METHODOLOGY AND FIRST RESULTS OF SELECTIVE CONE STIMULATION OF HUMAN EYE VIA SILENT SUBSTITUTION TECHNIQUE

P. Beßler*, S. Klee*, P. Husar** and G. Henning*

* Institute of Biomedical Engineering and Informatics, Technische Universität Ilmenau, Germany
** Department of Medical Technology, Saarland University Hospital, Homburg, Germany

patrick.bessler@tu-ilmenau.de

Abstract: For electrophysiological examination of colour vision defects and of wavelength specific neural pathways, selective excitation of cones is needed [1]. Physical impulses have to give a desired effect at psychophysiological level. By use of appropriate colour models associated with the silent substitution technique these possibilities are given [2], [3]. For generation of suitable stimulations via silent substitution technique all kinds of display-colours, given in the RGB space, must be mapped onto the biological system of L -, M - and S - cones. Thus at certain combinations of colour the activation of the cones is known. By calculating of different colour combinations the activation of different cones types can be modified. With these calculated colour values a flash stimulation sequence for a TFT-display was generated. The first examinations are accomplished at test persons. Two trials (S - cone and L – and M - cone response) at both eyes accomplished. The analysis of the VEP data in the EEG shows a significant delay of the S - cone response against the L - and M - cone response. First results show that it is possible to excite the cones selectively via silent substitution technique. Further investigations in this field, at more test persons, are necessary to verify the results and generalise the electrophysiological effects.

Introduction

Glaucoma is one of the most widespread eye diseases. It is number one of reasons for blindness. Often the rise of the intraocular pressure is a reason for stall of optical nerve. Thus the field of vision decrease and without any therapy blindness is the consequence. The early diagnosis of this clinical picture is very important on this account to detect these diseases and stop the process with drugs or surgery.

Measurement of intraocular pressure and subjective perimetry are the most applied methods in the diagnostic of glaucoma at present [4]. The possibilities of psychophysiological and electrophysiological examination methods for diagnosis of glaucoma are determined currently [5], [6]. For electrophysiological examination of colour vision defects and of wavelength specific neural pathways, selective excitation of cones is needed [1]. Many clinical studies show disorders in colour perception of the blue channel by glaucoma patients or persons with suspicion of glaucoma [1], [7], [5] ,[8]. By selective cone excitation colour vision defects and associated clinical pictures can be detected [9], [10].

For selective excitation the physical stimulus of stimulators must be reach the desired effect at psychophysiological level. This possibility is provided by appropriate colour models associated with the silent substitution technique [2], [3].

Initial point of this development was the search for an alternative to the known method “chromatic adaption” from Estevez and Spekreijse. In the 1970th the “chromatic adaption” was a method to isolate the several photoreceptors. The authors used the “principle of univariance” of Rushton as work base and named their method “spectral compensation”. To stimulate one type of photoreceptor and get no response from the other photoreceptors, the “spectral compensation” is applied in psychophysiological and electrophysiological examinations. Already 1949 Donner and Rushton adopt a nearly equal method: the “light substitution”. For these idea the name “silent substitution” has achieve today [3].

By the use of several colour models, physiological properties of the human eye and vision associated with the silent substitution technique, stimulation algorithms can be generated. Therewith an excitation of the blue channel without an excitation of the red-green channel and vice versa is possible. The response signals in the EEG of the visual cortex can be measured an interpreted. So it is possible to early detect colour vision deficits and glaucoma in order to counteract.

Materials and Methods

To calculate the colour values for selective cone excitation via silent substitution technique, the technical RGB - space must be mapped onto the biological LMS - space. One base of the silent substitution technique are “metamer colours”. These are different colour impulses based on distinct spectral power distributions, witch produce the same colour impressions to the observer. Metamer colours have equal properties, so the additive colour composition has a great importance [17]. Thus, in colour change during the stimulation and associated change of spectral power distribution the colour impression of the several cones can be hold constant. To stimulate several cone types and have no colour stimulus at other cones with different area of sensitivity this method is necessary. For an effect at biological level at LMS - space, thus for activation of several cones, the colour changes must be optimized.

Commercial TFT - displays create the displayed colour via additive colour composition. Those and other important properties, like spectral, static and dynamic properties of the stimulators must be determined. For application at silent substitution technique these facts must be known. [11]

To transfer the technical RGB - values to the biological LMS - activation, several steps are necessary. At first the spectrum after adjustment to white must be known. Also the context between the luminance of the stimulator and the attuned colour values of primary colours, the gamma curve, is very important because it is a non-linear context. Therewith the luminance of colours can be adjusted via the primary colour rate. For the setting of calculated colour combinations for the desired colour changes via silent substitution technique this is very important. There are different possibilities for transformation between the technical RGB - space and the biological LMS - space. To guarantee the comparability of the light sources in a technical system, a transformation of the RGB - colour values to the tristimulus values in XYZ - space are necessary. By multiplication of the RGB - colour values with the transformation matrix $M_{RGB \rightarrow XYZ}$ the transformation is realized. The spectra of the three primary valences and white will be convoluted with the colour matching functions. The results are the tristimulus values XYZ for the chosen RGB values. From the XYZ - values the chromaticity coordinates xyz can be calculated. If the system is adjusted to white then the brightness of white in the virtual colour space is one (Y_W=1). Consequently the transformation matrix $M_{RGB \rightarrow XYZ}$ can be destined and the colour values can be transferred to the virtual XYZ - system. From the virtual XYZ - space to the biological LMS - space are two transformation matrices known. One matrix was developed by Hunt [12], and the other one by Stockman and Sharpe [2]. The investigations of Schlegelmilch show both transformation matrices are equitable [13]. Based on the matrices $M_{RGB \rightarrow XYZ}$ and $M_{XYZ \rightarrow LMS}$ the relationship between the technical RGB - space and the activation at biological LMS - space can be calculated. Therefore the transformation matrices $M_{RGB \rightarrow LMS}$ and $M_{LMS \rightarrow RGB}$ are developed and used. So the relative activation of the cones caused by any colour combination is known. The activation of several cones can be modified on the basis of selective adjusted colour combinations. For optional cone types it is possible to switch these cones "silent" by optimisation of colour combinations. For example it is possible to calculate two colour combinations without a difference in activation for L - and M - cones but a maximum difference in activation for S - cones (L_1=L_2, M_1=M_2, $S_1 \neq S_2$). Therefore an optimisation is necessary. The initial value in RGB - space will be alleged and the activation in LMS - space can be determined. The L - and M - cone activation must be constant, the S - cone activation should be maximal. To check the technical feasibility and plausibility, the optimized LMS - space values must be mapped back onto RGB - space. If the RGB - values not feasible then the combination next to the calculated is chosen and its activation in LMS - space are determined. The alternating approximation to the technical feasible optimum occurs in further calculation steps on this procedure.

The stimulation was presented by a 30" TFT - panel MYRICA V30-1 (Fujitsu Siemens). For the selected, white adjusted, commercial TFT - display, two stimulations were calculated, on described method. Following values are absolute activation values of S - cone stimulation for a 10° observer.

$$\begin{bmatrix} L_1 \\ M_1 \\ S_1 \end{bmatrix} = \begin{bmatrix} 0.1527 \\ 0.1889 \\ 0.0356 \end{bmatrix} \qquad \begin{bmatrix} L_2 \\ M_2 \\ S_2 \end{bmatrix} = \begin{bmatrix} 0.1527 \\ 0.1889 \\ 0.8663 \end{bmatrix}$$

These are the values for L - and M - cone stimulation.

$$\begin{bmatrix} L_1 \\ M_1 \\ S_1 \end{bmatrix} = \begin{bmatrix} 0.0243 \\ 0.0301 \\ 0.1435 \end{bmatrix} \qquad \begin{bmatrix} L_2 \\ M_2 \\ S_2 \end{bmatrix} = \begin{bmatrix} 0.9249 \\ 0.8557 \\ 0.1435 \end{bmatrix}$$

With the colour values, calculated for optimal cone activation, a flash stimulation sequence for the selected stimulator was generated. The silent substitution stimulation was presented as circle with an eccentricity of 20° and a fixation point in the centre. Around the circle is an adaption area. The adaptation area eliminates the rod response.

Simultaneously to the stimulation the EEG - signal is recorded. For presentation of stimulation sequences and recording of the EEG and VEP the examination system Theraprax® (eldith GmbH, Ilmenau, Germany) has been used. The EEG - signals were recorded at Oz vs. reference = Fz (10 - 20 - system). By the use of digital signal processing the VEP - responses were preprocessed. With the software MATLAB®, MathWorks Inc. analysis of VEP - signals from the EEG - data are done. The drift of electrodes and other interferences like 50Hz line frequency and their harmonics are cancelled. Furthermore a detector for alpha waves, and EMG - interferences are implemented. The signals of several trials were averaged.

A second stimulation to suppress the S - cone response was generated. The calculation of this stimulation is analogue to the calculation for suppression of L - and M - cone response. Thus the VEP - responses of the L - and M - cones can be investigated. With this method the differences in processing of the colour channels can be investigated.

Figure 1 show the measuring station and measuring system. With this measuring station the first examinations are done.

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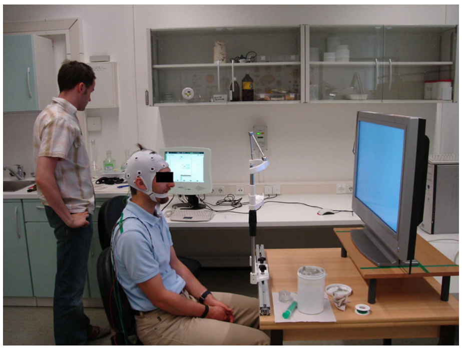

Figure 1: measuring system for EEG - measuring during stimulation via silent substitution technique

First investigations occur on two male subjects. The test persons are 26 and 47 years old and without known visual defects.

Results

The rates of the colours which were calculated for silent substitution were implemented in a stimulation sequence. The subjective impression which is generated from colour change is shown in Figure 2. During the change of the two calculated colours for S - cone response the subjective impression of a bright cycle with points in the centre is originated. This impression only occurs by application of the calculated colour combinations. Consequently this special stimulation method has an effect to the vision sense cells. By great activation of the blue channel the cones are saturated. If the stimulation sequence changes to lower activation then the normal sensitivity for stimuli is not restored in that time. The phenomenon of afterglow appeared. A subjective impression occurs which is objective inexistent. That impression is shown in Figure 2. That phenomenon only occurs by these special calculated great differences in activation. Consequently via silent substitution technique selected cone types can be excited.

Figure 2: Subjective vision impression during the alternation of colours of the silent substitution

During the stimulation of calculated colour combination for silent substitution technique a subjective vision impression arise, which is objective inexistent. This effect occurs only at very large differences in activation and via silent substitution technique a selective cone type can be activated whereby similar effects develop.

For first EEG examinations the stimulation sequences, as described in chapter methods, are presented on the stimulator. After pre-processing the triggered signal parts are averaged. The evaluated VEP - signals of S - cone response and L - and M - cone response of the two test persons are shown in Figure 3 and Figure 4.

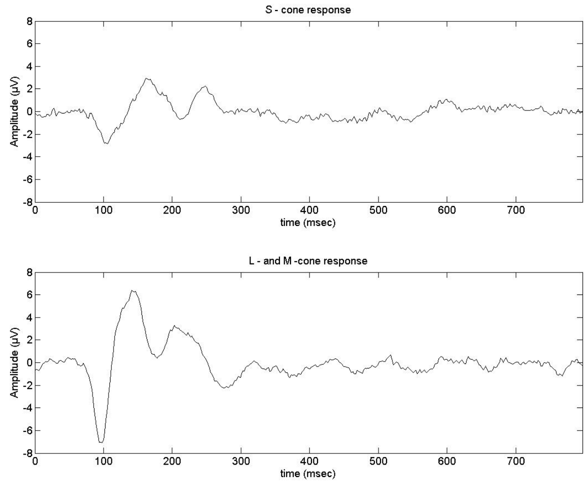

Figure 3: S - cone response (top) and L - and M - cone response (bottom) of the first test person at silent substitution technique

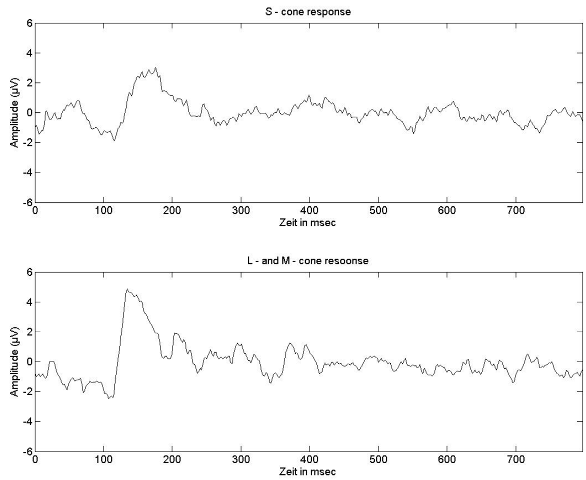

Figure 4: S - cone response (top) and L - and M - cone response (bottom) of the second test person at silent substitution technique

From the pictures is recognisable that for both test persons the amplitude of the L - and M - cone response is greater than the amplitude of the S - cone response. Alike the blue channel response is slower. In Figure 3 the mean wave of blue channel is located at 162 ms, the mean wave of red - green channel is located at 140 ms at test person 1. At test person 2 the response times is 166 ms respectively 135 ms. There are clearly differences in response time distinguishable. A steeper rise of responses in red - green channel is also visible. As further distinctive feature the signal form is to consider. For quantification of these differences suitable parameters must be developed. For example the signal of S - cone response falls to zero level after the first response wave. The declension of L - and M - cone response is not so strong. Taking everything into account a difference between the response signals after excitation is existent. So may be evidenced the described method of silent substitution technique is acting and several cone types and colour channels can be stimulated. The response signals of several cone types can be analysed. Consequently it is possible that colour vision deficits can be objective qualified and quantified. The results of the two test persons are not significant for universality but the first results are promising. Further investigations in this field and more examinations at test persons are necessary to generalise the electro-physiological effects and to verify the results.

Discussion

The theoretical fundamentals and derivations for stimulations via silent substitution technique are published. At practical implementation of the method, the technical parameters with influence to the stimulation method are considered. On the basis of objective examinations and analysis of VEP signals is demonstrated, that the method of selective cone excitation respectively colour channel stimulation is working. The detailed biological procedures must be resolved. The definitely S - cone response is assumed in the signal, but could not reproducible verified as S - cone response. The time difference between VEP signals of the two developed stimulations are circa 20 ms. These are first consideration of selective colour channel excitation and different properties regarding the signal processing of the colour channels. Differences in latency, form and other parameters of VEP signals must be enhanced and researched to get an assured evaluation and significant results. Therefore it is necessary to discuss the diagnostic relevance of this method with specialists at ophthalmology and electrophysiology. To provide first assumptions respectively to give significant statements huger groups of test persons are necessary. The intraindividual reproducibility is well however, the interindividual reproducibility must be checked at large groups. Furthermore examinations at patients are necessary to check the diagnostic validity of this method. Universal parameters for distinctions between healthy test persons and patients can be developed if applicable.

Conclusions

Summing up the analysed EEG data show the selective colour channel stimulation via silent substitution technique is possible. Based on theoretical models selective stimulation algorithms can be developed. First results show the silent substitution technique can be used for examination of human colour vision. The assumed responses of the stimulated cone types are identifiable at EEG. So the cone responses can be analysed and appraised. Therewith the objective qualification and quantification of colour vision deficits is possible. Investigations for verification with a great amount of patients and probands are in process.

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