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RESEARCH ARTICLE

Isolating early cortical generators of visual-evoked activity: a systems identification approach

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Abstract The VESPA (visual-evoked spread spectrum analysis) method estimates the impulse response of the visual system using a continuously varying stimulus. It has been used recently to address both basic cognitive and neurophysiologic questions as well as those surrounding clinical populations. Although the components of the average VESPA response are highly reminiscent of the early components of the visual-evoked potential (VEP) when measured over midline occipital locations, the two responses are acquired in different ways and, thus, they cannot be regarded as being equivalent. To further characterize the relationship between the VESPA and the VEP and the generative mechanisms underlying them, we recorded EEG from 31 subjects in response to checkerboard-based VEP and VESPA stimuli. We found that, across subjects, the amplitudes of the VEP C1 component and the VESPA C1 component were highly correlated, whereas the VEP P1 and the VESPA P1 bore no statistical relationship. Furthermore, we found that C1 and P1 amplitudes were significantly correlated in the VESPA but not in the VEP. We believe these findings point to the presence of common generators underlying the VESPA C1 and the VEP C1. We argue further that the VESPA P1, in light of its strong relationship to the VESPA C1, likely reflects further activation of the same cortical generators. Given the lack of correlation between the VEP P1 and each of these three other components, it is likely that the underlying generators of this particular component are more varied and widespread, as suggested previously. We discuss the implications of these relationships for basic and clinical research using the VESPA and for the assessment of additive-evoked versus phase-reset contributions to the VEP.

Keywords EEG · Visual-evoked potential · VESPA · C1

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Introduction

The event-related potential (ERP) technique is a widely used and extremely valuable tool in both research and clinical settings for the evaluation of sensory and perceptual processing (Handy 2004). The effects of cognition and

mental disorders on specific components of the ERP have added much to our understanding of the human brain both healthy and otherwise. The VESPA (visual-evoked spread spectrum analysis), a generalization of the standard ERP technique, has been used over the last few years by our group to address basic cognitive and neurophysiologic questions (Frey et al. 2010; Lalor et al. 2007, 2009), as well as issues surrounding pathologic dysfunction in clinical populations (Lalor et al. 2008, in press). Unlike the classic transient visual-evoked potential (VEP) which is usually obtained using discrete stimuli, the VESPA is an estimate of the visual system's impulse response and is obtained by continuously modulating a specific feature of a stimulus in accord with a pre-computed signal. In the majority of studies, the contrast of a visual stimulus such as a checkerboard has been modulated by a stochastic Gaussian signal, and a linear estimate of the impulse response has been derived. The resultant VESPA response obtained at midline occipital sites presents positive and negative deflections at latencies in close correspondence with the early components of the standard pattern-reversal VEP when averaged across subjects (Lalor et al. 2006).

However, despite this temporal correspondence, the spatial profile of the VESPA response is distinct from that of the average VEP. The VESPA response to centrally presented stimuli initially develops over midline occipital scalp similar to the early component (C1; 60–80 ms) of the transient VEP, but the subsequent lateral spread of activation found in the VEP after $\sim$100 ms is absent in the VESPA. The circumscribed midline scalp distribution of the contrast modulated VESPA has led to the suggestion that it is particularly sensitive to neural populations in early visual cortices (Lalor and Foxe 2009). Additional support for this suggestion comes from the fact that the typical VESPA analysis explicitly assumes a linear relationship between the particular feature being modulated and the activity of the brain. The outcome of this assumption is likely to be a measurement that largely targets neuronal ensembles that respond to the modulation of a stimulus along a chosen parameter (e.g., luminance contrast, as in the present study). No such explicit assumption is made when obtaining a VEP using time-locked averaging and, as such, the VEP may incorporate information from a more diverse neuronal population.

Under the assumptions of the contrast VESPA, an ideal neuronal ensemble would be one in which the contrast response function is monotonic and has an extended dynamic range. There is strong evidence in macaques (e.g., Sclar et al. 1990; Rolls and Baylis 1986; Cheng et al. 1994; Lu and Roe 2007) and humans (e.g., Avidan et al. 2002; Tootell et al. 1995, 1998; Bartels et al. 2008) that as one progresses up the visual hierarchy, cells possess ever more contrast-invariant responses to suprathreshold contrasts. Indeed, parametric variations of luminance and contrast are most faithfully represented by primary visual cortex (Goodyear and Menon 1998; Whittingstall et al. 2010).

Given the differing assumptions made when determining the VESPA and VEP, a better understanding of the generation of the VESPA response is integral to the continued employment of this technique in basic and clinical research. One potentially fruitful route to that end is through comparison with its widely used and long studied counterpart, the VEP. Given that, on average, the VESPA matches the VEP both spatially and temporally during the first component but thereafter diverges from the VEP in terms of the stability of its distribution over time, we set out to further compare the early components of the VEP and VESPA across individuals. Intra-individual correspondence between VEP and VESPA components is interpreted here as an indication of overlapping generators among the responses, whereas divergence between these two responses are interpreted as indicative of differences in their underlying generators. In contrast to the VEP, our findings support the localization of the VESPA response, across its full temporal extent, to early visual cortices. Furthermore, based on correspondence between the two responses, we discuss the implications of these findings for current models of ERP generation with regard to the relative contributions of phase reset of ongoing oscillations and superposition of additive-evoked activity (Makeig et al. 2002; Shah et al. 2004; Sauseng et al. 2007).

Materials and methods

Subjects

In order to maximize the statistical power of the analysis presented here, we elected to utilize data collected from three studies conducted at different locations, herein referred to as data sets **A**, **B**, and **C**. Data set **A** was collected at Trinity College Dublin, Ireland; **B** at St. Vincent's Hospital, Dublin; and **C** at Albert Einstein College of Medicine, Bronx. Each study employed an essentially identical stimulus setup. Data set **A** was obtained from 9 male subjects aged 21–23 years. Data set **B** was obtained from 11 subjects (8 male) aged between 21 and 41 years. Lastly, data set **C** was obtained from 11 subjects (9 male) aged between 20 and 47 years. This resulted in an overall data set of 31 subjects (26 male) aged between 20 and 47 years. All subjects reported normal or corrected-to-normal vision. All subjects provided written-informed consent once the goals of the experiment were explained to them. All procedures were approved by the Ethics Committees of Trinity College Dublin and St. Vincent's Hospital, and the Institutional Review Board of the Albert

Einstein College of Medicine. Subjects were paid a modest fee for their participation. Results from data set **B** have been published previously (Lalor et al. 2006).

Stimuli and experimental procedure

For all experimental runs, the stimulus consisted of a checkerboard pattern with equal numbers of light and dark checks. Each check subtended a visual angle of 0.65°–0.75° both horizontally and vertically, while the checkerboard as a whole subtended visual angles of 5.25°–6.05° vertically and horizontally. The variation in visual angle was due to slightly different viewing distances in the different recording locations. In all experimental runs, the checkerboard was presented in the center of a monitor with a gray or black background.

Two experimental conditions were undertaken by each subject. The first was a standard pattern-reversal VEP paradigm wherein the phase of the checkerboard pattern was reversed with an inter-stimulus interval (ISI) of 1,000 ms (data sets A and B) or 750–1,250 ms (C). These pattern-reversal stimuli were presented in blocks of 120, and subjects undertook between two and five of such blocks. The checkerboard used to elicit the VEP had a contrast of 100 % in terms of the range of the monitor.

For the continuous VESPA stimulus, the refresh rate of the monitor was set to 60 Hz and on every refresh, the contrast of the checkerboard pattern was temporally modulated by a stochastic signal with a constant mean luminance. The stochastic stimulus contrast signals used had their power distributed uniformly between 0 and 30 Hz (see Lalor et al. 2006 for details). For each VESPA block, the stimulus was presented continuously for 120 s and each subject completed between two and five of such blocks.

Data recording and preprocessing

EEG data were recorded from 128, 64 and 168 electrode positions for data sets **A**, **B** and **C,** respectively. For all data sets, the EEG was filtered over the range 0–134 Hz and digitized at a rate of 512 Hz using the BioSemi Active Two system. Subsequently, the EEG was digitally filtered with a high-pass filter with passband above 2 Hz and −60 dB response at 1 Hz and a low-pass filter with 0–35 Hz passband and −50 dB response at 45 Hz. Because of the differing numbers of electrodes recorded at each location, we conducted our analyses on two measures of the EEG data. The first involved using the global field power (GFP), which is a single, reference-independent measure of response strength over the entire scalp (Lehmann and Skrandies 1980). The second, which was based on the fact that the VEP and the VESPA are primarily located over occipital cortex (Lalor et al. 2006), involved analyzing data from the standard midline occipital electrode location Oz re-referenced to the frontal midline electrode location Fz, as defined by the 10–20 system. Data from these two electrode locations were available in all three data sets.

Analysis

VEPs were obtained by performing signal averaging time-locked to the phase reversals of the checkerboard stimulus using a 500 ms window of data beginning 100 ms pre-stimulus. Epochs containing filtered EEG that exceeded ± 100 μV were not included in the averaging procedure.

VESPAs were obtained by assuming that the EEG response to the continuous VESPA stimulus consisted of a convolution of the stochastic control signal with an unknown impulse response (plus noise). Given the known stochastic stimulus signal and the measured EEG, the impulse response, that is, the VESPA, was estimated using the method of linear least squares (see Lalor et al. 2006, 2009 for details). The VESPA was estimated using a sliding window of 500 ms of data starting 100 ms pre-stimulus. No artifact rejection or correction was carried out in the VESPA analysis.

Results

Figure 1 illustrates the VEP and the VESPA at electrode location Oz (re-referenced to Fz) averaged over all 31 subjects. Given the apparent visual correspondence, we elected to compare the C1 (first negativity around 75 ms) and P1 (positivity around 100 ms; also known as the P100) components of the VEP and VESPA across subjects. We defined the C1 measure as the mean amplitude in the interval 66–88 ms, which we determined as an appropriate window for the analysis based on the grand average. Similarly, we defined the P1 measure as the mean amplitude in the interval 90–123 ms.

There was a strong dependence between the C1 component amplitudes for the VEP and the VESPA across subjects as determined by Pearson's correlation, both for the amplitude at Oz ($r = 0.528$, $p = 0.002$; Fig. 2a) and for the GFP ($r = 0.497$, $p = 0.005$). To ensure that this was not driven by outliers, we also conducted a non-parametric Spearman correlation on the data from Oz, which again demonstrated a significant relationship ($r = 0.378$, $p = 0.037$). In contrast, no relationship was found between the P1 amplitude of the VEP and that of the VESPA for either the analysis based on amplitude at Oz (Pearson's $r = 0.029$, $p = 0.875$; Spearman's $r = -0.077$, $p = 0.678$; Fig. 2b) or the GFP (Pearson's $r = 0.196$, $p = 0.291$).

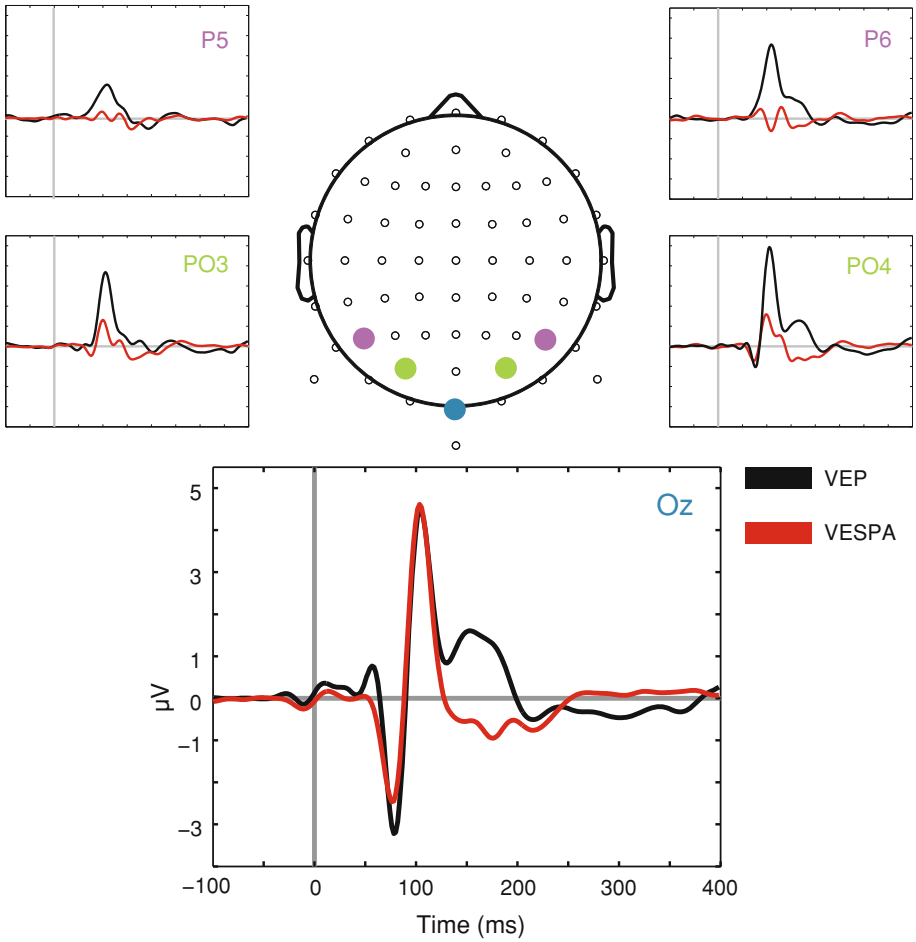

Fig. 1 Grand average ($N = 31$) VEP (*black line*) and VESPA (*red line*) waveforms at five electrode locations: Oz, PO4, PO3, P6, and P5

While every effort was made to ensure that the stimulus presentations in each laboratory were as similar as possible, we wished to confirm that the correlation we observed in the C1 at electrode Oz did not result from unaccounted for, systematic differences between data sets. To that end, we conducted an ANCOVA to test whether VEP C1 amplitude could be significantly predicted by VESPA C1 amplitude while accounting for any variance arising from data set. This test confirmed the VEP-VESPA C1 relationship ($F(1,25) = 10.85$, $p = 0.003$), and no main effect of data set ($F < 1$).

In order to investigate the relationship between components *within* methods, we computed correlations between the C1 and P1 components for both the VEP and VESPA responses (Fig. 3). The amplitude of the VEP C1 bores no relationship to the amplitude of the VEP P1 (Pearson's $r = 0.001$; $p = 0.994$), whereas the VESPA C1 and the VESPA P1 were strongly correlated (Pearson's $r = -0.757$; $p < 10^{-6}$). This latter relationship further suggested a correlation between the VEP C1 and the VESPA P1, which we confirmed (Pearson's $r = -0.639$; $p = 0.0001$).

Figure 4 illustrates the topographic distribution of the C1 and P1 components for the VEP and VESPA methods averaged over all subjects. The spline interpolation—which allowed us to average across data sets with different numbers of channels—and topographic plotting were conducted using code from the EEGLAB toolbox (Delorme and Makeig 2004; http://www.sccn.ucsd.edu/eeglab/).

Discussion

We have shown a strong correlation between the VESPA C1 and the VESPA P1 components across subjects. In light of this relationship, as well as the close topographic overlap of the VESPA C1 and VESPA P1 (Fig. 4b), we suggest that the VESPA P1 may reflect activation of the same visual areas that are responsible for the generation of the VESPA C1. Moreover, the relationship between the VESPA C1 and VEP C1, as well as the relationship between the VESPA P1 and VEP C1, is suggestive of common generators underlying the entirety of the VESPA and the VEP C1. These relationships stand in contrast to the lack of a reliable correlation between the VEP C1 and VEP P1, and the large-scale shift in topography of the VEP from the circumscribed midline C1 to the bilateralized P1 (Fig. 4).

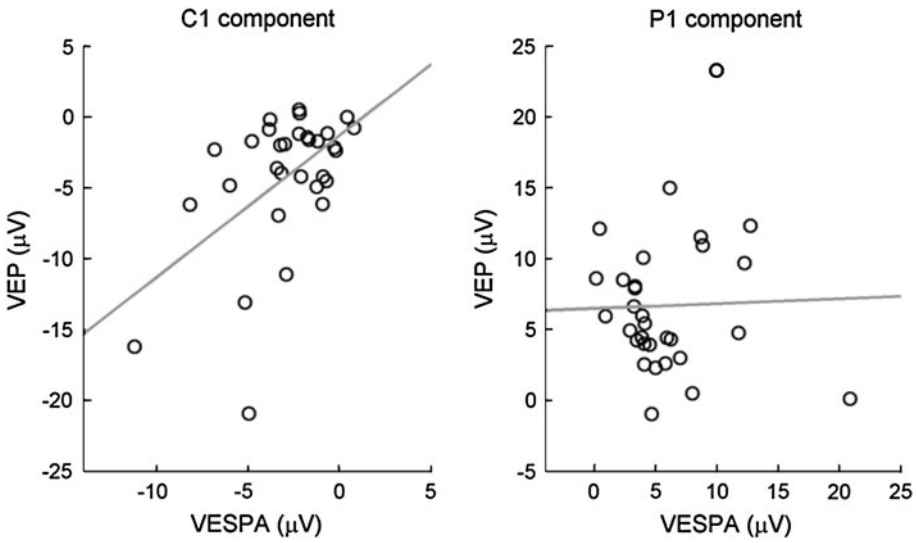

Fig. 2 The C1, but not the P1, was correlated across methods. **a** VESPA C1 amplitude versus VEP C1 amplitude for each of the 31 subjects as measured at electrode Oz (Pearson's $r = 0.528$, $p = 0.002$). **b** VESPA P1 amplitude versus VEP P1 amplitude for each of the 31 subjects as measure at Oz (Pearson's $r = 0.029$, $p = 0.875$). The *solid lines* represent the best linear fit to the data

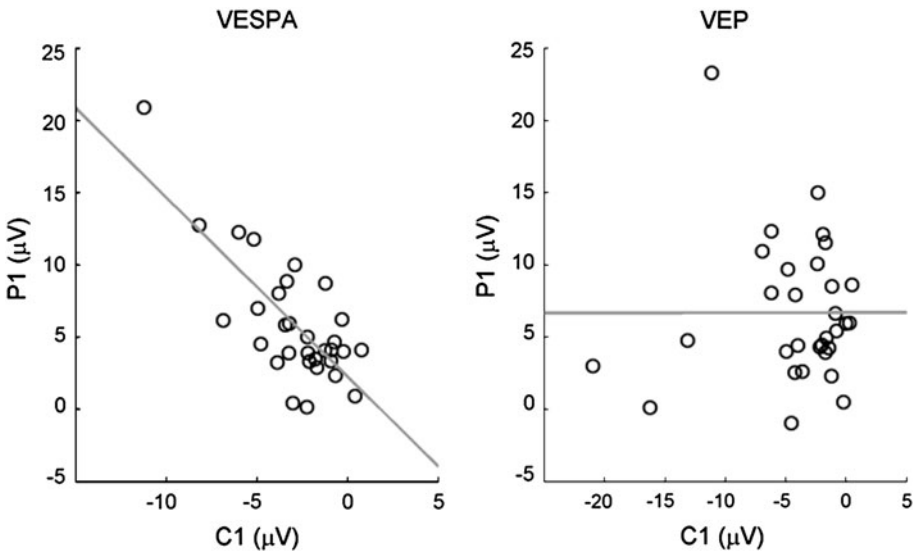

Fig. 3 The C1 and P1 components were correlated in the VESPA, but not the VEP. **a** VESPA C1 amplitude versus VESPA P1 amplitude for each of the 31 subjects as measured at electrode Oz. (Pearson's $r = -0.75742$; $p = 8.1077\ e^{-7}$). **b** VEP C1 amplitude versus VEP P1 amplitude for each of the 31 subjects as measured at electrode Oz. (Pearson's $r = 0.001$; $p \sim 1$). **c** The *solid lines* represent the best linear fit to the data

A vast body of literature indicates that the C1 component of the VEP reflects initial afferent activity in V1 (Jeffreys and Axford 1972; Clark et al. 1995; Di Russo et al. 2001, 2005; Foxe and Simpson 2002; Foxe et al. 2008; Kelly et al. 2008; but see Ales et al. 2010; Kelly et al. in press). If the VEP C1 indexes activity in V1, the lack of a correlation between the VEP C1 and VEP P1 supports previous research positing additional P1 generators lying outside of striate cortex (Clark et al. 1995). Furthermore, given the high correlation that we have shown between the C1 component of the VEP and the C1 component of the VESPA, in conjunction with their similarities in timing (Fig. 1) and topography (Fig. 4), we suggest that these two components, while acquired using two distinct techniques, represent the same neurophysiological process within V1. Finally, we propose that the high correlation between the VESPA C1 and VESPA P1 (and VEP C1) indicates that the VESPA P1 is likely representative of a second phase of activity within V1, either resulting from slower feed-forward input or recurrent activity. Indeed, such multiphasic patterns of postsynaptic activity have been frequently observed in intracranial local field potential (LFP) recordings in area V1 (Schroeder et al. 1991, 1998; Whittingstall and Logothetis 2009) and have been linked with the initial components of concurrently recorded scalp EEG (Schroeder et al. 1991).

Further grounds that the contrast modulated VESPA is dominated by striate activity lies in how the VESPA is computed. The VESPA is derived based on the assumption of a linear relationship between stimulus contrast and the EEG. It is known that the operations of the visual system obey linear models less and less as one moves from the retina to higher cortical areas (Sclar et al. 1990; Cheng et al. 1994; Carandini et al. 2005). This means that in the

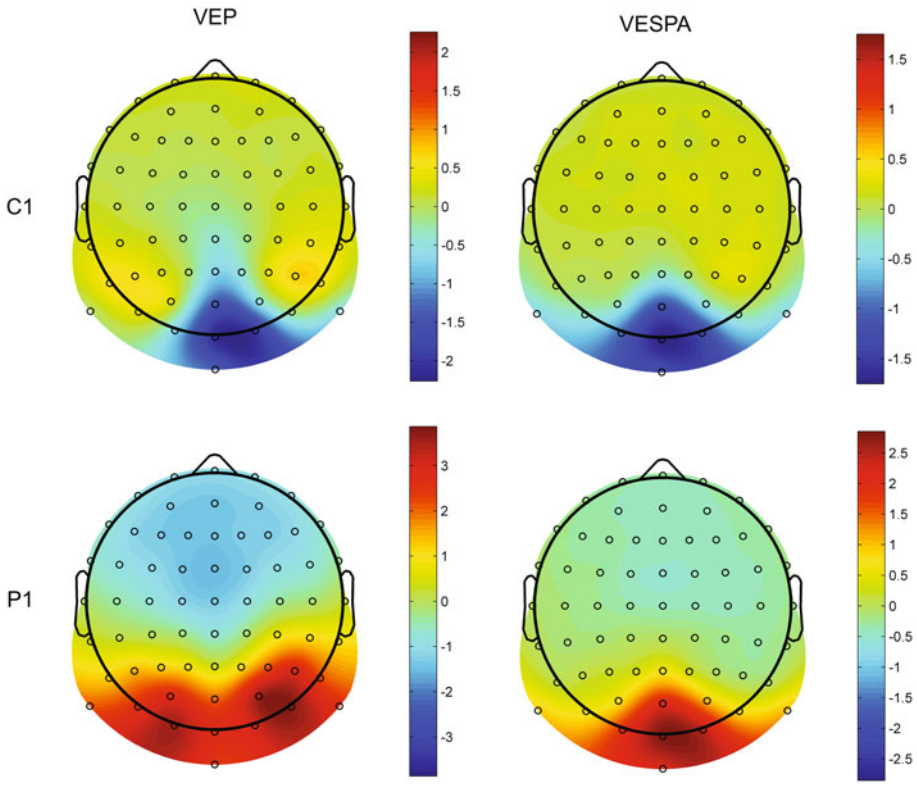

Fig. 4 Spline-interpolated scalp distribution of the C1 component (average value in the interval 66–88 ms) and the P1 component (average value in the interval 90–123 ms) for both the pattern-reversal VEP and the VESPA averaged over all subjects

VEP, the C1 is likely to be more linear in its response to contrast changes than the P1 which, as is strongly reflected in its highly distinct topography, also includes contributions from extrastriate areas (e.g., Schroeder et al. 1995; Di Russo et al. 2001; Murray et al. 2001; Foxe and Simpson 2002) as well as nonlinear delayed re-entrant feedback to V1 (Noesselt et al. 2002). Thus, the comparisons between the linear VESPA components and a relatively linear VEP C1 reveal correlations where those between the VESPA components and a nonlinear VEP P1 do not. Dramatic dissociation between the VESPA and VEP P1 components in comparisons between healthy controls and patients with schizophrenia provides further evidence for their non-correspondence (Lalor et al. 2008).

Our findings indicate that the contrast modulated VESPA may very nearly index striate cortical activity exclusively. Further work is required to assert this with certainty, and the degree to which the assumption of linearity in the VESPA obscures feed-forward nonlinear activity within striate cortices remains to be determined. Nevertheless, our findings allude to the potential power of the VESPA and similar systems identification techniques (Klistorner et al. 1997; Slotnick et al. 1999; Sutherland and Crewther 2010) for estimating the impulse response of neural populations in relative isolation, given the appropriate parametric manipulation of the input. In fact, many previous papers have already pointed to a specific striate cortical origin for kernels estimated using system identification techniques. Many of them did so based on the fact that, using multiple inputs in the upper and lower visual fields, the acquired kernels display components that invert across the horizontal meridian (Baseler et al. 1994; Slotnick et al. 1999; Fortune and Hood 2003; James 2003; Zhang and Hood 2004; Klistorner et al. 2005; Maddess et al. 2006). As detailed elsewhere (Lalor et al. in review), this property is shared by the VESPA, which, when combined with the extremely focal scalp topography of the VESPA across the entire C1–P1 timeframe, strongly points to a V1 origin. Indeed, the explicit assumption that the VESPA is linearly related to contrast changes may mean that the VESPA is even more dominated by V1 activity than the aforementioned kernel estimation techniques that typically use discrete events such as pattern reversals (e.g., Slotnick et al. 1999) or pulses (e.g., James 2003) controlled by binary temporal waveforms.

In addition to our interpretation of a common source in V1 for the generation of the VEP C1 and the VESPA, a further interpretation can be made in terms of common cellular subsystem contributions. Specifically, the correlations between the C1 of the VEP and the C1 and P1 components of the VESPA are consistent with the proposal that all three of these components are dominated by parvocellular activity (Foxe et al. 2008; Lalor et al. 2008). Foxe et al. (2008) provided evidence that the C1 component of the VEP may be primarily parvocellular in origin, while Lalor et al. (2008) suggested that the VESPA—when modulated

between 0 and 100 % contrast by a Gaussian random process as in the present study—is likely to be dominated by parvocellular activity. Further work is required to tease apart the relative contributions of the magnocellular and parvocellular pathways to the components of the VEP and VESPA and to specifically ascertain whether magnocellular contributions to the VEP P1 component may be one of the reasons for the lack of correlation between methods seen in our data. Again, this possibility would have ramifications for previous research showing deficits in the VEP P1 in patients with schizophrenia with no corresponding reduction of the VESPA P1 (Lalor et al. 2008), especially given the fact that visual deficits in schizophrenia have often been linked specifically with magnocellular dysfunction (e.g., Butler et al. 2007). Future efforts in this direction may be guided by the principles employed in previous research using second-order Wiener kernel estimation based on M-sequences (Klistorner et al. 1997; Slotnick et al. 1999; Sutherland and Crewther 2010). Advances toward this goal may also be made by biasing the stimuli toward the M and P pathways both in terms of their physical features (e.g., Lalor and Foxe 2009) and by exploiting the VESPA's flexibility in terms of temporal statistics.

Potential generative mechanisms of the VEP and VESPA: evoked superposition and phase reset

Recent debate surrounding ERP generation has focused on two distinct mechanisms: one in which the average ERP results from a simple additive process whereby time-locked supplementary electrophysiological activity is added to the ongoing EEG (the 'additive-evoked' model; Mazaheri and Jensen 2006; Mäkinen et al. 2005; Rousselet et al. 2007; Shah et al. 2004), and a second in which the average ERP arises from a stimulus-locked reset in the phase of ongoing EEG oscillations (the "phase-reset" model; Başar 1999; Makeig et al. 2002; Sayers et al. 1974). The difficulties involved in determining the relative contributions of each mechanism to the average ERP have been thoroughly detailed (Sauseng et al. 2007). For example, demonstrating correspondence between the frequency characteristics of ongoing oscillations and those of an ERP, while necessary, is nevertheless insufficient evidence to support the phase-reset model, since certain mediating factors may lead to this relationship (e.g., inter-individual differences in transmission speeds). Given our aim in this article, to relate the generative mechanisms of the VESPA to those of the VEP, it is important to consider how the VESPA fits into the phase-reset/additive-evoked debate.

The VESPA analysis, based as it is on a linear convolution, assumes that increasing the stimulus contrast (input) will increase the response (output). This is largely in accordance with the physiology of primary visual cortex where cells display a monotonic relationship between contrast and both firing rate (Albrecht and Hamilton 1982) and membrane potential response (Contreras and Palmer 2003). Importantly for our EEG work, this also holds at a population level for primary visual cortex as indexed by optical imaging (Lu and Roe 2007) and fMRI (Boynton et al. 1996). Although it has been shown that a hyperbolic ratio function better describes the relationship between contrast and response in primary visual cortex (Contreras and Palmer 2003), the assumption of linearity in V1, especially in simple cells, is likely reasonable when using a Gaussian input stimulus that spends 68 % of its time between 33 and 67 % contrast (Albrecht and Hamilton 1982; Sclar et al. 1990).

It is true, however, that the physiological conditions assumed to underlie VESPA generation are not the only ones capable of producing a VESPA response. It is mathematically possible to acquire a VESPA-like response from a uniform population of oscillators that stochastically phase-reset to contrast change. In such a model, each oscillator would have a monotonically increasing probability of phase-reset with contrast change magnitude. Central to this scenario is the requirement of an asymmetry in some property of the cortical response to increases versus decreases in contrast. This asymmetry could be in terms of a difference in number or type of cells phase resetting to increases versus decreases (e.g., ON and OFF cell groups) or differences in the phase of reset (e.g., to "high" versus "low" excitability states), for example. While differences in response properties and cell populations for increases versus decreases of contrast have been characterized for evoked spiking responses within visual areas (e.g., Gawne and Martin 2002), the influence of such basic factors as the direction of the contrast change on phase-reset parameters, to our knowledge, has not been studied.

An intuitive argument against a phase-reset model of VESPA generation is that changes in contrast happen so rapidly that an appreciable number of oscillatory cycles on the scale of the frequency content of evoked potentials (around 5–10 Hz) could not play out before being phase-reset again. One could propose, however, that cells do not follow the VESPA input signal in a continuous manner, but are rather driven beyond a reset threshold in a more discretized manner to large, transient changes in contrast that are contained in the ongoing VESPA input. As such, relatively infrequent phase resets allow for cells to play out a number of cycles of an oscillation before the arrival of another suprathreshold transient. Regardless of whether the superthreshold transient causes phase-reset or additive-evoked activity, such a model may undermine the supposition that the VESPA is acquired in response to continuous stimulation. Evidence against this model comes from the existence of VESPA responses to contrast modulation over

a very delimited range and at low contrasts (e.g., 0–10 %; Lalor and Foxe 2009), and from the fact that single V1 neurons have been shown to discriminate small contrast changes as well as, and often even better than, the overall discrimination performance of the organism (e.g., Geisler and Albrecht 1997). In addition, the successful estimation of VESPA-like kernels using binary M-sequences that involve checkerboard reversals on average every ~30 ms highlight that responses can be obtained without a long time interval between suprathreshold stimuli (Slotnick et al. 1999).

With this in mind, we maintain that the VESPA likely represents an impulse response that almost exclusively reflects evoked activity, specifically the relative changes in membrane potential in response to changes in stimulus contrast. We further surmise that any quantitative relationship between a VEP component and a VESPA component suggests that that particular VEP component contains contributions from an evoked process. Any dissimilarity between components of the VEP and VESPA, however, would not constitute conclusive evidence for or against a generative model based on either phase-reset or evoked activity. Thus, because the VESPA C1 is significantly correlated with the VEP C1, arguments for the generation of the VESPA by an evoked process also count toward establishing an additive-evoked generator of the VEP C1. While it has been shown recently that, in particular cognitive contexts, oscillatory phase resetting can occur in V1 (Lakatos et al. 2009), the very low power of ongoing oscillatory activity in the local field potentials of macaque V1 (Shah et al. 2004) suggests that phase-reset is unlikely to generate robust C1 responses. Our results support this latter conclusion.

Others have suggested that, while phase resetting in V1 may not contribute significantly to the VEP (Sauseng et al. 2007), the later P1–N1 complex, which has been localized in part to extrastriate regions, may be generated by phase-reset (Gruber et al. 2005). While further work needs to be carried out to conclusively resolve this issue, it is worth nothing that the similarities in frequency and the clear temporal continuity between the C1 and P1 in the VEP at electrode Oz (Fig. 1) do not suggest entirely differing generative mechanisms. We take the very existence of an evoked VESPA P1 as evidence that evoked activity occurs around 100 ms after the presentation of a stimulus. In fact, Di Russo et al. (2005) demonstrated that among the generative sources of the VEP P1 is a V1 source that also accounts for the generation of the preceding VEP C1 (Di Russo et al. 2005). This source may correspond to the VESPA and, as such, it is likely that there is a significant primary cortical-evoked contribution to the VEP P1, although additional phase-reset contributions cannot be ruled out.

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