

Rapid Objective Assessment of Contrast Sensitivity and Visual Acuity With Sweep Visual Evoked Potentials and an Extended Electrode Array

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PURPOSE. Sweep visual evoked potentials (sVEPs) provide an implicit, objective, and sensitive evaluation of low-level visual functions such as visual acuity and contrast sensitivity. For practical and traditional reasons, sVEPs in ophthalmologic examinations have usually been recorded over a single or a limited number of electrodes over the medial occipital region. Here we examined whether a higher density of recording electrodes improves the estimation of individual low-level visual thresholds with sVEPs, and to which extent such testing could be streamlined for clinical application.

METHODS. To this end, we tested contrast sensitivity and visual acuity in 26 healthy adult volunteers with a 68-electrode electroencephalogram (EEG) system.

RESULTS. While the most sensitive electrophysiologic response was found at the traditional medial occipital electrode Oz in a small majority of individuals, it was found at neighboring electrodes for the remaining participants. At the group level, lower spatial frequencies were also associated with right lateralized responses. More generally, visual function was evaluated more sensitively based on EEG recorded at the most sensitive electrode defined individually for each participant. Our data suggest that recording over seven posterior electrodes while limiting the testing session to less than 15 minutes ensures a sensitive and consistent estimation of acuity and contrast sensitivity threshold estimates in every individual.

CONCLUSIONS. The present study shows that sampling from a larger number of posterior scalp electrodes is relevant to optimize visual function assessment and could be achieved efficiently in the time-constrained clinical setting.

Keywords: EEG, visual acuity, contrast sensitivity, sweep visual evoked potentials, spatial frequency

According to the World Health Organization,¹ 253 million people are visually impaired, mostly as a result of uncorrected refractive errors or unoperated cataracts. The diagnosis of ophthalmologic pathologies is based on the evaluation of visual acuity, contrast sensitivity, Vernier acuity, or other visual parameters, typically with explicit behavioral measures, such as naming of Snellen letters for visual acuity, or naming of letters in the Pelli-Robson Chart for contrast sensitivity. Although largely used in a clinical setting, these behavioral tests are difficult, sometimes impossible, to perform with pre- or nonverbal patients, for instance infants. Even in human adults, performance at these tests can be influenced by confounding motivational and decisional factors, or intellectual abilities.

Recording electrophysiologic signals on the human scalp offers an alternative or complementary approach to assess visual function, particularly in difficult to test populations.² In particular, stimulating the visual system at a relatively fast fixed frequency rate, a flickering light for instance, leads to an electrophysiologic response on the electroencephalogram (EEG) exactly at the frequency of stimulation³ which,

transformed in the frequency domain, is typically referred to as a steady-state visual evoked potential (SSVEP^{2,4,5}). In the sweep VEP,⁶ the visual property under measurement, for instance spatial frequency, is progressively increased or decreased during the periodic visual stimulation. The point at which the frequency domain EEG response emerges or disappears significantly from noise level provides a threshold of visual acuity.⁷ Similarly, increasing or decreasing the stimulus contrast allows the determining of a contrast sensitivity threshold.⁸

The sVEP approach has substantial advantages to measure visual function. First, it does not require understanding of instructions and explicit responses of the tested participant, for instance to name letters or objects, or determine gratings' orientation. Hence, this approach is of particular interest to test infants or individuals with intellectual disabilities. Early detection of visual parameters abnormalities in infants is essential to diagnose and treat pathologies such as amblyopia, for which an early correction is recommended given the risk of irremediable visual function loss. The optimal age for treatment is not clear, but a correction before the age of 7 or even 3 years,



depending on the study, seems advisable.^{9,10} Moreover, while a patient could potentially simulate visual function loss with explicit behavioral tests in cases of hysteria or malingering,¹¹ he/she would be unable to do so with an implicit electrophysiologic index as measured with sVEP. Second, unlike standard event-related potential (ERP) measures¹² such as the flash potential, the electrophysiologic response of interest confines to a predetermined frequency known by the experimenter, increasing objectivity,⁴ and requiring minimal analysis procedures. Third, sVEP is typically associated with a higher signal-to-noise ratio than conventional ERP measures,⁴ increasing sensitivity. Finally, the method assesses visual function with a dynamic display, changing at a relatively fast rate, in conditions that are closer to the temporal constraints of vision in real-life environments.

Sweep VEPs to low-level visual parameters have traditionally been recorded at a medial occipital electrode Oz, in between O1 and O2 of the 10-20 electrode system,¹³ which is included in ~80% of reviewed publications, with very few other posterior electrodes (mean of electrodes recorded: 4; SD $\pm$ 2; mean over occipital region: 2, Table 1).^{7,14-31} This focus on a limited scalp region is due to the largest EEG amplitude frequently being recorded on this electrode with simple visual stimuli; it also traces back to a tradition in this area of research, when the first sVEPs were developed,^{14,15} and large arrays of electrodes and scalp topographic analyses were not available. Moreover, the time constraints in clinical settings require a trade-off between measure sensitivity and consultation efficiency, so that recording at only a few electrodes has become prevalent.

However, it has never been demonstrated that the Oz location on the scalp captures the sVEP with the highest sensitivity (i.e., signal-to-noise ratio, SNR), for parameters such as visual acuity and contrast sensitivity, either at the group level or across individuals. Moreover, the optimal number and location of electrodes for a full evaluation of these visual functions remain largely unknown. One of the only studies addressing this issue compared visual acuity and contrast thresholds obtained for two electrode placements of five electrodes in the occipital region, with a 2- to 3-cm shift of the electrodes between the two placements.¹⁸ This study showed no significant effect of electrode placement on visual acuity and contrast thresholds. However, even though the authors compared these two placements, they did not compare electrodes individually. For instance, whether a more sensitive threshold evaluation could be obtained with electrode Oz versus electrode PO8 was not assessed. Moreover, how the threshold values were determined in that study is not clear.

Another issue related to the limited spatial sampling in traditional sVEP investigations is that the highest SNR may be measured at Oz at the peak of the response, but the scalp topography may change across spatial frequency or contrast values during the sVEP. Identifying the highest suprathreshold SNR might be particularly important for the diagnosis of amblyopia for instance. Indeed, a greater suprathreshold amplitude helps to evaluate the suprathreshold depression induced by neutral density filter (NDF) in grating stimuli. This measure may contribute to the diagnosis of amblyopia because the proportion of eyes with NDF-induced suprathreshold depression is greater for normal control eyes than for amblyopic eyes.³²

For these reasons, here we aimed at determining whether human visual function assessment could be optimized by using an extended electrode array, including 64 electrodes of an extended 10-20 system, with four additional electrodes in the occipitotemporal region.

METHODS

Participants

The research protocol followed the tenets of the Declaration of Helsinki and was approved by the University of Louvain's Human Biomedical Ethics Board under the Belgian registration number B403201732407. We tested 26 healthy volunteers, including 17 females, aged 19 to 29 years (mean age 24, SD $\pm$ 3). Written informed consent was obtained from all participants after they were informed about the goal of the study.

One participant was excluded because she was taking psychiatric medication. In the final sample of 25 participants, none reported any significant neurologic or psychiatric disease, nor did they take any medication with major neurologic or psychiatric effect. All participants were right-handed. The Freiburg Visual Acuity & Contrast Test³³ (FrACT) at a viewing distance of 2 m was used to assess their subjective visual acuity with tumbling E's, and sensitivity to contrast with Landolt C's. Their visual parameters fell within the normal range, with a binocular visual acuity better than 0 logMAR and a sensitivity to contrast ranging from 0.4% to 3.9% of Michelson contrast, at a wide spatial frequency range, as sensitivity to contrast was assessed using Landolt C's.³⁴

In addition, 12 out of the 25 emmetropic participants were tested with converging lenses of various powers to artificially alter their visual acuity. Their artificially altered visual acuity was measured behaviorally using the FrACT test at 2 m with tumbling E's, and using eye charts at 5 m displaying Snellen letters and Landolt C's. The visual acuities measured with the FrACT test displaying tumbling E's correlated with those measured with eye charts showing Snellen letters and Landolt C's, respectively with a correlation of 0.91 and 0.90. In the remainder of this article, we will refer to the participants without artificially altered visual acuity as the "emmetropic" group (group E), and the participants with artificially altered visual acuity as the "artificially ametropic" group (group AA).

Participants received a monetary compensation at the end of the recording session.

Stimuli and Procedure

Stimuli were vertical sinewave pattern-reversing gratings with blurred edges, displayed at a rate of 10 Hz or 20 reversals per second, presented on an LCD monitor (ViewPixx3D; VPixx Technologies, Quebec, Canada) with a resolution of 1920 (horizontal) $\times$ 1080 (vertical) pixels and a refresh rate of 120 Hz. The mean luminance of the monitor was 132 cd/m².

At a viewing distance of 2 m, the stimulus patch subtended 20° of visual angle. Binocular visual acuity and contrast sensitivity were measured by respectively sweeping the spatial frequency or contrast of the grating over a range of 18 logarithmically spaced values. There were four stimulation conditions (Fig. 1). In the first two conditions, visual acuity was measured by gradually increasing or decreasing the spatial frequency of the grating between 2.7 and 40 cycles per degree (cpd) for group E, and between 3.8 and 50 cpd for group AA, with the Michelson contrast of the grating set at 30% for both groups. We used a relatively low level of contrast to minimize after-effects such as headaches, after several participants reported visual discomfort after looking at the stimuli with a higher contrast for 20 to 30 minutes of testing.

In the last two conditions, contrast sensitivity was measured by either progressively increasing or decreasing the Michelson contrast of the grating between 0.1% and 16%, with the spatial frequency of the grating set at 1.5 cpd. Visual stimulation lasted 20 seconds in all conditions with the grating contrast-reversing at each of the 18 logarithmic steps during 1 second. It included

TABLE 1. Localization and Number of Electrodes Used in Reviewed Studies

Authors	Date	Journal Name	Electrodes Localization	Electrodes Number
Abdullah SN, Vaegan, Boon MY, Maddess T	2012	<i>Clin Neurophysiol</i>	Pz, Oz, 2 elect. between Pz and Oz, 2 elect. right to Pz, 2 elect. left to Pz (+ reference and earth)	10
Allen D, Banks MS, Norcia AM	1993	<i>Vision Res</i>	3 cm above the inion, 1 cm above and 3 cm to the right of the inion (+ reference and ground)	5
Almoqbel FM, Yadav NK, Leat SJ, Head LM, Irving EL	2011	<i>Graefes Arch Clin Exp Ophthalmol</i>	Oz (placed either above the inion at 10% of the inion-nasion distance or 1.5 cm above the inion), O1, O2, PO7, PO8 (+ reference and ground)	7
Arai M, Katsumi O, Paranhos FR, Lopes De Faria JM, Hirose T	1997	<i>Graefes Arch Clin Exp Ophthalmol</i>	Oz, Pz (used as the reference) + ground	3
Bach M, Maurer JP, Wolf ME	2008	<i>Br J Ophthalmol</i>	Oz, LO and RO, respectively 15% (of the half-head circumference) left and right of Oz (+ reference at FPz)	4
Gottlob I, Fendick MG, Guo S, Zubcov AA, Odom JV, Reinecke RD	1990	<i>J Pediatr Ophthalmol Strabismus</i>	Oz, referenced 3 cm above Cz on the midline (channel 1), and right of Oz (channel 2), with ground electrode on Cz	4
Hou C, Good WV, Norcia AM	2007	<i>Invest Ophthalmol Vis Sci</i>	O1, O2, Oz (+ reference and ground electrodes at Cz and Pz)	5
Kelly JP, Borchert K, Teller DY	1997	<i>Vision Res</i>	Oz (+ reference electrode at Cz and ground electrode midway between Cz and Oz)	3
Kromer R, Serbecic N, Krastel H, Beutelspacher SC	2014	<i>Acta Ophthalmol</i>	Active electrode at the occiput (+ reference electrode on the forehead, ground electrode at the apex)	3
Lauritzen L, Jørgensen MH, Michaelsen KF	2004	<i>Pediatr Res</i>	O1, O2, Oz (each referenced to Oz) and O1, O2 (each referenced to Cz)	4
Mackay AM, Bradnam MS, Hamilton R, Elliot AT, Dutton GN	2008	<i>Invest Ophthalmol Vis Sci</i>	Oz-Fz, LO-Fz, RO-Fz (with ground at a mastoid)	5
Norcia AM, Tyler CW	1985	<i>Vision Res</i>	1 cm above the inion, 3 cm to the right at the same level	2
Norcia AM, Tyler CW	1985	<i>Electroencephalogr Clin Neurophysiol</i>	1 cm above the inion, 3 cm to the right at the same level	2
Norcia AM, Sato T, Shinn P, Mertus J	1986	<i>Electroencephalogr Clin Neurophysiol</i>	3 cm above the inion on the midline, 3 cm to the left of the inion	2
Norcia AM, Wesemann W, Manny RE	1999	<i>Vis Neurosci</i>	Oz vs. 3 cm laterally and Oz vs. 6 cm forward on the midline. In some recordings, Oz vs. 9 cm up and Oz vs. 6 cm lateral derivations.	3
Peterzell DH, Norcia AM	1997	<i>Vision Res</i>	6 cm above (near Cz) and 3 cm to the right of (near O2) a reference electrode placed 3 cm above the inion on the midline (near Oz)	3
Ridder WH III, McCulloch D, Herbert AM	1998	<i>Invest Ophthalmol Vis Sci</i>	2 cm above the inion on the midline (+ reference and ground electrodes on the earlobes)	3
Skoczinski AM, Norcia AM	1999	<i>Invest Ophthalmol Vis Sci</i>	O2, Pz (+ reference at Oz and ground 3 cm left of the reference)	4
Tyler CW, Apkarian P, Levi DM, Nakayama K	1979	<i>Invest Ophthalmol Vis Sci</i>	3 cm above the inion and 3 cm above and lateral; the ear served as ground	3

For review, see Refs. 7, 14–31.

a 1-second prelude, identical to the first step, at the beginning, and a 1-second postlude, identical to the last step, at the end of the sequence. Participants were instructed to maintain fixation throughout the experiment on a green circle of 0.1° visual angle overlaid on the center of the stimulus. For group E, there were two blocks of four trials for each type of sequence (2 × 16 trials in total), and for group AA, two blocks of three trials for the increasing spatial frequency sequence. Trials were separated from each other by 5 seconds of white noise during which the participant could take a short break.

Within each block, sequences measuring contrast sensitivity and visual acuity were presented in alternate order, as were the ascending or descending sweep directions. The sequence order was randomized for each participant. For example, for one participant, the first two sequences measured contrast

with increasing contrast and visual acuity with increasing spatial frequency, the next two sequences tested contrast with decreasing contrast and visual acuity with decreasing spatial frequency. For another participant, the first sequence tested visual acuity with decreasing spatial frequency, the next tested contrast with increasing contrast, and the final two sequences tested contrast sensitivity and visual acuity with opposite sweep directions. Sequences were repeated in the same order for the second block of the testing. Total testing time including breaks was less than 30 minutes.

EEG Acquisition

Recording took place in a darkened room. Scalp EEG was recorded at a sampling rate of 512 Hz with a 64-channel system

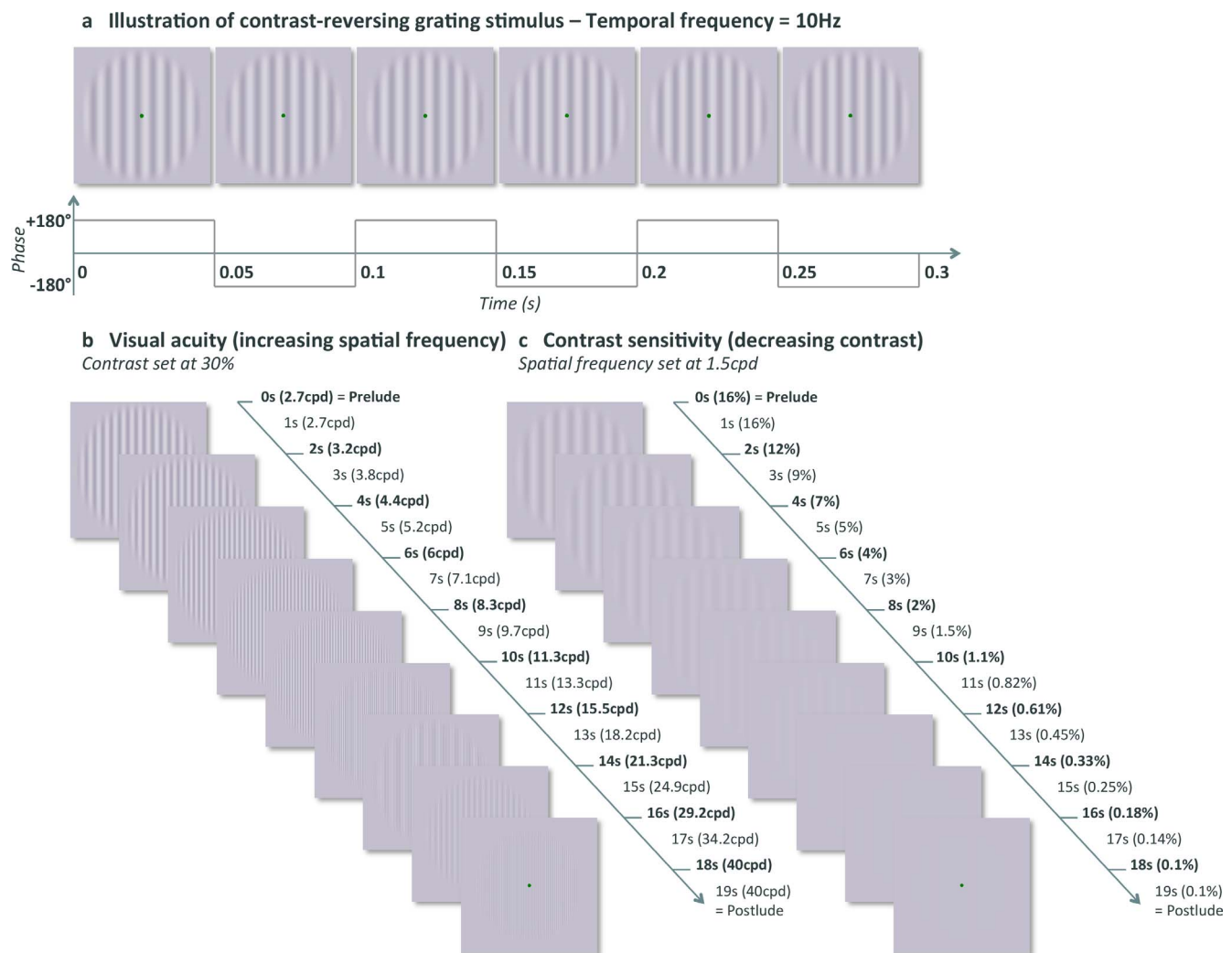


FIGURE 1. (A) Example of a contrast-reversing grating stimulus at the temporal frequency of 10 Hz. The image displayed at (0.05, 0.15, 0.25 seconds, etc.) is a spatial translation of the image presented at (0, 0.1, 0.2 seconds, etc.). To put it differently, the sinusoidal grating changed phase by 180° every 50 ms, corresponding to 20 changes per second. (B, C) Examples of two of the four 20-second sweep sequences used in this experiment. In each case, a vertical sinusoidal grating, contrast-reversing at 10 Hz, was shown through a circular aperture with blurred edges and a central fixation dot. (B) Visual acuity was measured with the contrast-reversing grating increasing in spatial frequency over 18 logarithmically spaced steps from 2.7 to 40 cpd for group E, and from 3.8 to 50 cpd for group AA, with contrast held constant at 30%. (C) Contrast sensitivity was measured with the grating contrast decreasing logarithmically over 18 steps from 16% to 0.1%, with spatial frequency held constant at 1.5 cpd.

(Biosemi Active 2; BioSemi B.V., Amsterdam, The Netherlands), with electrodes corresponding to the standard 10-20 system locations, and four additional electrodes (Fig. 2) placed over the occipitotemporal region (PO9, PO10, I1, I2). Eye movements were recorded via four facial electrodes placed at the left and right lateral canthi, and above and below the right eye. Facial electrodes were used to identify blinks and saccades, to determine when to start the stimulation (i.e., after the participant had stopped blinking), to control the quality of their fixation during stimulation, and to monitor participants' visual comfort during testing. Electrode offsets were kept below 50 mV and the experimenter manually initiated the stimulus and the recording after observing an artefact-free EEG signal for at least 10 seconds.

EEG Analysis

Preprocessing. The EEG data was band-pass filtered off-line between 0.1 and 100 Hz with a fourth order zero-phase

Butterworth filter and re-referenced to the average of the 68 scalp channels. For each participant and condition, the preprocessed EEG data was averaged across trials, and cropped into 1-second epochs corresponding to each step of the sweep sequence, excluding the prelude and postlude, without any correction for artefact. A discrete Fourier transform was applied to each epoch, resulting in a frequency resolution of 1 Hz. Baseline-corrected amplitudes were then computed by subtracting the mean amplitude of 12 surrounding frequency bins (i.e., six on each side), from the amplitude at each frequency bin, excluding the immediately adjacent frequency bin. The resulting EEG amplitude at the second harmonic of the contrast-reversal frequency (i.e., 20 Hz) was taken as an index of the sensitivity to the stimulus. The second harmonic was chosen because of the pattern reversal nature of the grating stimulus.⁴ In this stimulation mode, there is no global onset or offset mode, and each pattern alternation should lead to a response of the same amplitude in early visual pathways. This results in an EEG response with the same periodicity as

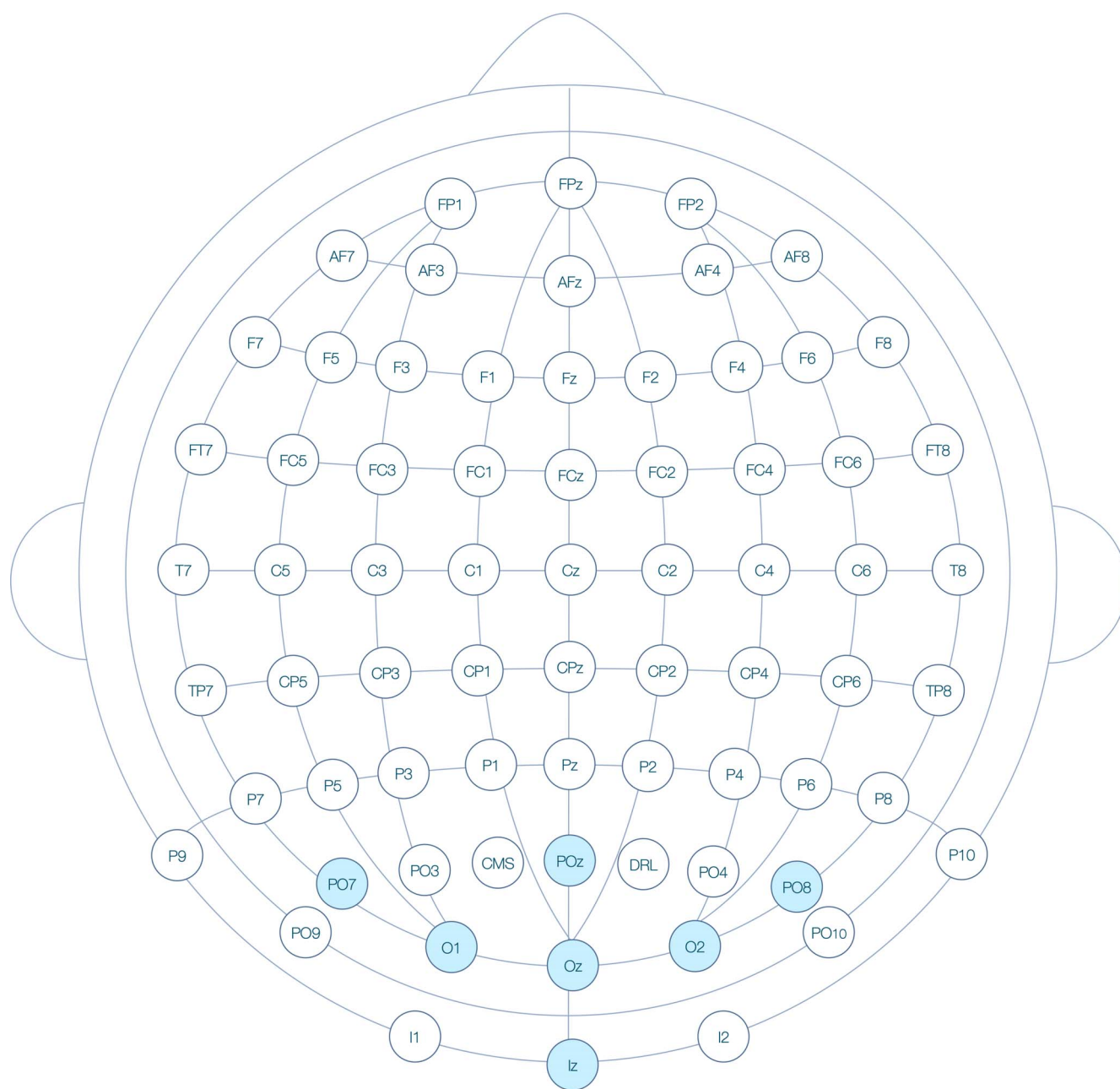


FIGURE 2. Location of scalp electrodes of the 64-channel Biosemi Active 2 system with four additional electrodes over the occipitotemporal region, PO9, PO10, I1, and I2. The electrodes that are recommended to assess low-level visual function in future recordings are shaded.

the number of reversals, at twice the frequency of the pattern reversal rate (2f), and an EEG spectrum containing only even harmonics (2f, 4f, 6f, etc.; Fig. 3A). In the remainder of the article, the term “amplitude” refers to baseline-corrected amplitude.

Most Sensitive Electrode Selection. To determine visual acuity and contrast sensitivity thresholds, we first selected the “most sensitive electrode” (MSE) for each participant and each condition. The MSE was defined as the electrode with the highest mean baseline-corrected amplitude over seven to nine steps of the sweep sequence. These steps were defined as the epochs either above or below the average thresholds found in previous comparable experiments.^{4,18,20,25,30,35} More precisely, for visual acuity, this corresponded to the nine steps with

spatial frequency from 2.7 to 9.7 cpd for group E, and to the seven steps from 3.8 to 9.4 cpd for group AA. For contrast sensitivity, this corresponded to the nine steps with contrast from 1.5% to 16%.

To illustrate, for participant 1, we defined the MSE for decreasing contrast sequences by first averaging the baseline-corrected amplitudes over contrasts between 1.5% and 16%, then selected the electrode with the highest average baseline-corrected amplitude. For participant 1, this electrode was O1 (top 4 electrodes: O1 = 0.63 μ V, PO7 = 0.55 μ V, PO3 = 0.45 μ V, Oz = 0.45 μ V).

Threshold and Correlation Estimation. Next, we estimated sensitivity by transforming the amplitude spectrum at the MSE at each epoch into Z-scores, taking into account the

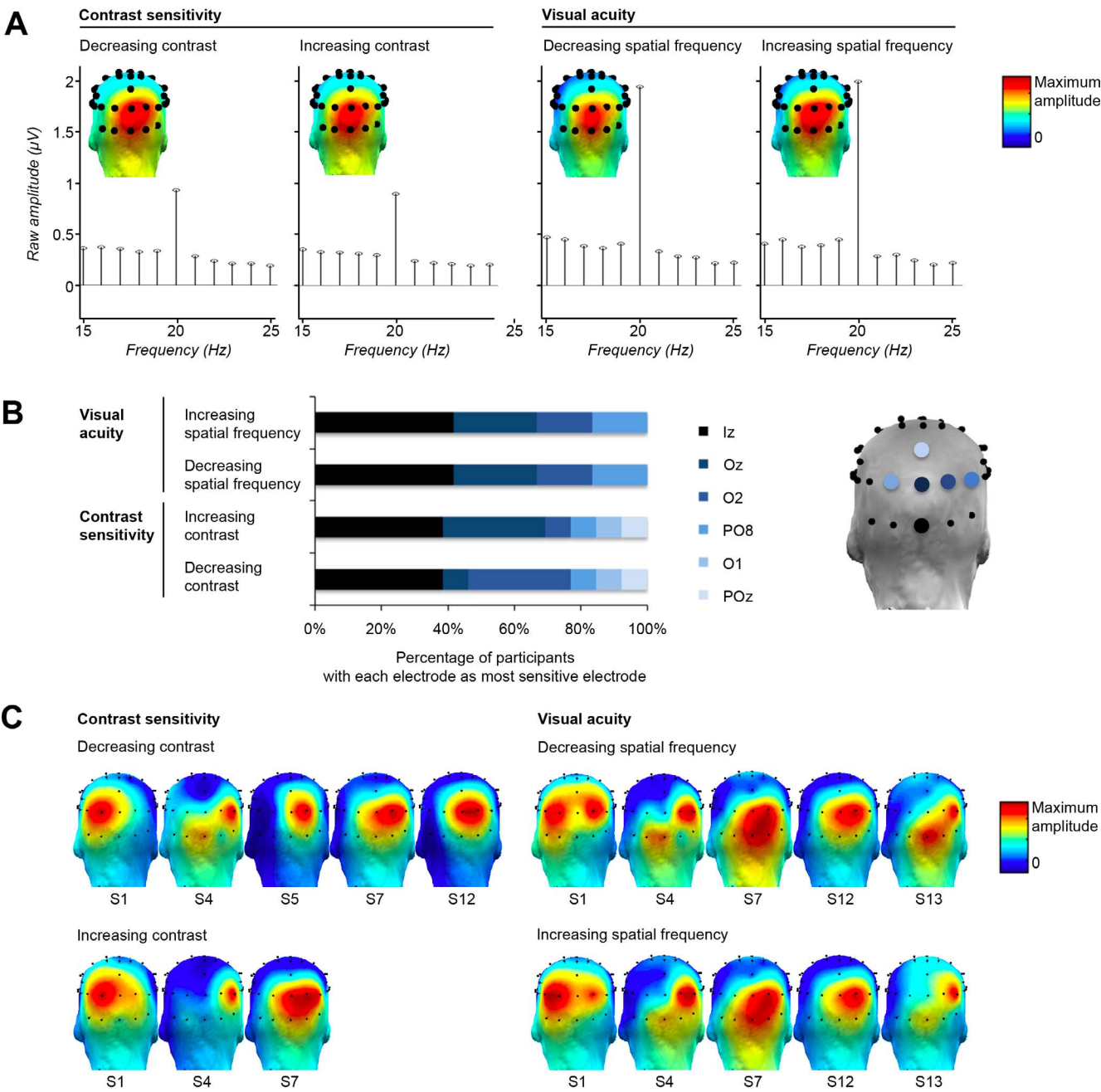


FIGURE 3. (A) Mean raw amplitude spectra of the four conditions across the nine supra-threshold steps at electrode Oz, presenting large and significant peaks at the second harmonic (20 Hz). The three-dimensional scalp topographies at the back of the head represent the group-average baseline-corrected amplitude at the second harmonic (20 Hz), averaged across the nine suprathreshold steps. The scalp topographies presented peaks around medial occipital channels Oz and Iz. (B) Location of the most common MSE for individual participants in each condition. The MSE is determined based on the average response across the nine suprathreshold steps. For contrast sensitivity, this corresponds to contrasts from 1.5% to 16%. For visual acuity, this corresponds to spatial frequencies from 2.7 to 9.7 cpd. (C) Atypical EEG topographies, for which the MSE is localized laterally (i.e., at O2, PO8, PO4, O1, PO7, PO3), mostly in the right occipital region (for S4, S5, S7, S12, S13) but also in the left occipital region (for S1). The scalp topographies represent the block-average baseline-corrected amplitude at the second harmonic (20 Hz) averaged across the 9 suprathreshold steps.

12 surrounding bins on either side of the frequency of interest according to:

$$\frac{(\text{amplitude at the frequency of interest} - \text{average amplitude of surrounding bins})}{\text{standard deviation of surrounding bins}}$$

For participants without artificially altered acuity, the threshold

was defined as the epoch preceding the first or last epoch with a significant response at 20 Hz, with the condition that the four adjacent epochs corresponding to suprathreshold values contained at least three significant responses. For instance, in a sequence with decreasing contrast, the contrast sensitivity threshold is set at the last step associated with a significant response and having a significant response among at least three of the four preceding steps. Thus, if the response significance

of the first 10 steps are as follows: 1, 0, 0, 1, 1, 1, 0, 0, 0, 0, with 1 meaning significant and 0 nonsignificant, the seventh step will be defined as the threshold. If the significance pattern is 1, 1, 1, 1, 0, 1, 1, 0, 0, the threshold will be set at the ninth step. The Z-score thresholds were set at 3.1 (significance level of 0.001) at the block-average level, at $Z > 2.33$ (significance level of 0.01) at the single-block level, and at $Z > 1.64$ (significance level of 0.05) at the individual trial level. A one-tailed hypothesis was considered in the three cases.

For participants with artificially altered visual acuity, the threshold selection condition was softened to three adjacent epochs corresponding to suprathreshold values containing at least two significant responses. In addition, the Z-score threshold was set at $Z > 1.64$ with a one-tailed hypothesis at the block-average level.

Finally, to evaluate the correlation between blocks, we first computed, for each epoch of the sequences assessing acuity, the average between participants of the EEG amplitude at each participant's MSE in block 1. Next, we applied the same computation in block 2 and evaluated the correlation between the averages at each epoch in blocks 1 and 2. Lastly, we took the average between this correlation for the sequences with increasing and with decreasing spatial frequency. The computation was identical for the sequences measuring sensitivity to contrast.

EEG Interpretation

We initially analyzed the EEG data of the 13 participants without artificially altered visual acuity. Unless otherwise specified, we refer to these participants in the results below.

We first evaluated the scalp topography of these participants' EEG response at the group-average, which is the average across stimulation blocks and individual participants; and block average levels, which is the average across stimulation blocks for each participant. A response associated with the highest SNR located outside of electrode Oz would demonstrate the relevance of using an extended electrode array. Next, we analyzed the evolution of scalp topographies throughout stimulation sequences, with increasing/decreasing contrast or spatial frequency. If the most sensitive EEG response was located at Oz at threshold but outside of this electrode at suprathreshold values or vice versa, this would also be of interest since the visual function is characterized by an analysis of the EEG signal at both thresholds (e.g., to determine visual acuity and contrast sensitivity) and suprathreshold values (e.g., to contribute to the diagnosis of ophthalmologic pathologies like amblyopia). With the purpose to efficiently use sVEP in a time-constrained clinical setting, we then tested whether a smaller number of trials, for instance, a single block for each condition, would provide a reliable assessment of visual function. To that end, we first evaluated the correlation between blocks, encompassing suprathreshold and threshold values; computed the visual acuity and contrast thresholds at the block-average, single-block and individual trial levels; and determined if these thresholds were consistent. Finally, we assessed whether the sVEP thresholds of participants with and without artificially altered visual acuity were related to their behavioral thresholds.

RESULTS

Response Overview

At the group-average level, the most sensitive response was recorded centrally in the medial occipital region, near Iz and Oz (Fig. 3A). This was also true for most individual participants

(i.e., 50%–70% according to the condition tested), with the most sensitive response being most frequently recorded within this region (Fig. 3B). However, for nearly half of the participants (6/13), the most sensitive response was localized over lateral occipital channels, mostly in the right hemisphere (O2, PO8, PO4), but also in the left hemisphere (O1, PO7, PO3; Fig. 3C). Hence, in order to properly assess visual function for each individual, taking into account individual scalp topographies with an extended electrode array appears important. Figure 4 compares the average EEG response across participants with typical and atypical topographies at their most sensitive electrode with their average response at electrode Oz. Overall, threshold assessment was more reliable on the MSE compared to Oz: while thresholds could be defined at the MSE for all 13 participants of group E at the block-average and single-block levels, this was not the case for Oz (Table 2).

Moreover, for the four conditions, different thresholds were obtained with the two approaches: lower threshold for contrast sensitivity and higher for visual acuity with the MSE approach. Taking the average between increasing and decreasing stimuli and between participants, contrast sensitivity thresholds were 2.7% and 3.4% ($\Delta = 0.7\%$), respectively, for the MSE and for Oz, and visual acuity thresholds were 23 cpd and 21.6 cpd ($\Delta = 1.4$ cpd). Considering the thresholds determined individually, there was a statistically significant difference between thresholds defined at the MSE and thresholds defined at Oz, both for visual acuity ($P = 0.02$) and contrast sensitivity ($P = 0.004$). The difference in thresholds was even greater for participants with atypical topographies. Their contrast sensitivity thresholds were 2.4% and 4.2% ($\Delta = 1.8\%$), respectively, for the MSE and for Oz, and visual acuity thresholds were 20.5 cpd and 17.4 cpd ($\Delta = 3.1$ cpd).

Response Evolution Across Steps

Next, we studied the evolution of EEG topographies with increasing/decreasing contrast and spatial frequency (Fig. 5A). While in the sequences measuring sensitivity to contrast, the most sensitive EEG response was in the medial occipital region throughout the sequences, there was a right lateralization of the response with lower spatial frequencies in the visual acuity conditions. To further examine this shift in response topography, we determined the number of participants whose most sensitive responses were located over left, medial, or right occipital regions across the nine suprathreshold steps of the visual acuity sequences (Fig. 5B). The most sensitive EEG signal was mostly located at O2, PO8, and PO4 at lower spatial frequencies (2.7, 3.2, and 3.8 cpd). At higher spatial frequencies, the most sensitive EEG amplitude was mostly measured at Iz, Oz, and POz. Importantly, this right lateralization at low spatial frequencies is observed for both participants with typical and atypical scalp topographies (Fig. 5C), indicating the consistency of this pattern across observers. Overall, analysis of the suprathreshold responses demonstrates the interest of using an extended electrode array.

sVEP Use in Practice

We finally turn to implementing sVEP to assess visual function in the time-constrained clinical context. In order to determine whether a smaller number of trials than used here would provide a reliable visual function assessment, we first visually assessed the consistency of the overall EEG response, at threshold and supra-threshold values, between blocks 1 and 2. The traces obtained for blocks 1 and 2 were virtually identical (Fig. 6A), and Z-scores for blocks 1 and 2 were also very close

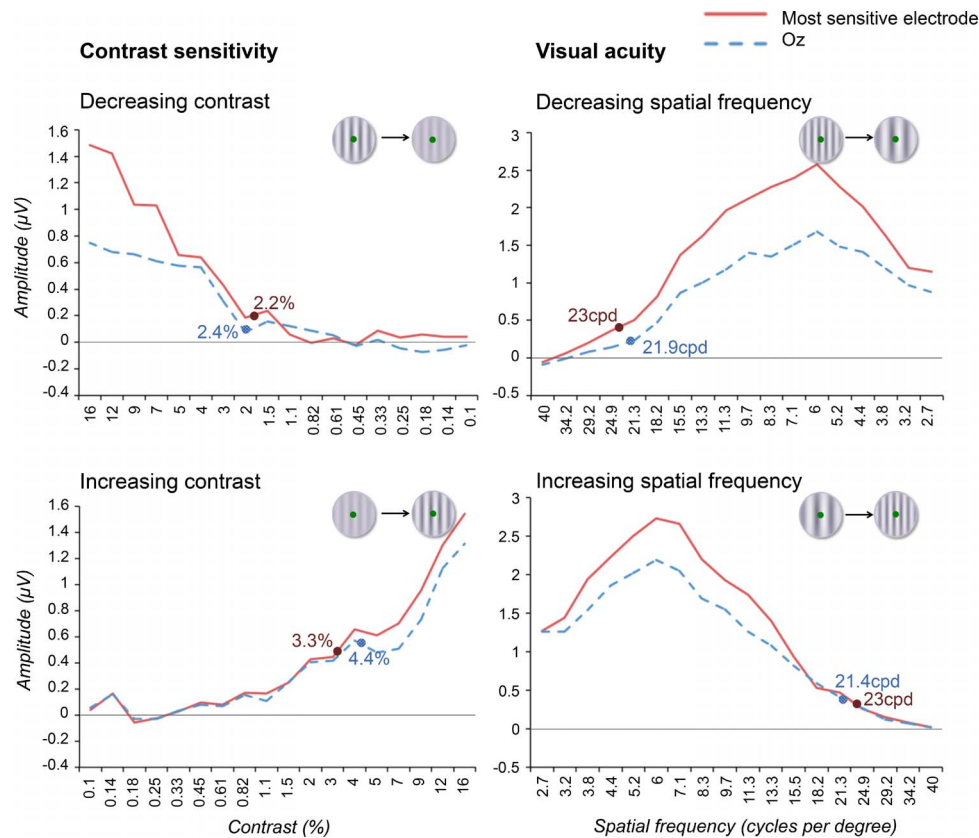


FIGURE 4. For the four conditions, group-average (i.e., average across blocks and across all participants with typical and atypical topographies), baseline-corrected EEG amplitude at the second harmonic (20 Hz) for the MSE and for Oz and group-average thresholds computed based on the amplitude spectrum at the MSE and at Oz.

(Fig. 6B). For the stimulation sequences measuring acuity, the correlation between blocks 1 and 2 was 0.99, with a 95% confidence interval of [0.97, 1] for sequences with both increasing and decreasing spatial frequency. For the sequences assessing sensitivity to contrast, it was 0.97, with a 95% confidence interval of [0.93, 0.99] for the sequences with decreasing contrast, and [0.91, 0.99] for the sequences with increasing contrast. These high correlations suggest that a

reliable assessment of threshold and supra-threshold values could be obtained with a single block for each condition.

We then focused on the consistency between blocks at threshold values. To that end, we first computed the contrast sensitivity and visual acuity thresholds at the block-average and single-block levels (Fig. 7A). In line with the average thresholds found in previous comparable experiments^{4,8} we found contrast thresholds of 1% to 9% and acuity thresholds of ~10 to 40 cpd. Since we were interested in assessing the consistency of thresholds between blocks, we then evaluated the mode of the thresholds at the block-average, single-block and individual trial levels (Fig. 7B). Thresholds assessed for block 1 were visually consistent with thresholds determined for block 2, and with thresholds determined for the average of both blocks. This consistency between blocks would allow to halve testing time, leading to a reliable and objective assessment of visual function in less than 15 minutes, making it highly useful in clinical contexts.

Finally, we assessed the correlation between behavioral and sVEP thresholds for participants both with and without artificially altered visual acuity. In the “emmetropic” group, there was no correlation between the sVEP and behavioral measures. This outcome was predictable: although the participants have reported to be emmetropic since their last visit to the ophthalmologist, we measured small differences of behavioral acuities, which may result from their motivation or tiredness. Such factors may vary during an experiment, and differently affect sVEP and behavioral acuities.

What is more important is to show that the sVEP measures relate directly to more drastic (e.g., pathologic) loss of visual acuity reported behaviorally. To this end, we included 12 extra

TABLE 2. Number of Participants

	Contrast Sensitivity		Visual Acuity	
	Decreasing Contrast	Increasing Contrast	Decreasing Spatial Frequency	Increasing Spatial Frequency
Blocks 1 and 2	12	13	13	13
Block 1	13	13	12	13
Block 2	11	12	12	13
Trial 1	10	11	12	12
Trial 2	9	8	12	12
Trial 3	11	10	11	11
Trial 4	8	9	12	10
Trial 5	10	8	12	11
Trial 6	10	10	11	12
Trial 7	8	9	10	12
Trial 8	9	9	12	12

Out of the 13 participants of group E, for which a threshold could be defined based on the Z-score criteria applied to the amplitude spectrum at electrode Oz (see “Methods”).

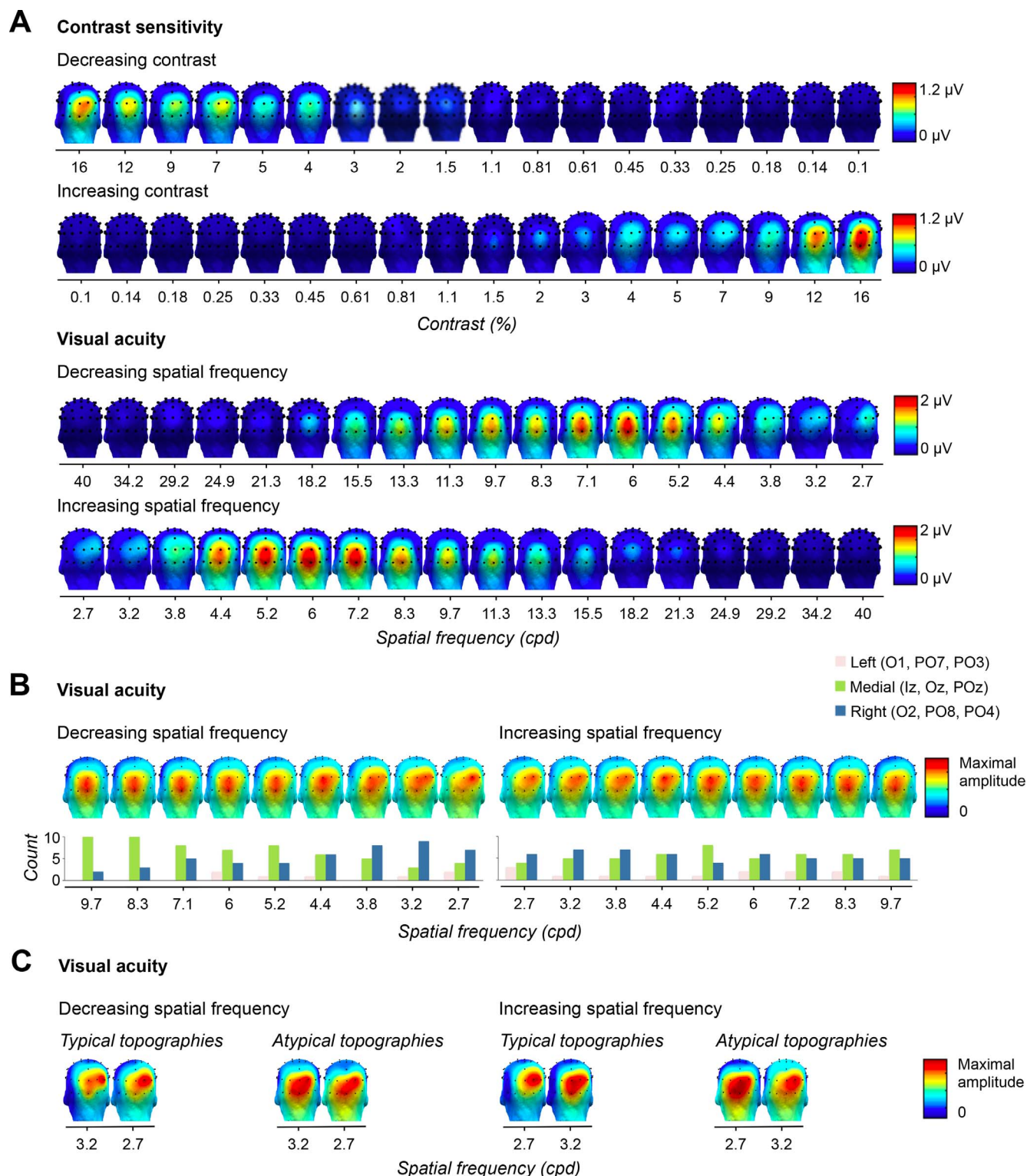


FIGURE 5. (A) Evolution of the EEG visual response as a function of contrast and spatial frequency. Note that here the scalp topographies represent the group-average baseline-corrected amplitudes at the second harmonic (20 Hz) and for each sweep step. (B) For the visual acuity conditions, scalp topographies of the group-average baseline-corrected EEG amplitude at the second harmonic (20 Hz) for each of the nine suprathreshold steps, and count of participants for whom MSE is in the left, medial, or right occipital regions. The scalp topographies of the visual acuity sequences presented peaks in the right occipital regions at low spatial frequencies (2.7, 3.2, and 3.8 cpd). (C) Topographies of the visual acuity sequences, with peaks in the right occipital regions at low spatial frequencies for typical and atypical topographies.

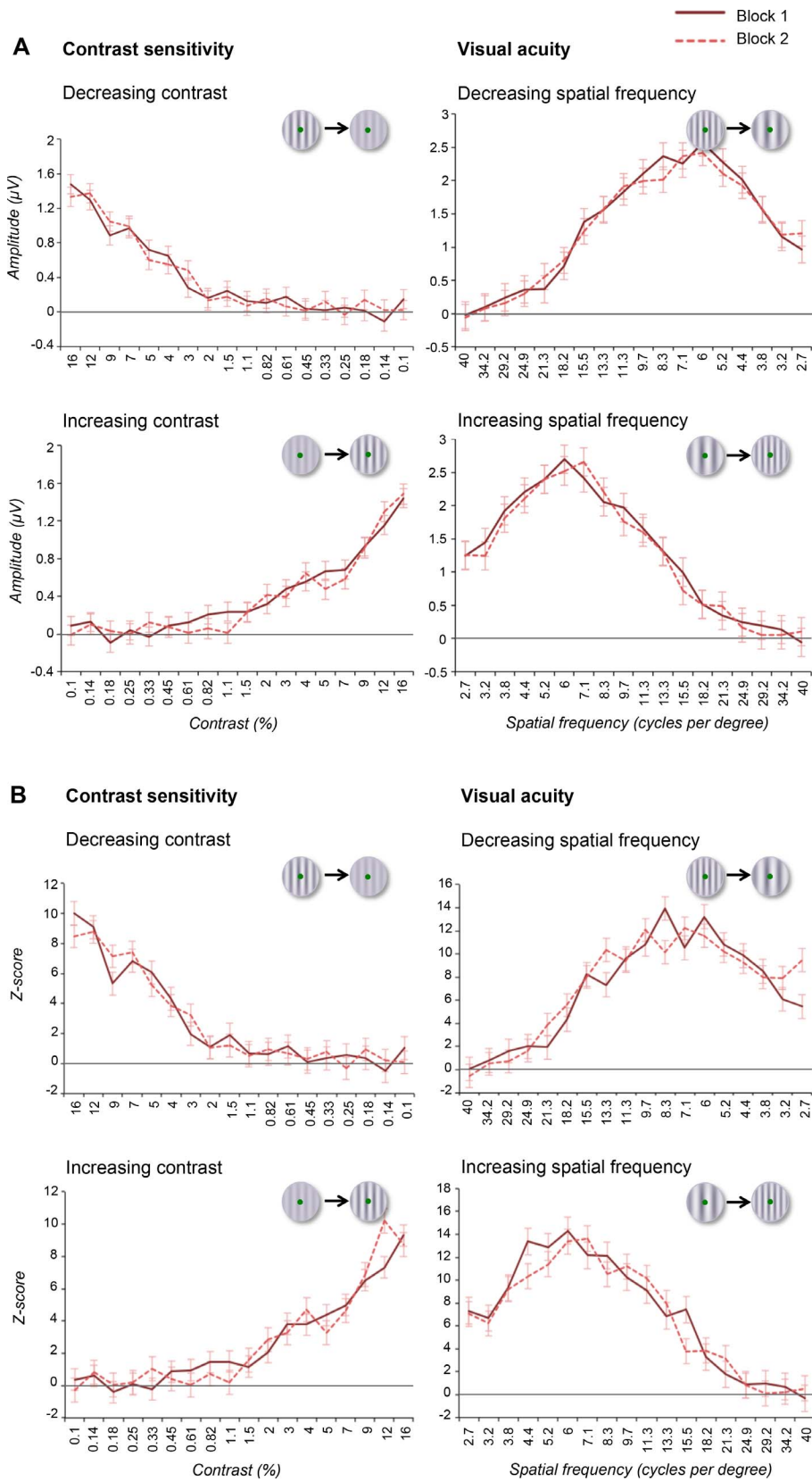


FIGURE 6. (A) For the four conditions, single-block baseline-corrected EEG amplitude, and (B) single-block Z-score at the second harmonic (20 Hz) for the MSE. Error bars represent the standard errors of these averages.

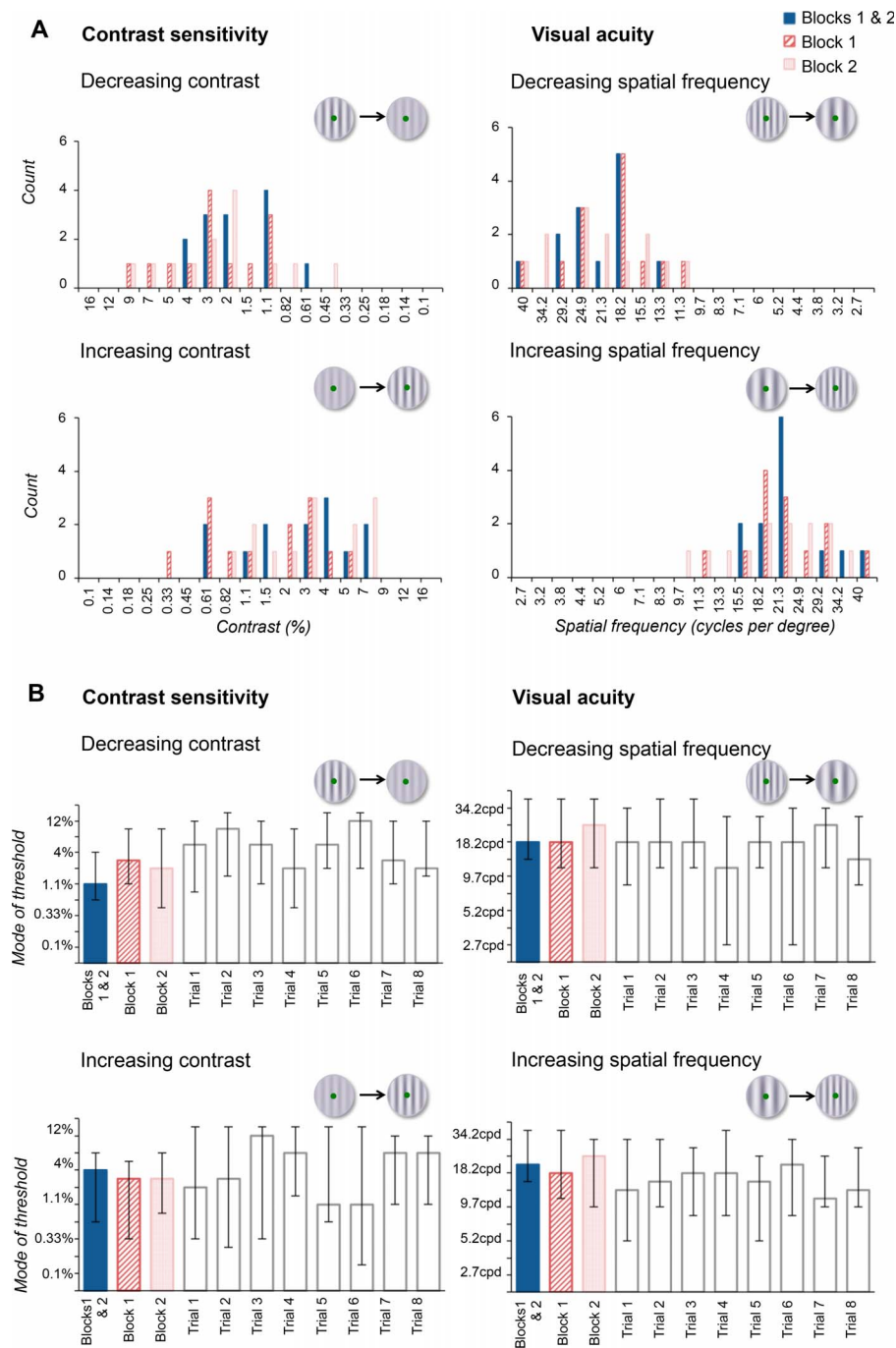


FIGURE 7. (A) Distribution of contrast sensitivity and visual acuity thresholds determined based on the Z-score criteria for the block-average and single-block levels. (B) Mode and minimum/maximum, represented by error bars, of contrast sensitivity and visual acuity thresholds for the block-average, single-block, and individual trial levels. These thresholds were all determined based on the Z-score criteria.

participants with artificially altered visual acuity, using converging lenses of various powers. Figure 8 below shows the relationship between the neural and behavioral measures when these data points are included ($r = 0.93$). Note that this correlation drops significantly when using Oz only ($r = 0.72$; $P = 0.03$). Additionally, in line with the main findings of our paper, thresholds were better defined on each participant's individual MSE compared to Oz: while thresholds could be determined for all participants at the MSE, they could be determined on Oz for 12/13 participants of group E and only for 6/12 of participants of group AA.

This not only underlines the importance of selecting electrodes individually for the evaluation of visual function with sVEP, but it also confirms the usefulness of this technique to diagnose ophthalmologic pathologies like amblyopia in nonverbal or preverbal participants.

DISCUSSION

In this study, we aimed to evaluate the clinical contribution of a more comprehensive electrode array to the assessment of visual function. To do so, we measured contrast sensitivity and

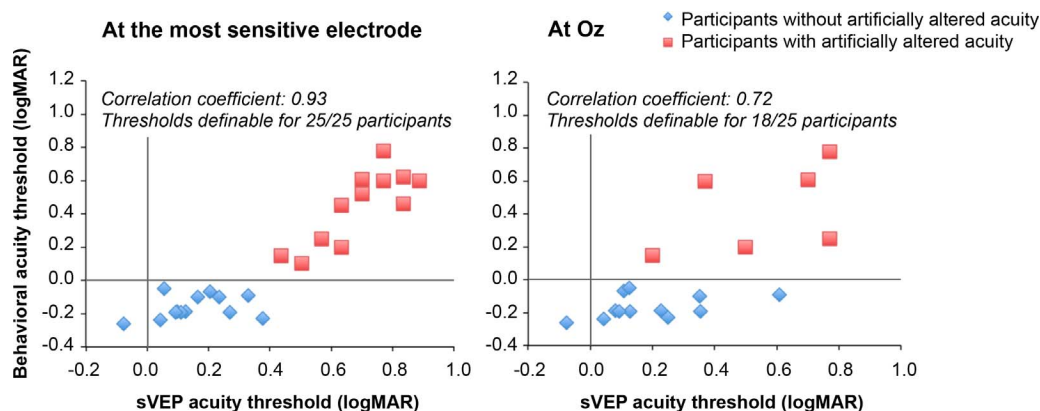


FIGURE 8. Correlations between behavioral and sVEP acuity thresholds, measured at the most sensitive electrode (*left graph*) and at Oz (*right graph*), for the 13 participants and 12 participants, respectively, without and with artificially altered visual acuity using converging lenses.

visual acuity with 64 electrodes plus 4 additional electrodes over the occipitotemporal region. Our data demonstrate the importance of sampling from a larger number of scalp electrodes for the evaluation of visual function. More specifically, we showed that, while the signal of maximal amplitude is often recorded at the medial occipital region (Iz, Oz, POz) for a majority of participants, it is lateralized for nearly half (approx. 46%) of the participants. As a result, not only could thresholds be determined for more participants with their individual MSE relative to Oz, but the threshold values were also different: lower for contrast sensitivity and higher for visual acuity. Moreover, measuring a greater suprathreshold amplitude may help diagnose amblyopia, as suprathreshold amplitudes are differently impacted by a neutral density filter with a grating stimuli, depending on whether the participant has normal or amblyopic eyes.³²

Our testing of visual acuity has shown a lateralization over the right occipital region for low spatial frequencies. This is in line with findings by Merigan and Maunsell³⁶ that in the macaque monkey brain these spatial frequencies follow a specific pathway posterior to the thalamus: they are quickly processed in the magnocellular pathway. Moreover, it has been hypothesized that the magnocellular layer may predominantly project to the right hemisphere.³⁷ In humans, the perception of high spatial frequency (HSF) sinusoidal gratings activates the foveal representation in all retinotopic areas of the occipital cortex, while LSF sinusoidal gratings activate more peripheral representations in the same cortical areas,^{38,39} which could explain the pattern of lateralization found here: a mostly medial topography for HSF versus lateral for LSF. Moreover, even at the level of visual retinotopic areas, the right hemisphere appears to be preferentially specialized in the processing of LSF information and the left hemisphere preferentially specialized in HSF information processing^{40–42} (see Ref. 43 for review). In particular, Peyrin et al.⁴⁴ showed that, in the case of brief exposure duration, as in the sVEP used here, low and high spatial frequencies are predominantly processed by the right and left hemispheres, respectively. However, we acknowledge the potential interaction between the perception of temporal and spatial frequencies. At relatively high temporal frequencies, such as 10 cycles per second in this experiment, higher spatial frequencies are less well perceived.⁴⁵ Hence, we cannot exclude that using a lower reversal rate would shift the acuity thresholds higher, though the signal-to-noise ratio might be reduced due to the smaller number of stimulations per second. Although further study is necessary to clarify this issue, our observation highlights the

interest of using an extended electrode array to examine such suprathreshold response dynamics that would otherwise have been missed with the common sparse electrode positions. It would be desirable in the future to vary spatial frequency in the contrast sensitivity testing to assess the correlation between the sensitivity of measures and spatial frequency and to better understand the lateralization dynamics.

In line with Norcia et al.,⁴ we have shown that the sweep VEP is an efficient method to assess visual acuity and contrast sensitivity. A reliable evaluation of these two ophthalmologic parameters can be obtained within an equivalent or even shorter testing time than for the typical psychophysical procedures such as naming of Snellen letters. More specifically, we show that stable thresholds could be obtained with as little as four 20-second trials for each visual parameter. This then allows for a consistent and sensitive measurement of visual acuity and contrast sensitivity that can be completed in a testing time, excluding setup and placement of electrodes, of less than 15 minutes.

In practical terms, the electrodes we recommend to use, in order to precisely determine each patient's individual most sensitive electrode, are Iz, Oz, POz, O1, PO7, O2 and PO8 (Fig. 2). This includes an electrode lower than Oz, Iz, which is never included in the studies published before, as listed in Table 1, as well as POz, also never included. Electrodes PO8 and PO7 were recorded only in one of these studies.

Using active electrodes, for instance with the Biosemi system, the setup and placement of seven electrodes can realistically be achieved in about 5 minutes, since it is not needed to prepare the skin. The total duration of testing, including installing electrodes and visual stimulation, could be reduced to approximately 20 minutes. Future studies would need to validate this technique's efficiency and evaluate its appreciation by different patient populations.

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