p=0.003, corrected for continuity p=0.004).

	Parametric (students-t test)			Non-parametric (Wilcoxon Matched-Pairs Signed-Rank Test)		
Comparison ampl. skin/dtl	df (two-tailed 0.05)	t	p-value(two-tailed)	T (two-tailed 0.05)	z (corrected for continuity)	p-value(two-tailed)
amplitudes a-wave	10	2.17063	0.0551	10	-2.93406 (2.8896)	0.003 (0.004)
amplitudes b-wave	10	2.22719	0.0500	10	-2.93406 (2.8896)	0.003 (0.004)

Table3: t-Tests – VEP amplitude; Tests ran with quantified values shown in table2 ; results parametric approach left column; results non-parametric statistical approach right column

The bar-plot below, Figure 11, visualizes the data underlying the statistical approaches used, showing the data is different.

Figure 11: Bar-Plot data a-wave and b-wave

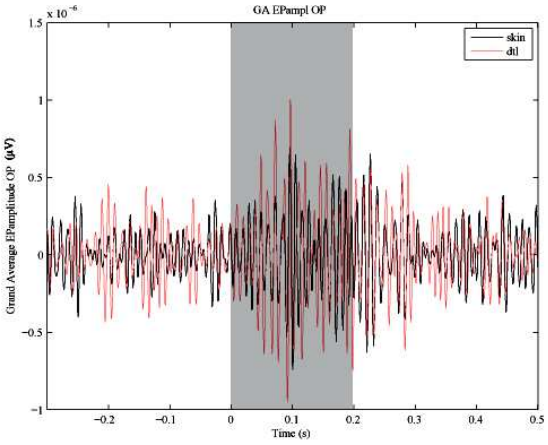


y- axis: comparison of a wave, b wave extremes regarding amplitude ,and comparison of b wave extremes in respect of high frequency oscillations. x-axis: Amplitude in volt (V)

Oscillatory potential.

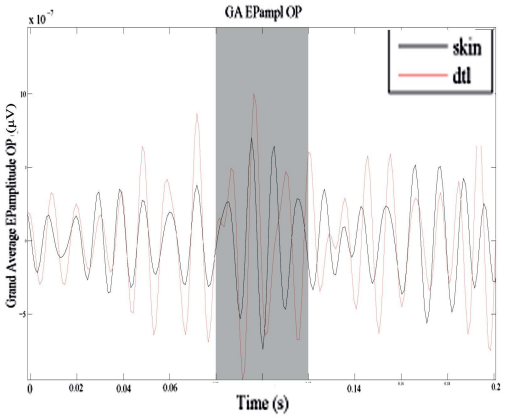
First the visualization of the grand average of all participants, depicted below in Figure 12, has been made. Indicating that there is synchronicity between high frequency oscillations in b-wave extremes in DTL- and skin electrode.

Figure 12: Oscillatory Potential – Grand average



x-axis time (s), y-axis amplitude in μV; black curve skin electrode, red curve DTL electrode, Time of interest shaded from zero sec. to 0.2 sec.

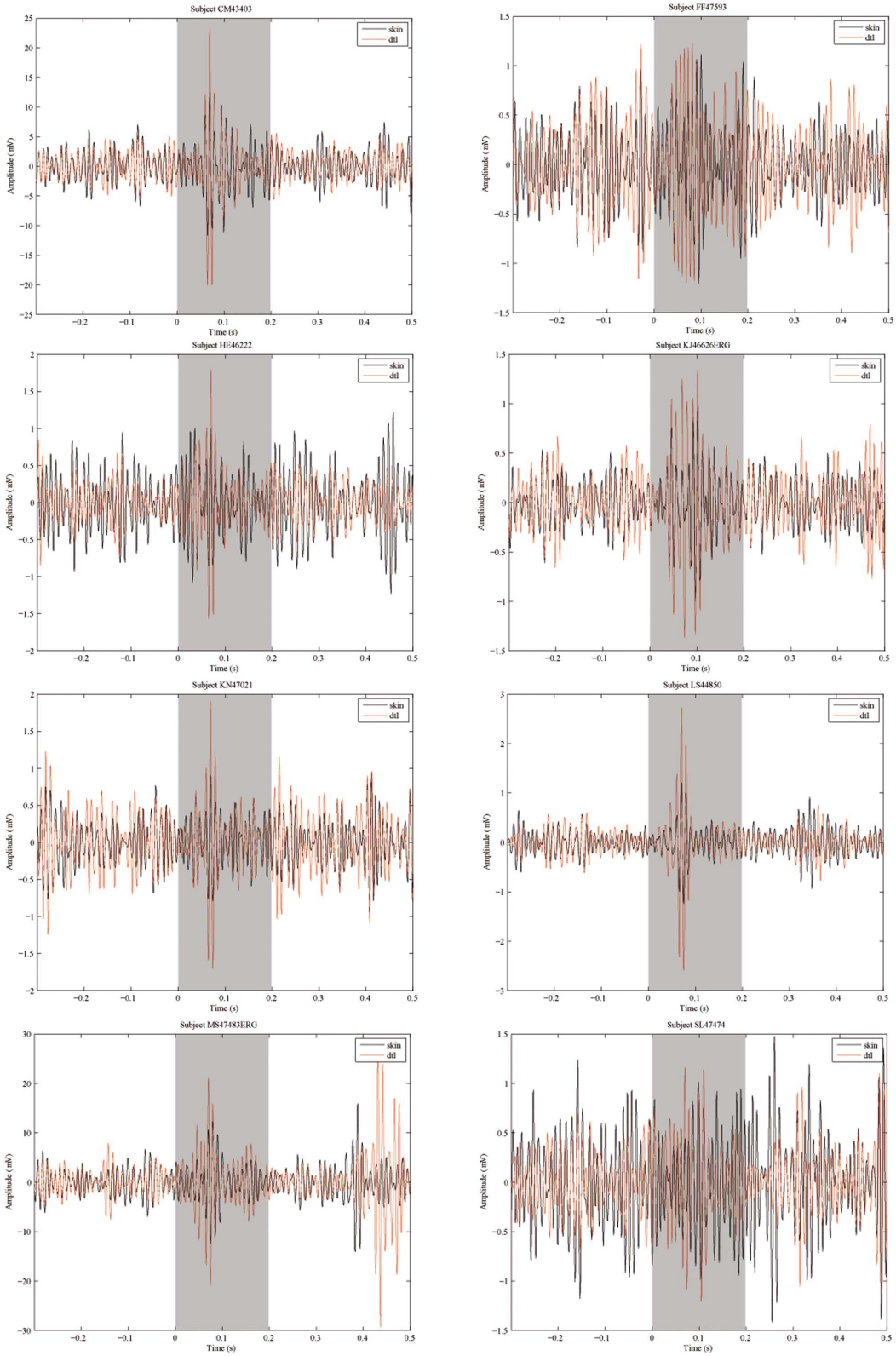
Figure 13: Oscillatory Potential – Grand average (zoom-in)



x-axis time (s), y-axis amplitude μV; black curve skin electrode, red curve DTL electrode, Time of interest shaded from 0 to 0.2 sec.

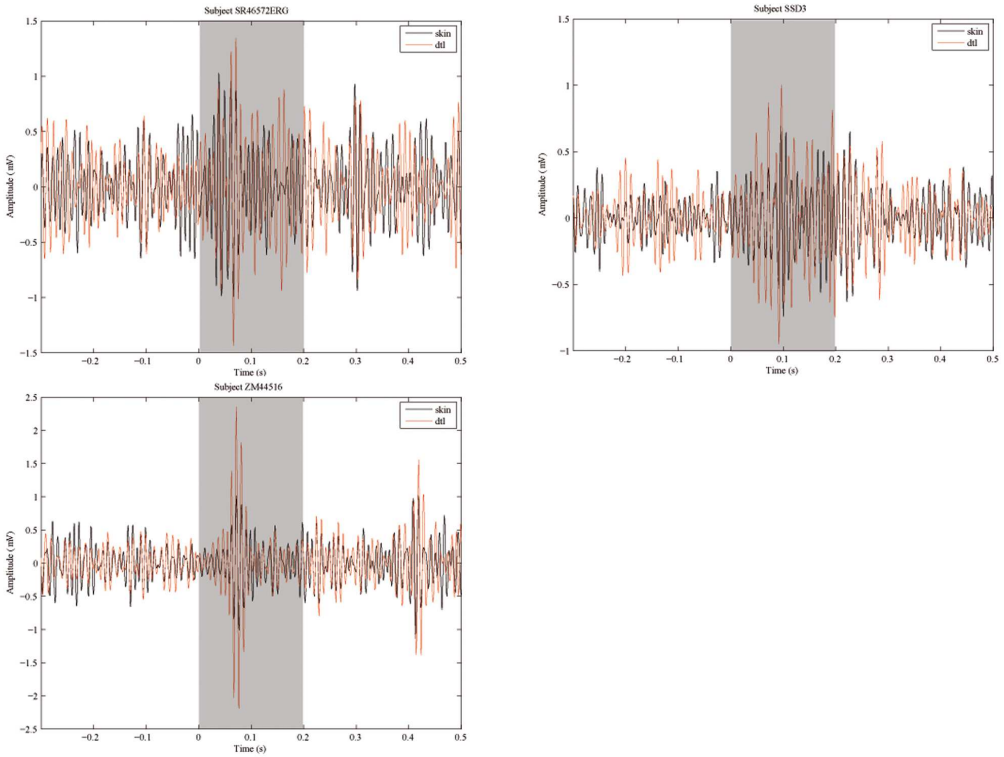
To show that both signals measure similar contents the synchronicity between both channels during the VEP at the time of the b wave extreme has been further examined. Figure 13 depicts the same data but zoomed in with an excerpt of 0-0.2 seconds on the x-axis- The y-axis shows the amplitude in μV. Succeeding the eleven participant-averages over trials regarding oscillatory potential are shown in Figures 14 and 15.

Figure 14: Oscillatory Potential - all participants depicted, each window shows one participant trial average



x-axis time (s), y-axis Oscillatory potential amplitude in μV; black curve skin electrode, red curve DTL electrode, time of interest shaded from 0 to 0.2 sec.

Figure 15: Continuation of Figure 14 - Oscillatory Potential - all participants depicted, each window shows one participant trial average



x-axis time (s), y-axis amplitude in µV; black curve skin electrode, red curve DTL electrode, Time of interest shaded from 0 sec. to 0.2 sec.

Table4 quantifies the plots depicted in Figure 14 and Figure 15 to provide the reader a deeper impression of the data-set.

	b- wave Extremes	
	OP skin	**OP dtl**
Subject	in µVolt	in µVolt
1	8.64	23.18
2	0.67	1.22
3	0.59	1.80
4	0.76	1.25
5	0.42	1.91
6	0.48	1.91
7	4.63	2.73
8	0.38	21.09
9	0.87	1.35
10	0.28	0.87
11	0.21	2.36

Table4 Oscillatory Potential quantified for each participant listed in the shaded column on the left
b wave extremes of skin electrode and DTL electrode in µV listed on the right between 0 and 0.2 sec.

A statistical comparison of skin electrode and DTL electrode has been made. Figure 16 shows the test for normality. A-wave and b-wave data were not normally distributed.

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
b-wave gamma skin	0,0162945	0,0264066	2,37769	4,79249	0,576387	< 0,0001	No

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
b-wave gamma dtl	0,0542455	0,0829221	1,91849	1,56946	0,556865	< 0,0001	No

Figure 16: Shapiro-Wilk's test for Normality - Distribution oscillatory potential

The two-tailed students-t test for paired samples and a Wilcoxon Matched-Pairs Signed-Rank test has thus been computed in order to compare DTL and skin electrode in respect of phase coherence. Assuming that the oscillatory potential would be more visible in the stronger b-wave extreme, the analysis focused on that. Table5 states the results of these computed tests.

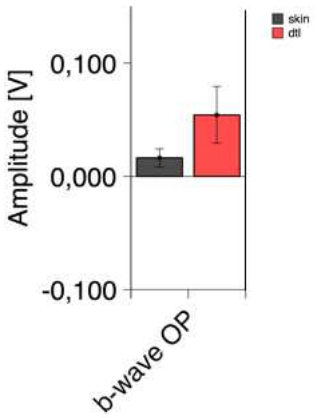
	Parametric (students-t test)			Non-parametric (Wilcoxon Matched-Pairs Signed-Rank Test)		
Comparison OP skin/dtl	df (two-tailed 0.05)	t	p-value(two-tailed)	T (two-tailed 0.05)	z (corrected for continuity)	p-value(two-tailed)
OP b-wave	10	1.78526	0,105	10	-2.22277 (2.17832)	0.026 (0.029)

Table5 statistic approach regarding Oscillatory Potential in b-wave extreme. Tests ran with quantified values shown in table 4. results parametric approach left column; results non-parametric statistical approach right column

The parametric students-t test as shown in table5 did not reach significance (t=1.78, p=0.105). In contrast, the non-parametric Wilcoxon Matched-Pairs Signed-Ranks test reached significance (z=-2.22277, corrected for continuity z=2.17832, p=0.026, corrected for continuity p=*0.029*).

The bar-plot below Figure 17 visualizes the data underlying the statistical approaches used.

Figure 17: Bar-Plot summarizing data



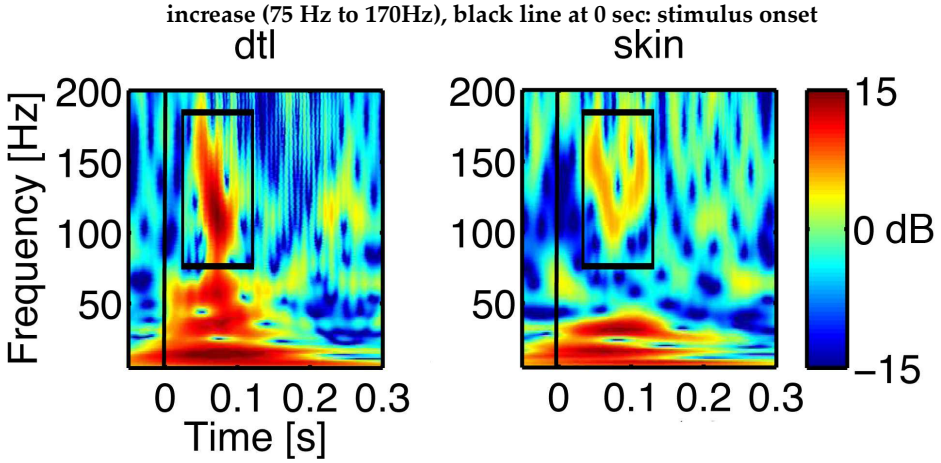
y- axis: comparison of a wave, b wave extremes regarding amplitude ,and comparison of b wave extremes in respect of high frequency oscillations. x-axis: Amplitude in volt (V)

Time frequency analysis

"Time-frequency analysis identifies the time at which various signal frequencies are present, usually by calculating a spectrum at regular intervals of time" (wavemetrics.com, 08.09.2013).

To visualize the oscillatory potentials contained in the signal, a time-frequency representation of power (TFR) has been computed as depicted in Figure 18.

Figure 18: Time-frequency resolution of power,
x-axis time (s), y-axis Frequency (Hz); Time of interest marked in black squares: high-frequency power increase (75 Hz to 170Hz), black line at 0 sec: stimulus onset

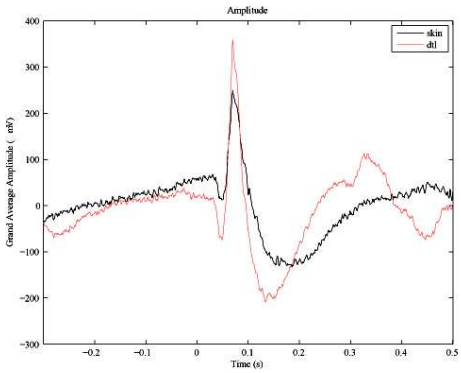


warm colours: power increase relative to prestimulus baseline
cold colours: power decrease relative to prestimulus baseline

Signal-to-noise Ratio.

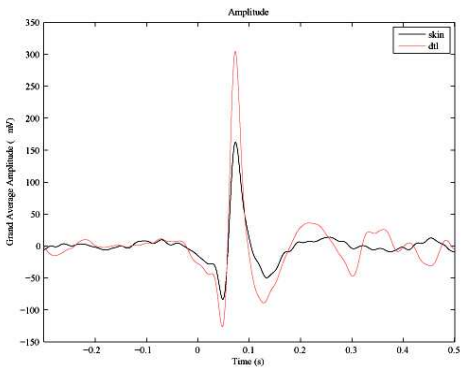
After filtering the data, a comparison of both signals with regard to same noise levels has been done. The difference in signal composition before and after applying the bandpass filter from 5 Hz to 45 Hz is depicted in Figure 19 and Figure 20. The desired retinal signal is not corrupted by this operation.

Figure 19: SNR without Band-pass filter 5-45Hz; showing different noise levels in both signals.



x-axis time (s), y-axis: amplitude μV; red curve DTL electrode, black curve skin electrode

Figure 20: SNR with Band-pass filter 5-45Hz, smoothed signal ready for Signal-to noise-ratio application.



x-axis time (s), y-axis: amplitude μV, red curve DTL electrode, black curve skin electrode

After computing SNR, the two electrodes have been examined with a parametric two-tailed students-t test for paired samples and a non-parametric Wilcoxon Matched-Pairs Signed-Rank test. Figure 21 shows the test for normality. A-wave and b-wave data regarding skin electrode thus are normally distributed. The data of DTL electrode is not normally distributed.

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
a-wave SNR skin	-13,2136	6,35353	-0,849812	0,0372909	0,932933	0,4413	Yes

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
a-wave SNR dtl	-8,58545	5,82587	-0,646714	-1,74191	0,872487	0,0834	No

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
b-wave SNR skin	12,7453	8,08447	1,12466	0,142681	0,88865	0,1338	Yes

Shapiro-Wilk's Test for Normality (α = 0,10)							
Variable	*Mean*	*Std. Dev.*	*Skewness*	*Kurtosis*	*W*	*p*	*Normality ?*
b-wave SNR dtl	13,9607	12,1085	1,83334	3,43453	0,812041	0,0136	No

Figure 21: Shapiro Wilk's Test for Normality - Distribution of SNR samples

Table 6 shows the results of the computed tests.

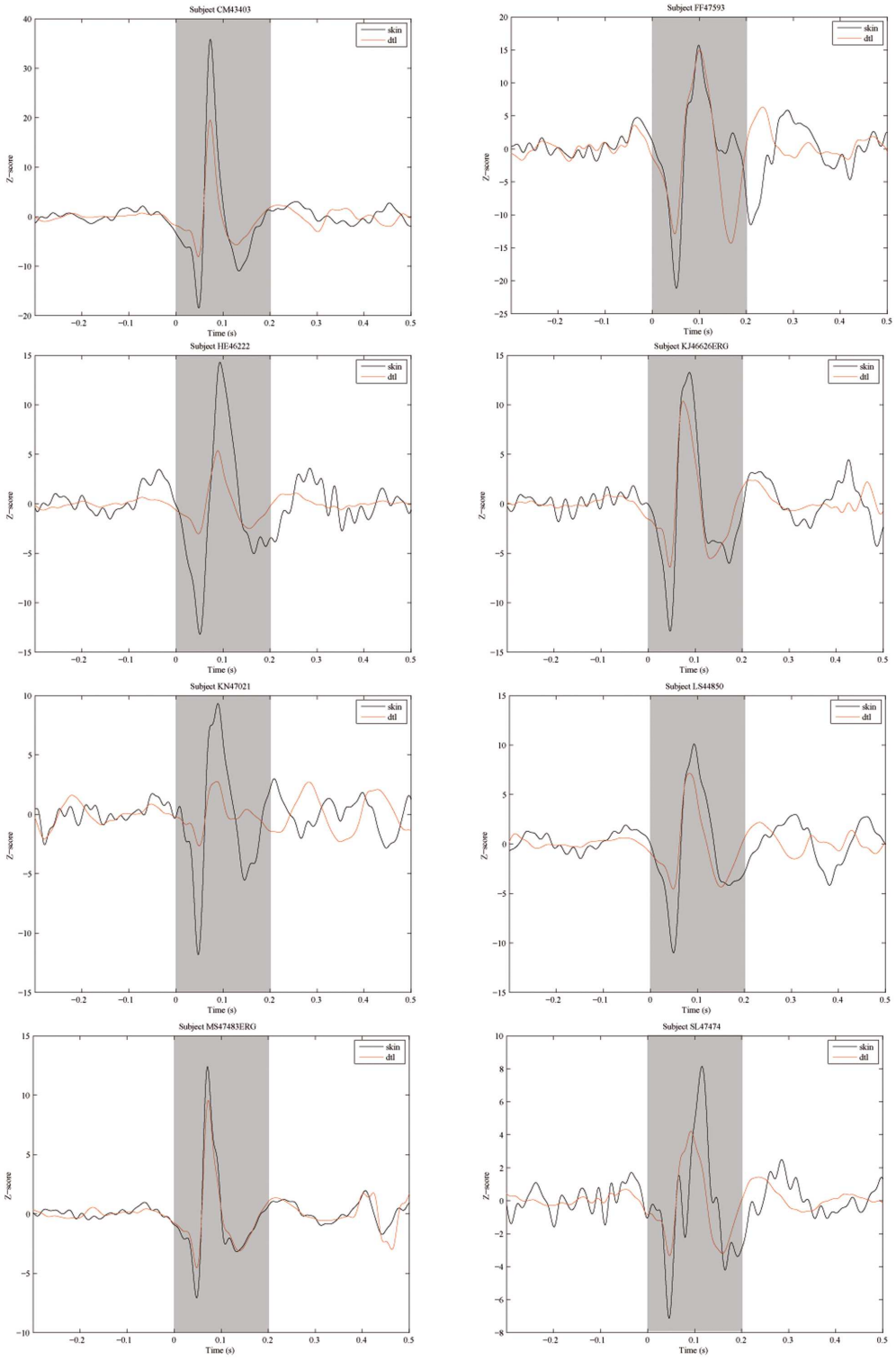
	Parametric (students-t test)			Non-parametric (Wilcoxon Matched-Pairs Signed-Rank Test)		
Comparison SNR ratios skin/dtl	df (two-tailed 0.05)	t	p-value(two-tailed)	T (two-tailed 0.05)	z (corrected for continuity)	p-value(two-tailed)
ratios a-wave	10	2.50678	0.0310	10	-1,86713 (1,82267)	0,068
ratios b-wave	10	0.3961	< 0.5	10	0 (-0,0444554)	< 0,5

Table6: t-Test Signal-to-Noise-Ratio; T-test ran with quantified values in table 7. results parametric approach left column; results non-parametric statistical approach right column

While the comparison of the a-wave ratios reached significance in the parametric students-t test *(t=2.50678, p*=0.0310*),* it did not with b-wave ratios (*t*=0.3961, *p*<0.5). The Wilcoxon Matched-Pairs Signed-Rank test did not reach significance in both comparisons. A-wave ratios (*z*=-1.86713, corrected for continuity *z*=1.82267, *p*=0.062, corrected for continuity *p*=0.068) and b-wave ratios (*z*=0, corrected for continuity *z*=-0,044455, *p*<0.5).

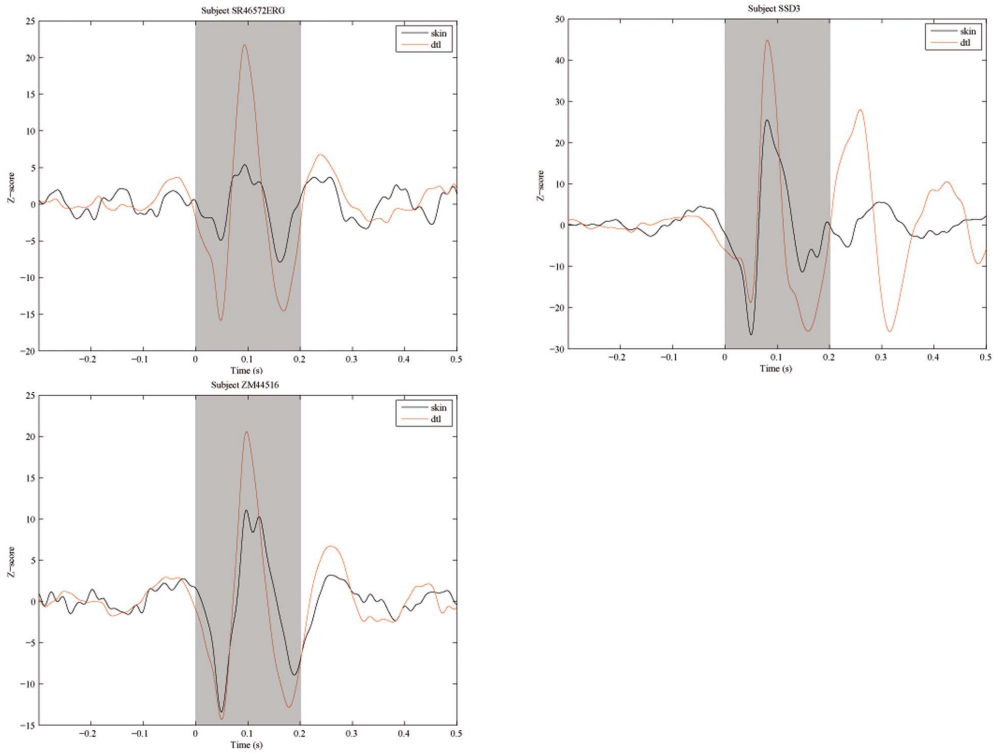
Depicted below, Figures 22 and 23, show the SNR for each participant.

Figure 22: Signal-to-Noise-ratio - all participants depicted, each window shows one participant trial average after SNR application



x-axis time (s), y-axis amplitude μV; black curve skin electrode, red curve DTL electrode, Time of interest shaded from 0 sec. to 0.2 sec.

Figure 23: Continuation of Figure 22 – Signal-to-Noise-ratio all participants depicted, each window shows one participant trial average after SNR application



x-axis time (s), y-axis amplitude in μV; black curve skin electrode, red curve DTL electrode, Time of interest shaded from 0 sec. to 0.2 sec.

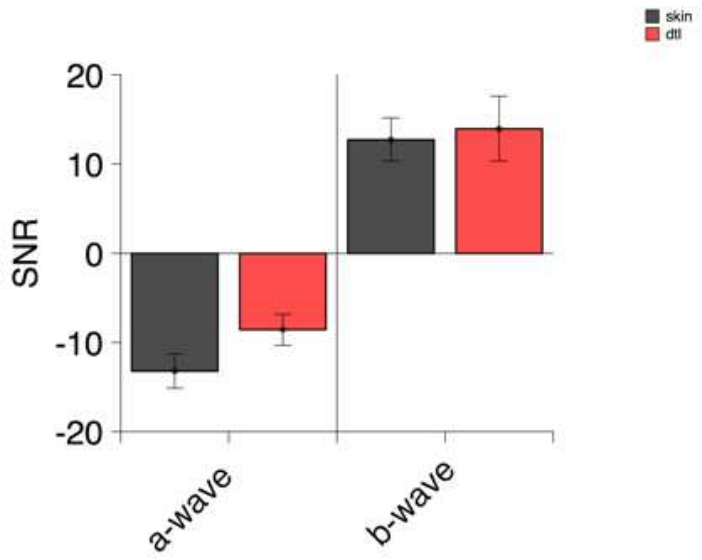
Table7 quantifies the data values of Figures 22 and 23, depicting a ratio of signal amplitude and noise average.

	Extremes			
	a-wave		b-wave	
	ratio skin	**ratio dtl**	**ratio skin**	**ratio dtl**
Subject				
1	-18.25	-8.10	29.12	14.84
2	-20.20	-12.88	15.33	15.02
3	-12.52	-3.03	13.54	5.36
4	-12.85	-6.40	12.28	9.91
5	-11.59	-2.66	9.12	2.77
6	-10.96	-4.55	8.09	7.14
7	-7.07	-4.54	7.89	7.09
8	-7.12	-3.33	2.80	4.22
9	-4.91	-15.86	5.40	21.77
10	-26.53	-18.79	25.55	44.87
11	-13.35	-14.30	11.07	20.58

Table7: Quantification of Signal-to-Noise-Ratio – quantified for each participant listed on the left

The bar-plot below, Figure 24, visualizes the data underlying the statistical approaches used, indicating that data does not differ drastically. In particular regarding b-wave comparison of skin and DTL electrode (right column)

Figure 24: Bar-Plot - comparison of a and b wave extremes after applying SNR



x-axis comparison of a-wave and b-wave extremes in z scores after applying SNR; y-axis: SNR z-scores from from -20 to 20; warm colours: z-score of DTL electrode; cold colours: z-score of skin electrode

Discussion

Desired retinal signal

Due to a careful methodical approach regarding the appliance of electrodes and the rejection of artifact-contaminated trials, as well as the high stimulus-onset-synchronicity between DTL- and skin electrode, it seems probable that the desired signal has been recorded.

VEP amplitudes

As literature covers that intensely, the DTL electrode should outline the skin electrode regarding recorded signal strength distinctly. This is because of the direct contact of the DTL with the retina. Present results cover that. Yet, the difference has not been as clear as expected. This may refer to the experimental design, regarding light adaptation and other configurations varying slightly across different inquiries. In addition, this research approach often has to deal with small sample size, which makes reproducibility more difficult. Yet, it might also show that the DTL and skin electrode do not differ in signal recording as strong as reported in the past, maybe to developments in recording techniques in respect of impedance. Given that in the past skin electrodes have been disqualified in some respect due to its lower signal strength, the experimenters investigated further aspects of the recorded signal.

Visually inspecting the present results, the signals differ distinctly while showing high stimulus congruency. Meaning, that a and b wave extremes show high synchronicity, implying that the experimental design has been feasible measuring VEP with both instruments, DTL- and skin electrode.

Tracing back the results of former studies, a significant difference in both signals regarding signal strength has been expected. A computed students-t test yet did not reach significance, implying there being no significant difference. Although the p-values of the a-wave (p= .53) and b-wave (p= .50) do barely not reach

significance and give at least a tendency. After inspecting the data visually that result has been surprising to the experimenters.

After testing samples with a Shapiro Wilk's Test for Normality the decision has been made, that non-parametric testing is required. A non-parametric Wilcoxon Matched-Pairs Signed-Ranks test was computed. This approach then provided different results. Both comparisons of skin and DTL electrode, the a-wave (p= 0.003, corrected for continuity p=0.004) and b-wave (p=0.003, corrected for continuity p=0.004) reached significance with this test, indicating that the DTL electrodes generally recorded higher peak voltages than the skin electrodes. Although only two samples in the present study have been normally distributed the parametric students-t test has been routinely used to double-check the statistical analyses. The Wilcoxon Matched-Pairs Signed-Rank test however has to be considered in that case, assuming that it has more statistical power in data that is not distributed normally.

Oscillatory potentials

As examination of amplitude alone might barely give an acceptable statement about the instrument's qualification, the present report focused next on the feasibility of DTL- and skin electrode to measure oscillatory potential contained in the recorded signal.

Neuroscience lately has highlighted the importance of different synchronization processes in the brain. These are, for instance phase coupling and frequency coupling. Especially valuable in that respect is gamma frequency, found to be part of synchronization dynamics in the visual system. To be sure, that both electrodes do not significantly differ in measuring the high frequency spectrum, meaning that they effectively measure certain frequency-domains, data has been high-pass filtered at 75 Hz.

Present results show a synchronicity in the extremes of the b-wave, which has been examined because of its higher strength in comparison to the a wave extreme,

assuming that this entails higher coherence. Figure 12 and Figure 13 show the averaged oscillatory potential.

Although the primary visual inspection supported the impression that both signals do not significantly differ in phase coherence the values of the b-wave extremes have been extracted and a students-t test has been computed. The parametric students-t test did not reach significance (p=0.1). In contrast, the non-parametric Wilcoxon Matched-Pairs Signed-Rank test reached significance (p= 0.026, corrected for continuity p=0.029), indicating that the signals are somehow not coherent. More advanced statistical examination is therefore needed.

Looking at oscillatory potentials, the present study was particularly interested in finding gamma-frequency in the recorded signal. Showing the feasibility of both instruments used, to cover high-frequency dynamics, might be important to further qualify both instruments in analyzing processes in the visual cortex.

As Time-Frequency-Analysis shows, depicted in Figure 18, the recorded signal of both electrodes contain frequency in the gamma spectrum (from 80-150Hz), similar to those observed in the human visual cortex. Both electrodes seem thus able to measure gamma oscillations at the time of the stimulus-onset. Yet the recorded gamma in the DTL electrode is more powerful what might be associated with its ability to record stronger signal. Nonetheless, both electrodes skin- and DTL electrode provide satisfying data in that respect, implying that both electrodes are qualified to be used in further research aiming at high frequency.

Signal-to-noise-ratio

The signal-to-noise ratio has a long history in neuroscience to measure the quality of recorded neuronal signal, but has still not found its way into the analysis of the electrodes to be examined in the present report. Hence, the present report has been interested in the true comparability of DTL and skin electrodes in respect of

signal quality. Hence, just an amplitude disparity towards one measurement tool does not self-evidently prove the qualification of one electrode or the other to measure retinal signal in clinical or research trials.

Interpreting existing data that way, scientists claim DTL electrode being a more qualified tool for VEP-measurement, because of the multiplied amplitude of the VEP recorded. Taking a loss in wearing comfort, handling, preparation time, data consistency, and as the present report implies data quality as well.

To avoid that misconception of the data a SNR-analysis, as advanced classification strategy to get a practical and fair comparison between the two measures, has been applied. Thereby the power of the retinal signal in both electrodes has been compared to the level of the averaged background noise. It was therefore necessary to do a low-pass filtering in order to compensate for different noise-levels in both recorded signals. Visual inspection yet gives the impression that both signals approached each other after applying a low-filter without corrupting the recorded signal of retinal activity.

Inspecting the data for each participant visually after applying SNR the disparity between the recorded electrodes dropped drastically. As depicted in Figures 22 and 23 the present results show that skin electrode provides better signal quality in most participants. That surpassed the expectation that skin electrode recording might provide almost similar results. The impression that applying SNR would even invert the relations has been surprising. This impression however has not been consistently proved by the statistical approaches used.

A parametric students-t test and a non-parametric Wilcoxon Matched-Pairs Signed-Rank test have been computed to show that both signals do not differ significantly. While the parametric approach reached significance in the a-wave comparison (p=0.031) the b-wave comparison did not reach significance (p<0.5). The Wilcoxon Matched-Pairs Signed-Rank test instead, did not reach significance in both comparisons, recorded signal of skin and DTL electrode in a-wave (p=0.062,

corrected for continuity p=0.068) and b-wave (p=<0.5), indicating that there is in no significant difference in signal quality between the two electrodes after application of SNR.

General discussion

The findings show, that there is more to the measurement of retinal signal than just recording a high-amplitude signal. Mere signal strength might therefore not be a sufficient classification strategy in respect of signal quality. Yet, clinicians missed to question their results in an appropriate way and go one step further in their analyses. The present results indicate that the comparison of DTL electrode and skin electrode did not have comparable signal quality. In addition, visual examination of the recordings after application of SNR suggests that the skin electrode may even provide a slightly higher quality signal in some cases.

In addition, the application of the skin electrode has been much easier and quicker in comparison to the application of the DTL electrode. The DTL electrode was accompanied by discomfort to both, participants and experimenters, although the handling of the DTL electrode improved during the sessions. Thus, taking matters of signal quality, wearing-comfort, handling, and health-wise risks of usage of both electrodes into account, benefits of the skin electrode are plain.

Regarding further research of retinal activity and dynamics in visual cortex the present report recommends usage of skin electrodes.

In case that skin electrodes provide acceptable results in respect of measuring retinal activity, this could have huge impact on testing of clinical populations. These particularly sensitive populations (i.e., children, psychic populations) might be measurable as the skin electrode does not appear as intimidating as the DTL electrode. Using skin electrodes to measure ERG would increase the willingness of these particularly sensitive populations to participate in research studies, which in turn might lead to new insights into the mechanisms or symptoms of psychiatric

disorders.

In addition, the results of the present report might lower the methodical effort. On the one hand, experimenters would not need highly specialized equipment/electrodes to carry out studies that address retinal activity. On the other hand, involved staff would not need such specific instructions, which makes the realization of an inquiry more feasible. That opens up new application possibilities in clinical research as well as in basic research. Furthermore, an instrument that is easy to handle, might improve reproducibility of results.

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Michael Morgenroth

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Appendix

Naturwissenschaftliche Fakultät Fachgruppe Psychologie
Prof. Dr. Thomas Elbert / Prof. Dr. Brigitte Rockstroh
Universitätsstraße 10
E-Mail: thomas.elbert@uni-konstanz.de
Studie: **Beitrag der Retina zu Oszillationen im visuellen Cortex**

Untersuchungen mittels Elektroenzephalographie/Magnetoenzephalographie und Elektroretinographie

Erklärung:

Dr. Dalal zusammen mit Professoren Elbert und Rockstroh führen Untersuchungen durch, um aus der Messung elektrischer und magnetischer Aktivität des Gehirns mehr über die Arbeitsweise des menschlichen Gehirns zu erfahren. Derzeit gibt es zwar sehr gute Verfahren, um die anatomische Struktur des Gehirns abzubilden, die Verfahren, um die Funktionsweise des Gehirns zu erfassen, befinden sich jedoch noch in der Entwicklung. Die Messung von Magnetfeldern des Gehirns während bestimmter Funktionen des Wahrnehmens, Denkens und Erlebens kann Wissenschaftlern und Ärzten eine solche Funktionsmessung ermöglichen und zwar mit einer zeitlichen Genauigkeit, die den Prozessen des Denkens, Fühlens und Handelns entsprechen dürfte. Man bezeichnet diese Ortung von Aktivitätsquellen im Gehirn als MSI (abgekürzt aus dem Englischen “Magnetic Source Imaging”).

Das Gehirn verarbeitet Informationen aus der Umwelt zu Gedanken, Gefühlen, Wahrnehmungen dadurch, dass elektrische Impulse entlang der Nervenfasern weiter geleitet werden. Jeder dieser winzigen Stromflüsse verursacht ein ebenso winziges elektrisches und magnetisches Feld. Rhythmische Veränderungen dieser Nervenzellaktivität kann man z.B. von der Kopfoberfläche im sogenannten Elektroenzephalogramm/ Magnetenzephalogramm (EEG/MEG) sehen. Diese Aktivitäten verändern sich, wenn man z.B. einschläft oder wenn man Informationen aufnimmt, z.B. Töne oder Worte hört, Lichter oder Bilder sieht oder Gegenstände berührt, aber auch, wenn man sich auf etwas konzentriert, sich Bilder oder Töne merkt oder denkt.

Bei der Untersuchung, an der wir Sie bitten teilzunehmen, soll nun von Ihrem Gehirn die elektrische und magnetische Aktivität aufgezeichnet werden, während Ihnen bestimmte Stimuli dargeboten werden.

In diese Experiment wird zusätzlich zu der magnetischen Gehirnaktivität das Elektroretinogramm (ERG) abgeleitet. Das Ziel dieser Untersuchung ist zu erforschen, inwiefern das elektrische Signal in der Retina mit der elektro-magnetischen Hirnaktivität zusammenhängt. Zu diesem Zweck wird eine sehr feine Haarelektrode entlang des unteren Augenlids angebracht. Dieser Typ von Elektroden wird standardmäßig in augenärztlichen Untersuchungen verwendet und ist grundsätzlich mit keinen besonderen und/oder gefährlichen Nebenwirkungen oder Entzündungen verbunden. Nichtsdestotrotz werden Sie diese Elektrode während der Untersuchung spüren. Ebenfalls könnte es vorkommen, dass es während der Untersuchung zu einem verstärkten Tränenfluss kommt und/oder das Auge nach der Untersuchung etwas errötet. Wenn Sie an diesem Experiment teilnehmen erklären Sie sich damit einverstanden / bestätigen Sie,dass:

→ Ihnen eine ERG Elektrode entlang des unteren Augenlids angebracht werden darf

→ Sie darüber informiert sind, dass es zu einem verstärkten Tränenfluss und einer Errötung des Auges kommen kann.

→ **Sie uns sofort informieren, sobald Sie etwas Unangenehmes und/oder Seltsames in Verbindung mit der ERG Elektrode verspüren, und gegebenenfalls die Untersuchung abbrechen ohne dass Ihnen einen Nachteil entsteht.**

Im ersten Durchgang werden keine Reize dargeboten sondern lediglich die Ruheaktivität des Gehirns mit offenen Augen gemessen. In den restlichen Durchgängen werden Sie mit visuellen Stimuli (Lichtblitze, emotionale Bilder oder sich bewegende Stimuli) konfrontiert. Einige der in den Fotografien gezeigten Szenen können Darstellungen von Nacktheit, Sexualität, und Gewalt enthalten, die von manchen Personen als unangenehm empfunden werden können.

Wenn Sie an der Untersuchung teilnehmen

⇒ Wenn Sie an der Untersuchung teilnehmen, werden Ihnen zunächst einige Fragen zu Ihrer Person gestellt (z.B. ob Sie rauchen, Rechtshänder sind, wann Sie geboren sind, welchen Schulabschluss Sie haben etc.) und zu Ihrem Gesundheitszustand (z.B. ob Sie Medikamente einnehmen, einen Herzschrittmacher haben etc.)

⇒ Während der Untersuchung liegen oder sitzen Sie auf einer Liege in einem besonderen Raum. Die Messfühler für die **magnetische** Aktivität sind in einem großen Behälter, der eine helmförmige Einstülpung hat. Sie werden gebeten, Ihren Kopf in diese Einstülpung zu legen. Dabei bleibt Ihr Gesicht frei. Es werden kleine Messfühler auf Ihrer Stirn bzw. an Ihren Ohren befestigt, über die wir zu jeder Zeit die Lage und Bewegungen Ihres Kopfes feststellen können. Außerdem werden wir vor Beginn der Messung mit einem Griffel leicht über Ihre Kopfhaut fahren, um Ihre Kopfform zu messen.

⇒ Wenn **elektrische** Aktivität gemessen wird, wird Ihnen eine Art Badekappe aufgesetzt, auf der kleine Messfühler angebracht sind. Die Hautstellen unter den Messfühlern werden mit einer speziellen Paste eingerieben, die sich nach der Messung einfach abwaschen lässt.

⇒ Während der Messung sitzen Sie in einem besonderen Raum, dessen Tür geschlossen bleiben muss, um Geräusche abzuschirmen. Wir können Sie über eine Videokamera sehen und mit Ihnen über ein Mikrophon sprechen. Wenn Sie es wünschen, bleibt ein Mitarbeiter zusammen mit Ihnen während der Messung in dem Raum.

⇒ Es ist wichtig, daß Sie während der Messung ganz still liegen oder sitzen können und sich nicht bewegen. Es gibt aber regelmâssigen Pausen, in denen Sie sich bewegen können. Insgesamt wird die ganze Untersuchung 1-2 Stunden dauern.

Risiken:

Die M/EEG-Messungen werden routinemäßig und von geschultem Personal durchgeführt. M/EEG-Verfahren werden in der Forschung sowie im klinischen Alltag routinemäßig eingesetzt, somit bestehen für Sie keine Risiken. Im Prozess des Anbringens der Elektroden kann es zu leichten Hautirritationen kommen. Bitte informieren Sie den Versuchsleiter bei entsprechenden Unannehmlichkeiten.

Wie oben erwähnt, ist die Stimulation mit Lichtblitzen für gesunde Personen ungefährlich. **Sollten Sie oder ihre Familienmitglieder ersten Grades unter Epilepsie leiden**, so informieren Sie die Experimentatoren darüber. Das Experiment ist in diesem Fall abzubrechen.

Informieren Sie die Experimentatoren auch, wenn Sie unter Klaustrophobie leiden. Dies führt zum Abbruch des Experiments. Das Experiment wird in einem relativ kleinen Raum durchgeführt, welcher während der Dauer des Experiments geschlossen bleibt.

Es besteht ein kleines Infektionsrisiko durch natürlich vorkommende Keime, da die ERG-Elektrode direkt in Ihrem Auge platziert wird. Dieses Risiko wird durch folgende klinische Leitlinien effektiv minimiert: vor dem Anbringen der Elektroden desinfizieren die Experimentator/innen ihre Hände und ziehen Einweg-Handschuhe an. Eine neue Elektrode aus einer versiegelten Packung wird für jede/n Probanden/Probandin benutzt und nach Gebrauch entsorgt.

Einige Proband/innen könnten die Elektrode im Auge als unangenehmen Fremdkörper empfinden oder Reizung durch die Reibung der Elektrode wahrnehmen. Diese Risiken werden minimiert, indem die Elektrode vor Gebrauch mit einem Gel befeuchtet wird, das zur Verwendung im Auge vorgesehen ist. Eine neue Geltube wird für jede/n Probanden/in benutzt. Probanden in Pilotstudien haben berichtet, dass die Elektrode bei Verwendung des Gels kaum spürbar ist.

Bei Beschwerden, die durch die Elektrode oder das Gel verursacht werden, wird das Experiment sofort abgebrochen und die Elektrode entfernt. Bei Reizung wird Ihr Auge mit Salinlösung gespült.

Kosten:

Die Untersuchung dient ausschließlich wissenschaftlichen Zwecken. Es wird keine Rechnung gestellt und kein Antrag zur Kostendeckung durch die Krankenkasse. Sie erhalten für Ihre Teilnahme an der Untersuchung die Fahrtkosten zum Labor und/oder eine kleine finanzielle Entschädigung.

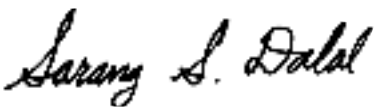
Rechte:

Ihre Teilnahme an der Untersuchung ist freiwillig. Durch Ihre Einwilligung gehen Sie keine Verpflichtungen ein. Sie können die Einwilligung in die Untersuchung jederzeit widerrufen, ohne dass Ihnen ein Nachteil entsteht. Sie können die Untersuchung jederzeit abbrechen, ohne dass Ihnen ein Nachteil entsteht.

Datenschutz:

Angaben zu Ihrer Person werden nicht an Dritte weitergegeben oder veröffentlicht. Um die Messwerte Ihrer Gehirnaktivität für die Auswertung zugänglich zu machen, werden diese für die Dauer der Untersuchung elektronisch unter einem Namenscode und Geburtsdatum gespeichert (ohne Adresse). Nur von den Unterzeichnenden autorisierte
Mitarbeiter/innen der Universität haben Zugang zu den erhobenen Messwerten. Die von Ihnen erhobenen Informationen werden nach Abschluss der Untersuchung gelöscht.

Sollten Sie weitere Fragen haben, beantworten wir Ihnen diese gerne. Den verantwortlichen Leiter der Studie, Dr. Dalal, erreichen Sie unter 07531/88-5706 oder sarang.dalal@uni-konstanz.de



Sarang S. Dalal, Ph.D.

Erklärung:

Ich habe die vorausgehende Erklärung gelesen und verstanden. Die/der von Professor Elbert oder Professor Rockstroh autorisierte/n Mitarbeiter/in

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hat mir die Untersuchung erläutert und allgemeine Fragen hinreichend beantwortet.

Ich nehme freiwillig an der Untersuchung teil und bin mit den Untersuchungsbedingungen und Datenschutzbestimmungen wie ausgeführt einverstanden.

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