Cognitive modulations of early visual cortex activity in humans

Rauss, Karsten

How to cite

RAUSS, Karsten. Cognitive modulations of early visual cortex activity in humans. Doctoral Thesis, 2010. doi: 10.13097/archive-ouverte/unige:5654

This publication URL: https://archive-ouverte.unige.ch/unige:5654
Publication DOI: 10.13097/archive-ouverte/unige:5654

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LEMANIC NEURO SCIENCE DOCTORAL SCHOOL

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FACULTÉ DE PSYCHOLOGIE
ET DES SCIENCES DE L'ÉDUCATION

Docteure Sophie Schwartz, directrice de thèse
Professeur Patrik Vuilleumier, co-directeur de thèse

COGNITIVE MODULATIONS OF EARLY VISUAL CORTEX ACTIVITY IN HUMANS

THESE

Présentée à la
Faculté de Psychologie et des Sciences de l'Éducation

de l'Université de Genève

pour obtenir le grade de
Docteur en Neurosciences

par

Karsten RAUSS

d'Allemagne

Thèse N° 46

2010

Publications

Pourtois G., Rauss, K. S., Vuilleumier, P. & Schwartz, S. (2008). Effects of perceptual learning on primary visual cortex activity in humans. *Vision Research* 48, 55-62.

Rauss K. S., Pourtois, G., Vuilleumier, P. & Schwartz, S. (2009). Attentional load modifies early activity in human primary visual cortex. *Human Brain Mapping*, 30, 1723-1733.

Rauss K. S., Pourtois, G., Vuilleumier, P. & Schwartz, S. (submitted). Stimulus synchrony modulates effects of endogenous attention on early visual processing.

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Thèse de KARSTEN RAUSS

Intitulée : Cognitive modulations of early visual cortex activity in humans

*La Faculté de psychologie et des sciences de l'éducation, sur préavis du jury de thèse formé par

Dr. Sophie Schwartz, co-directrice,Laboratoire de neurologie et d'imagerie de la cognition, Département des neurosciences fondamentales, CMU
Prof. Patrik Vuilleumier, co-directeur, Laboratoire de neurologie et d'imagerie de la cognition, Département des neurosciences fondamentales, CMU
Prof. Christoph Michel, Functional Brain Mapping Laboratory, Département des neurosciences fondamentales, CMU
Prof. Michael Herzog, Laboratory of Psychophysics, EPFL Lausanne
Prof. Gilles Pourtois, Department of Experimental Clinical and Health Psychology, Universiteit Gent, Belgique
Prof. John Foxe, Cognitive Neurophysiology Laboratory, Nathan Kline Institute for Psychatric Research, New York, USA

autorise l'impression de la présente thèse, sans prétendre par là émettre d'opinion sur les propositions qui y sont énoncées.

Genève, le 8 janvier 2010

Le Doyen :
Bernard Schneuwly

Thèse No 46
No d'immatriculation 06-312.466

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Remerciements Un grand nombre de personnes ont contribué à ce travail pendant ces trois dernières années. Je suis sûr que j'en oublie dans ces remerciements, et je ne sais pas dans quel ordre mettre ceux que je n'ai pas oublié. En ce qui concerne le premier point, si vous pensez que vous devriez figurer sur la liste en bas et que vous n'y trouvez pas votre nom, vous avez probablement raison et je suis désolé de mon oubli. Pour le deuxième point, dès que je n'arriverai plus à décider qui a contribué un peu plus ou un peu moins à cette thèse, l'ordre deviendra simplement alphabétique. J'aimerais donc remercier les personnes suivantes :

- Sophie Schwartz, pour avoir été la meilleure directrice de thèse imaginable ; pour son enthousiasme illimité ; pour ses critiques toujours constructives ; pour avoir toujours été là, des fois à l'heure.

- Gilles Pourtois, pour m'avoir appris presque tout ce que je sais sur l'EEG ; pour son enthousiasme aussi illimité que celui de Sophie ; pour ses questions lors de nos labmeetings ; pour avoir accepté d'être membre de mon jury.

- Patrik Vuilleumier, pour avoir créé un labo fantastique et un environnement de recherche extrêmement stimulant ; pour ses connaissances encyclopédiques ; pour ABIM.

- Christoph Michel, pour m'avoir appris ce que je ne savais pas sur l'EEG ; pour de nombreuses discussions stimulantes ; pour avoir accepté d'être membre de mon jury.

- John Foxe et Michael Herzog, pour avoir accepté d'être membre de mon jury et pour avoir fait le long trajet au dessus l'Atlantique et la frontière cantonale, respectivement.

- les membres du LabNIC, anciens et nouveaux, pour des heures, des jours et des années passés ensemble, au travail et ailleurs. Je suis particulièrement reconnaissant à Amal Achaïbou, qui serait première sur la liste même sans les nombreux *A* ; Mario Bonato, pour sa psychologie des étudiants en psychologie, et pour avoir été contre l'Italie (ou presque) ; Yann Cojan, pour la Bretagne ; Irina Constantinescu, pour de nombreuses clarifications ; Hamdi Eryilmaz, pour Istanbul ; Markus Gschwind, pour son pouvoir de pensée focalisée et pour m'avoir répété les joies de la liberté ; Christoph Hofstetter, pour m'avoir rappelé les limites de mes facultés en badminton ; Sebastian Korb, pour ses conseils de style ; Nadia Lucas, pour des motivations polyglottes ; Karim N'Diaye, pour Michael Jackson ; Camille Piguet, pour la montagne et plein de barbecues ; Aurélie Ponz, pour avoir insisté de parler français ; Sebastian Rieger, pour avoir apporté un coté bien allemand au labo, avec un accent écossais ; Virginie Sterpenich, pour des heures détendues de snowboard et pour ses capacités multidimensionnelles de motivation ; Wiebke Trost, pour avoir écouté du death metal et pour avoir supporté mes périodes plus bavardes ; Roland Vocat, pour des décisions rapides ; Ullrich Wagner, pour Susi.

- les membres du Functional Brain Mapping Lab, anciens et nouveaux, pour des discussions profondes sur la vie en général et le travail en particulier, et pour avoir écouté mes pensées à haute voix pendant que je consommais beaucoup trop de Coca Cola. Mes remerciements spéciaux à Verena Brodbeck, pour avoir ré-établi, à plusieures reprises, l'équilibre entre le travail et la vie ; Denis Brunet, pour Cartool ; Mélanie Genetti, pour sa compréhension ; Agustina Lascano, pour ses sandales et pour traduire Pablo ; Pierre Mégevand, pour ses connaissances de tout ce qui est suisse, de tout ce qui est neurosciences, et de tout en général ; Tonia Rihs, pour un bout d'Australie ; Vincent Rochas, pour le Palais Mascotte ; Gregor Thut, pour des discussions stimulantes, restées incomplètes à cause de Glasgow.

- Andrea Bender, Hans Spada et Simone Traber, pour m'avoir laissé partir plus tôt que prévu ; Sara Gonzalez Andino et Rolando Grave de Peralta, pour les solutions inverses utilisées dans cette thèse ; Christoph Kaller, pour m'avoir obligé de faire un choix ; Sven Thor, pour avoir été le deuxième visiteur le plus régulier d'Allemagne ; Josef Unterrainer, pour avoir proposé Genève ; Elsa Vuilleumier, pour toujours montrer la bonne direction ; Véronique Wavre et Natascha Wyss, pour m'avoir libéré pendant quelques mois de la recherche la plus difficile à Genève - celle d'un appartement ; Stefan Wiens, pour plein de discussions en Suède et en Suisse.

Finalement, mes remerciements les plus profonds vont à ma famille, pour leur soutien sans limite ; et à Christina, pour plein de choses, mais surtout pour sa patience.

Résumé La vision est la modalité sensorielle la mieux décrite, aussi bien du point de vue physiologique que du point de vue psychologique. Ceci est probablement lié au rôle important que joue cette modalité sensorielle dans notre vie quotidienne. En dépit de la précision de notre perception visuelle, nos yeux sont des instruments optiques de faible qualité, même en comparaison avec des appareils photo bas de gamme. Il s'ensuit que cette précision est le produit d'étapes ultérieures du traitement d'information dans le système visuel. Le cortex visuel des primates en général, et de l'Homme en particulier, constitue un système très complexe et développé. Selon des estimations courantes, plus de la moitié du cortex cérébral de certaines espèces de singes serait employée dans le traitement d'informations visuelles. Le grand nombre d'aires visuelles spécialisées dans certains aspects de ce traitement et les nombreuses connections bidirectionelles entre ces aires suggèrent des interactions très rapides au sein du système visuel lui-même ainsi qu'entre ce système et le reste du cortex.

Une question fondamentale dans ce domaine concerne la possibilité ou non de moduler la première étape corticale de la perception visuelle, par exemple par des facteurs cognitifs comme l'attention. Les études réalisées dans cette thèse ont pour objectif d'examiner en détail le traitement précoce de l'information dans le cortex visuel humain. En analysant les réponses électroencéphalographiques à des stimulations visuelles, nous montrons que la première composante du potentiel évoqué visuel, la C1, peut être modulée par l'attention et également suite à un apprentissage perceptif. Grâce à des améliorations méthodologiques, telles que l'adaptation des stimuli visuels aux caractéristiques physiologiques des aires visuelles les plus précoces, ces résultats originaux démontrent que des variables telles que l'attention ou l'apprentissage sont susceptibles de modifier le fonctionnement des régions visuelles primaires.

Les effets que nous rapportons suggèrent qu'une révision du modèle hiérarchique classique de la vision est nécessaire. Ce modèle assume notamment que le cortex visuel primaire (V1) traite uniquement les dimensions élémentaires des stimuli visuels et qu'il est essentiellement imperméable à l'influence de facteurs cognitifs. Nos résultats convergent avec des travaux électrophysiologiques menés chez les singes qui montrent que l'activité des neurones dans l'aire V1 est modulée par l'attention et ceci dès le début de cette activité, soit 50 à 100 ms après la présentation d'un stimulus visuel.

Nos travaux indiquent que la première étape de traitement de l'information dans le système visuel est flexible et sujette à des influences cognitives diverses. Ils élucident les mécanismes neuronaux qui sous-tendent l'interaction quasi-immédiate des informations sensorielles en provenance du monde extérieur avec des représentations internes et des buts préexistants. Nos résultats offrent aussi un éclairage nouveau sur l'immédiateté et la cohérence de nos perceptions de tous les jours.

But if we study the facts closely, we soon find no such constant connection between either judgement and retinal modification, or judgement and muscular modification, to exist. The judgement seems to result from the combination of retinal, muscular and intellectual factors with each other; and any of them may occasionally overpower the rest in a way which seems to leave the matter subject to no simple law.
– *William James*

I used to think that the brain was the most wonderful organ in my body. Then I realized who was telling me this.
– *Emo Phillips*

Abstract

The experiments conducted for this thesis examined the earliest stages of processing in human visual cortex. Using electroencephalographic recordings, it was observed that the first component of the visual evoked potential, the so-called C1, is affected by learning and attention. This contrasts with earlier studies which overwhelmingly reported no effects of higher cognitive processes on early visual cortex activity. It is suggested that methodological improvements such as the adaptation of stimulus parameters to the physiological characteristics of lower visual areas partly explain the new findings. Together with other recent studies, these results show that previously prevalent notions of primary visual cortex (V1) as an inflexible module for the treatment of low-level stimulus characteristics may need to be revised. The idea that V1 can act as an adaptive and flexible processor, previously based on animal studies, is thus starting to gain support from the human literature.

Contents

Chapter 1

Introduction

Vision is the best-studied sensory modality of the human nervous system, a situation that may be linked to its profound importance in our everyday lives. Primates in general and humans in particular possess highly developed visual systems that offer reliable and precise representations of their near and distant surroundings. This precision and reliability are, however, not due to our optical instruments themselves: the eyes only provide a relatively blurred image of the environment and their optical characteristics are in many ways inferior to those of any camera on sale today (Birbaumer & Schmidt, 1999). On the other hand, the brain systems involved in the processing of these blurred images are so advanced as to make any student of computer vision despair: for example, we are able to recognize the colour of an object under differences in ambient lighting that will throw any artificial system off track (Kandel & Wurtz, 2000), and our reactions to even very faint visual stimulation can be extremely rapid if the stimulus contains important information such as threat signals (Ohman, Flykt, & Esteves, 2001). These extraordinary capabilities are mirrored in the number and extent of brain areas involved in visual processing: current estimates assume that more than 50% of the neocortex of macaque monkeys are involved in visual processing (Felleman & Van Essen, 1991; Kandel & Wurtz, 2000). The importance of rapid information processing in the visual modality is evident even at the macroscopic level, with primary visual cortex (V1) being distinguished from other brain areas by a clearly visible band of myelinated intracortical axons, the stria of Gennari (Trepel, 2004; Wurtz & Kandel, 2000a). This anatomical difference forms the basis of the separation of visual cortex into striate (i.e. V1) and higher, extrastriate areas.

Both the importance of vision in everyday life and our detailed knowledge about the physiological and functional characteristics of the primate visual system make this modality an ideal candidate for studying the workings of higher, supramodal brain mechanisms such as attention, emotion, and learning. Attention in particular has been extensively studied in the visual systems of both animals and humans. As reviewed in Section 1.3, the results of numerous studies in these fields led to a dominant view that the profound effects of attention and other top-down processes on visual perception can act on relatively early stages of activity within the visual cortex, but that they do not affect activity during the earliest part of stimulus-evoked responses within V1. Contradictory results from animal experiments as well as a comparatively small number of human electroencephalography (EEG) studies casting doubts on this predominant view formed the basis of the present thesis.

In the following, I will first provide an overview of early studies on the characteristics of the first component of the visual evoked potential (VEP), the so-called C1, which is believed to have its principal origin in primary visual cortex. I will then present some of the experiments which established the notion that early primary visual cortex activity in general and the C1 component in particular are not affected by top-down mechanisms. Finally, I will review recent studies in both animals and humans which have cast doubts on this prevailing notion, and I will introduce the rationale of the experiments conducted for this thesis.

1.1 A Short History of the C1

In two EEG experiments using two rows of electrodes, Jeffreys and Axford (1972a, 1972b) described the characteristics of the earliest components of the VEP in humans. As opposed to most studies before and since, they presented stimuli peripherally, rather than foveally or on the visual field meridians. In addition, they systematically tested for differences between stimuli restricted to different quadrants and octants, with a particular focus on variations between upper and lower visual fields. Based on their results (see also Jeffreys, 1971) — including some of the earliest dipole simulations of human EEG data – and standard descriptions of the anatomy of the human visual system (Holmes, 1945), they concluded that the first of these components, characterised by an onset around 50 ms post-stimulus and peak latencies substantially below 100 ms, originated in V1.

Although it has since been demonstrated that higher, extrastriate visual cortex is already active at the peak latency of this earliest VEP component (Foxe & Simpson, 2002), the basic assertion that what Jeffreys and Axford (1972a) termed “C. I” (for ”component I”) has its principal sources in V1 has stood the test of time (Clark, Fan, & Hillyard, 1995; Di Russo, Martinez, Sereno, Pitzalis, & Hillyard, 2002; Im, Gururajan, Zhang, Chen, & He, 2007; Martinez et al., 1999; Pourtois, Grandjean, Sander, & Vuilleumier, 2004). The basic model proposed by Jeffreys and Axford (1972a) convincingly explains the most striking feature of the C1, which may also be the reason why the provisional name stuck: the component reverses its polarity depending on whether the upper or lower visual field is stimulated (see Fig. 1.1). Consequently, the standard nomenclature of numbered positive- and negative-going peaks does not fit. Some researchers have labeled the component as the NP80 (for ”negative-positive”; Lange, Wijers, Mulder, & Mulder, 1998; Wijers, Lange, Mulder, & Mulder, 1997) to indicate the distinctive polarity reversal. According to the Jeffreys and Axford model, this polarity reversal is due to the fact that V1 in the human principally covers the upper and lower banks of the calcarine sulcus, with the inversion between the external visual field and its central representation (Holmes, 1945) dictating that the upper visual field is represented on the lower bank of the calcarine and the lower visual field on the upper bank. Assuming a “canonical” calcarine running orthogonal to the interhemispheric fissure and roughly parallel to the parieto-occipital scalp, selective stimulation of the upper or lower visual field should excite populations of cortical neurons with opposing orientations, leading to the observed polarity reversal. Upper visual field stimulation then elicits a surface-negative component, and lower visual field stimulation leads to a surface-positive potential.

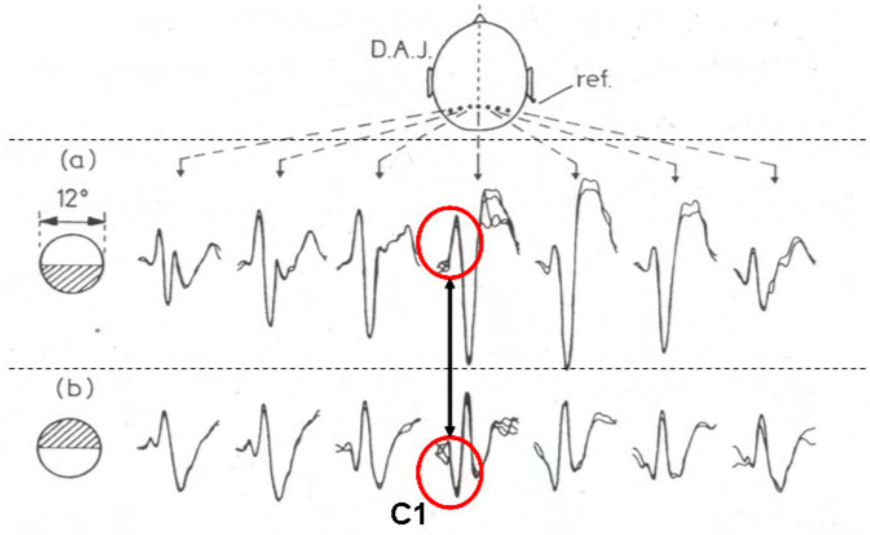

Figure 1.1: Recording setup and VEPs for simple upper and lower visual field stimulation as used by Jeffreys and Axford (1972a). Note the polarity inversion of the first component, which the authors termed ”C. I”. Positive voltages are up.

This model, also explains why a C1 component is absent in most VEP studies: if stimuli are presented foveally, their canonical representation should predominantly fall onto the outer occipital surface. As the representation of the fovea shows large differences in terms of size and location between individuals (Dougherty et al., 2003), any VEP components at this very early latency are effectively smoothed out. On the other hand, many authors presented stimuli centered on the horizontal meridian, whose representation usually falls into the fundus of the calcarine sulcus. In the case of bilateral stimulation, this would create opposing electrical fields in the two hemispheres that may cancel each other at the level of the scalp. In the case of unilateral stimulation, one may expect a bilaterally distributed component, but this has rarely been reported (however, see Im et al., 2007, below).

Several limitations need to be noted concerning this model, and Jeffreys and Axford were well aware of them, describing it as “almost certainly an oversimplification for most subjects” (Jeffreys & Axford, 1972a, p.18). First and foremost, individual differences in functional visual cortex anatomy are not limited to the representation of the fovea, but equally concern the location and extent of V1 and extrastriate visual areas, as well as the shape of the calcarine sulcus itself (Amunts, Malikovic, Mohlberg, Schormann, & Zilles, 2000; Dougherty et al., 2003; Hasnain, Fox, & Woldorff, 1998). Accordingly, atypical C1 topographies are frequently observed (Fig. 1.2), making C1 measurements notoriously difficult to compare across subjects and studies (Proverbio, Del Zotto, & Zani, 2007).

A second, related caveat concerns the representation of the horizontal meridian, which in the majority of subjects does not seem to coincide with the fundus of the calcarine, as its selective stimulation often evokes a negative C1 (Aine et al., 1996; Clark et al., 1995). This is in accordance with known differences between the cortical representations of the upper and lower visual field in humans: higher contrast sensitivity and spatial resolution are observed in the lower visual field (Lehmann & Skrandies, 1979; Liu, Heeger, & Carrasco, 2006; Skrandies, 1987; Talgar & Carrasco, 2002), corresponding to a larger extent of the neuronal populations representing this part of the visual environment in primates (Van Essen, Newsome, & Maunsell, 1984). It has been argued that environmental factors are responsible for this relative over-representation of the lower visual field (Skrandies, 1987). For example, higher spatial frequencies and lower contrast are usually present in the lower visual field of humans as we move through the environment and our visual systems may thus be hard-wired or trained to process such information more efficiently by expanding the neural populations coding for the lower visual field. The representation of the latter would thus encroach onto the lower back of the calcarine, producing the frequently observed negative C1 following stimulation on the horizontal meridian.

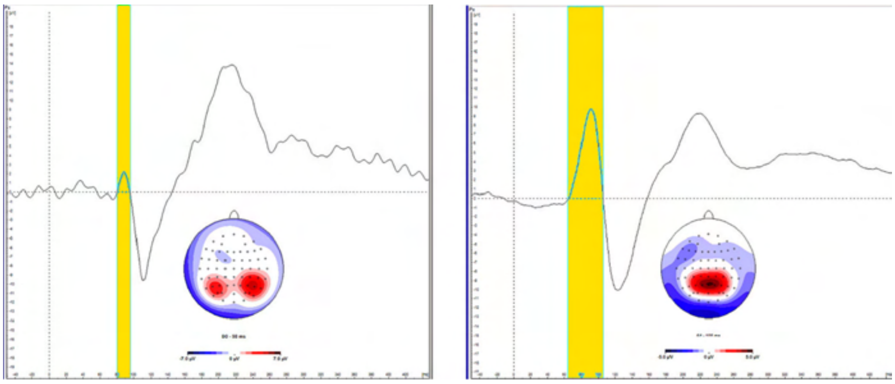

Figure 1.2: Single subject (left) and grand average (right) C1 from Experiment 1. Data were acquired following stimulation in the lower visual field. The subject shown on the left was excluded from analysis due to the atypical topography of the C1. Topographies are shown for the highlighted intervals; the time-window for the grand-average C1 is slightly larger due to blurring of the component when calculated across subjects, but equivalent differences in topography were observed for single time-frames. For details, see Results.

Notwithstanding these limitations, the general model as proposed by Jeffreys and Axford (1972a) is still frequently cited to explain the characteristics of the C1 (Clark et al., 1995; Di Russo et al., 2002; Martinez et al., 1999; Pourtois et al., 2004). Following the original report (Jeffreys & Axford, 1972a), a number of studies have explicitly addressed the component's characteristics and their results have led to the predominant view that C1 amplitude and latency are exclusively a function of physical stimulus characteristics and not subject to top-down influences. Before providing an overview of these studies in Section 1.3, I will briefly address an important conceptual issue.

1.2 Top-down Effects vs. Feedback

For an adequate assessment of the studies reviewed and the results presented in the following, it is important to distinguish between top-down modulations on the one hand and feedback effects on the other, as the latter are usually invoked as an alternative hypothesis to explain effects of higher cognitive processes on neural activity in early sensory cortices. As described below, it has repeatedly been argued that the absence of task effects on the C1 component reflects an impermeability of early visual cortex activity to higher cognitive processes. In turn, it is assumed that cognitive modulations at later stages of processing in retinotopic cortex are due to recurrent processing and thus only indirectly related to bottom-up activation.

This issue is of particular relevance in the context of the long-standing discussion about when selective attention first affects sensory processing (Deutsch & Deutsch, 1963; Lavie & Tsal, 1994; Lavie, 2005; Treisman, 1969). Thus, on the basis of the studies reviewed in section 1.3.2, it has often been concluded that attention can act early (i.e. at the level of extrastriate visual cortex), but not very early (i.e. at the level of striate cortex) during visual processing, an assumption that contrasts with theories suggesting that sensory processing may already be gated by attention at the level of the thalamus (Crick, 1984; McAlonan, Cavanaugh, & Wurtz, 2006).

From an experimental point of view, this issue is usually examined by analysing brain responses to temporally isolated stimuli presented for brief periods of time, so that the resulting neural activity (or at least its average across trials) can be clearly attributed to different processing stages of the same stimulus. In such a setting, the simplest and narrowest definition of feedback would be:

> *any influence of activity elicited by stimulus S in brain area B on the representation of S in brain area A, if A has received information about S before B.*

In this framework, any other effect of preceding neural activity in higher brain areas on stimulus processing within lower structures falls under the term top-down effects, irrespective of whether it spans intervals on the order of milliseconds (e.g. related to an immediately preceding experimental stimulus), minutes (e.g. linked to representations of different task instructions between different experimental trials or blocks), or years (e.g. depending on previously formed associations stored in long-term memory).

Although such a definition of feedback processes may appear overly narrow, it seems to reflect the prevailing view in most of the studies reviewed below. Also, this narrow view of feedback seems preferable to an equivalently narrow definition of top-down effects, which may result if memory-based processing is included under the term feedback: that is, if we assume that the effects of stimulus N+1 on the processing of stimulus N constitute a form of feedback, one is immediately confronted with the difficulty of defining a temporal window that distinguishes feedback from top-down effects. Thus, I will stick to the definition of feedback given above and the following, complementary definition of top-down effects:

> *any change in the activity elicited by stimulus S in brain area A linked to preceding or simultaneous activity in brain area B, if B has previously stored information relevant to the processing of S.*

The schema shown in Figure 1.3 illustrates these definitions. In the case of feedback, information is first transferred from lower to higher areas; it is then fed back onto the lower levels where it interacts with the still-activated representation of the same stimulus. In the case of top-down influences, on the other hand, the representation of a previously encountered stimulus (or task-instructions, or memory contents) initially acts on the lower areas receiving sensory information, so that processing of a subsequent stimulus is shaped by previously acquired information.

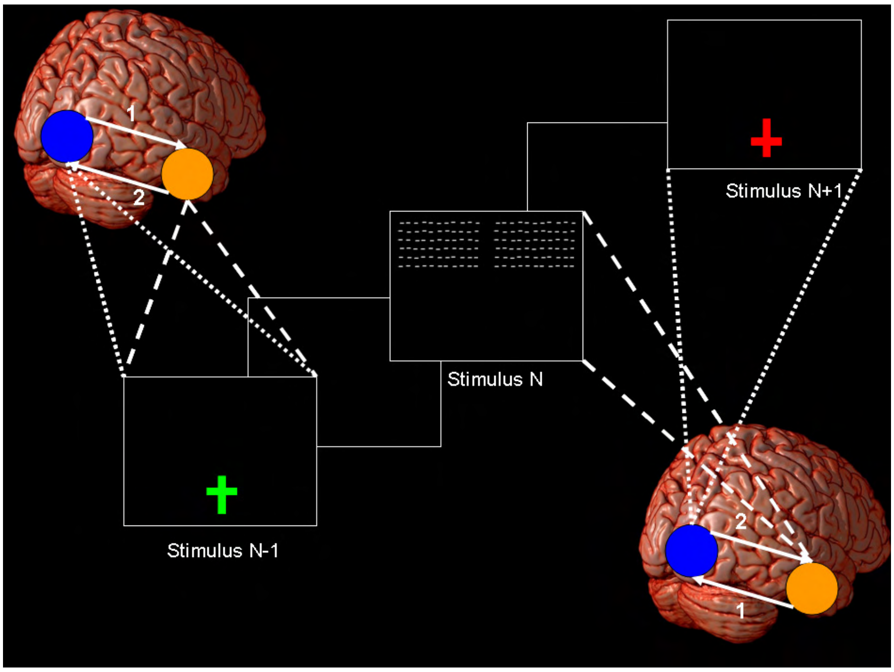

Figure 1.3: A schema of top-down and feedback effects as defined in the main text. The upper left half shows a classical feedback loop, where information about an individual stimulus is first passed on from lower to higher visual areas and subsequently fed back to lower levels, where it interacts with the still-activated representation of the same stimulus. The lower right half shows a generalized example of top-down effects: information about stimulus N stored in higher visual areas is projected back onto lower levels, where it may interact with early activity elicited by stimulus N+1.

In choosing a relatively narrow definition of feedback and a comparatively broad view of top-down effects, the latter may appear as an overly general concept comprising cognitive processes that are very different both in their temporal characteristics and their physiological underpinnings. In addition, these definitions have obvious shortcomings where natural viewing is concerned, which will be discussed in section 4.2. Notwithstanding these issues, I believe that this explicit if arguable definition is preferable to an ambiguous one, especially as it seems to reflect the usual operationalisation of the processes in question.

Finally, I would like to emphasize that the above definitions refer to different stages of the same process, namely the perception of a sensory stimulus. I do not wish to imply that these different aspects of stimulus processing correspond to separable anatomical substrates. On the contrary, given current evidence, the same interactions between higher cortical areas and local interconnections in sensory cortices may conceivably mediate both feedback and top-down effects (Crick, 1984; Gilbert, Ito, Kapadia, & Westheimer, 2000; McAlonan et al., 2006).

1.3 The C1 Component as a Reflection of Low-level Stimulus Attributes

In this section, I will provide detailed descriptions, first of the original studies establishing the retinotopic properties of the C1, then of the experiments that engendered the view that this component of the VEP is impermeable to top-down influences.

1.3.1 Mapping the C1 in Space and Time

While polarity reversals between upper and lower visual field stimulation had been demonstrated before, the extensive mapping of half-fields, quadrants and octants as well as of different eccentricities allowed Jeffreys and Axford (1972a) to characterize the earliest components of the VEP in unmatched detail. Using tachistoscopically presented patterns of isolated squares and a transversal row of electrodes centered 2.5-5cm anterior of the inion, they demonstrated (i) the characteristic polarity reversal of the C1 with upper vs. lower visual field stimulation; (ii) differences in C1 distribution following the stimulation of octants abutting the horizontal vs. vertical meridian, especially in the upper visual field; (iii) large individual differences in the degree of symmetry of the C1 following stimulation in the left and right visual field; (iv) additivity of quadrant stimulation, such that the sum of activity elicited by stimulating 2 adjacent quadrants is virtually equivalent to the corresponding half-field stimulation; (v) additivity of stimulation throughout the central 6° of the visual field, with the largest contribution to the C1 stemming from the area between $2\text{-}6^\circ$. Based on this wealth of data, the model described above was first formulated and substantiated by dipole simulations.

The number of studies referring to Jeffreys and Axford (1972a) has remained moderate but constant, with 50 articles citing the seminal study in the 1970s, 94 and 82 citations throughout the 1980s and 90s respectively and 67 citations so far in the current decade (source: ISI Web of Knowledge). Studies specifically investigating the component, however, are substantially fewer and early results were equivocal as to the localization of the neural sources of the C1. Specifically, a number of authors claimed that the C1 originated in extrastriate visual cortex (Lesevre & Joseph, 1979; Ossenblok & Spekreijse, 1991), whereas others (S. R. Butler et al., 1987) raised doubts about the model proposed by Jeffreys and Axford (1972a) because it did not explain the responses elicited by foveal stimulation (see also Clark et al., 1995; Di Russo et al., 2002; Onofrj et al., 1995).

It was not until Clark et al. (1995) provided compelling evidence for C1 sources in primary visual cortex that non-methodological studies started to take the component into account (see Section 1.3.2). The authors used high-density EEG to systematically map peripheral visual field activity elicited by circular checkerboard patterns. Based on waveform, scalp current density (SCD; Perrin, Pernier, Bertrand, & Echallier, 1989), and equivalent current dipole (ECD; Scherg & Berg, 1991) analyses, they largely confirmed the earlier findings of Jeffreys and co-workers (Jeffreys, 1971; Jeffreys & Axford, 1972a, 1972b) and showed that the retinotopic and topographic characteristics of the C1 are in accordance with its principal sources being located in V1. Their findings also underlined the fact that individual differences in V1 functional anatomy seem to be the rule rather than an exception, as shown by large variability in C1 topographies.

Subsequent mapping studies also used dipole modeling to confirm the hypothesized sources of early VEP components, but additionally employed structural and functional magnetic resonance imaging (MRI) to better constrain inverse solutions. For example, Di Russo et al. (2002) presented circular checkerboard patterns in each quadrant while recording high-density EEG, with subsets of participants undergoing structural and functional MRI, the latter used to map retinotopically organised visual cortices (Sereno et al., 1995). They observed striate cortical generators only for the C1 component, whereas early and late phases of the P1 component were localised to dorsal and ventral extrastriate visual regions, respectively. The subsequent N1 complex was attributed to dipolar sources in regions overlapping those from which the P1 originated, as well as deep-lying sources in the parietal lobe. Interestingly, the locations of dipolar sources mapped reasonably well onto fMRI activations in early visual cortex obtained with the same stimuli.

Foxe and Simpson (2002) addressed the question of timing along the visual hierarchy. Using detailed SCD analyses, they provided evidence for multiple-source activity during the C1 interval and very rapid propagation of activity especially along the dorsal visual stream (Wurtz & Kandel, 2000b). Activity in frontal regions was observed as early as 30 ms after C1 onset, indicating that feedback connections may affect activity in primary visual cortex within the first 100 ms post-stimulus and thus during the C1 interval. Based on these findings, Foxe and Simpson (2002) introduced the notion of an early C1 phase ($\mathrm{C1_e}$), comprising only the first 10-15 ms of the component, as the only part of the VEP that exclusively reflects V1 activity.

Vanni, Warnking, et al. (2004) used uni- and bilateral checkerboard patterns in separate EEG and fMRI sessions and acquired additional retinotopic mapping data. Stimuli were presented in the lower visual field and dipoles situated in primary visual cortex modeling the positive C1 could be clearly separated from sources in V3/V3A in the majority of seven subjects. On the other hand, substantial crosstalk between occipital sources was frequently present, such that sources in V1 and V2 could only rarely be distinguished. Similarly, for activity observed in V3/V3A during the rising phase of the C1, crosstalk from V1 could not definitely be excluded. Nevertheless, in accordance with the findings of Foxe and Simpson (2002), the authors concluded that activity in extrastriate visual areas contributes to the C1. Interestingly, very early activity was observed in an inversely modeled dipole (i.e. a source not seeded to fMRI activations) near V5. On the other hand, substantial delays of up to 20 ms were observed between peak source activity in areas V1, V2, and V3/V3A. In a companion paper (Vanni, Dojat, et al., 2004), the authors examined the timing of interactions between individual stimuli in early visual cortex and demonstrated that reliable non-linear summation effects first occurred at the level of V5, at around 80 ms following stimulus onset. Similar effects were also observed at lower levels of visual cortex, but here they occurred substantially later (e.g. beyond 150 ms for V1). These results are somewhat disparate from the findings of Foxe and Simpson (2002). However, Vanni and colleagues acquired fMRI data only for posterior brain regions, and the claim that frontal regions may already be activated at the time of the C1 peak was not investigated.

In a methodological study, Im et al. (2007) used the C1 component to assess the correspondence between fMRI activations in V1 and EEG inverse solutions. The authors presented circular checkerboard patterns at different but overlapping eccentricities along the horizontal meridian and found reasonably good correspondence between BOLD responses and EEG source reconstructions, with a median displacement of 7 mm between EEG source maxima and fMRI centers of activation in V1. Similar results using MEG were later reported by Poghosyan and Ioannides (2007). Considering the physiological basis of the BOLD signal (Logothetis, 2002; Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001), this relative correspondence between EEG- and MRI-based activation patterns may suggest some degree of intracortical processing during the C1 interval, in accordance with the results of Foxe and Simpson (2002). Interestingly, Im and colleagues used lateral posterior electrodes for measuring the C1 component and their figures suggest that the stimuli centered on the horizontal meridian indeed elicited positive ERP deflections at inferior parietal locations, in accordance with a strict interpretation of the cruciform model of V1 as proposed by Jeffreys and Axford (1972a).

In summary, there is substantial evidence corroborating the cruciform model of striate cortex organisation as first proposed by Jeffreys and Axford (1972a), while alternative models suggesting that the C1 reflects mainly extrastriate activity (Lesevre & Joseph, 1979; Ossenblok & Spekreijse, 1991) have received comparatively less empirical support. The experiments reported below were therefore based on this model, even though there is some doubt as to the exclusive contribution of V1 to the generation of the C1 component (Foxe & Simpson, 2002). For this reason, I will mostly speak about "early visual cortex activity" rather than "early activity in V1".

1.3.2 Null-findings on Top-down Effects

More complex paradigms were employed to examine the influence of top-down mechanisms on early VEP components, with a particular focus on spatial attention (for reviews, see Hillyard & Anllo-Vento, 1998; Hillyard, Teder-Salejarvi, & Munte, 1998). However, not all of these studies took into account the C1 due to stimulation parameters that did not reliably elicit this earliest component of the VEP (Handy, Soltani, & Mangun, 2001; Luck, 1995).

In an early multimodal study, Heinze et al. (1994) combined positron-emission tomography (PET) and EEG. Subjects were instructed to pay attention to either the left or the right side of bilateral stimulus displays flashed into the upper visual field. Changes in regional cerebral blood-flow were observed in the fusiform gyrus and used as seeds for inverse modeling of attentional effects on the P1. Despite the large differences in temporal resolution between the two methods, these seeded inverse solutions provided a good fit of the ERP data and relaxing the localisation constraints produced very similar solutions. The authors specifically noted the absence of very early attentional effects, both at the level of the C1 component and with respect to the PET data, which did not uncover any attention-related differences in V1.

Numerous EEG studies subsequently provided compelling evidence for the effects of spatial attention on early extrastriate VEP components (i.e., P1 and N1), but unequivocally reported an absence of such effects on the C1. Experimental paradigms were similar to that employed by Heinze et al. (1994), with subjects attending either the left or right visual field while uni- or bilateral stimulus displays were flashed into the periphery (Clark & Hillyard, 1996; Gomez Gonzalez, Clark, Fan, Luck, & Hillyard, 1994; Johannes, Munte, Heinze, & Mangun, 1995). Some experiments additionally examined the effects of colour (Anllo-Vento & Hillyard, 1996; Lange et al., 1998) and background luminance (Wijers et al., 1997), but also failed to find any attentional modulations of the C1 component.

This was corroborated by studies combining EEG/MEG and fMRI. For example, Martinez et al. (1999) obtained fMRI data (including retinotopic maps) and EEG recordings from the same subjects. The experimental setup was similar to that of Heinze et al. (1994), but with targets presented in a cluttered field of distractors. They found blood oxygen level dependent (BOLD) signal changes as a function of attention throughout retinotopically organized visual areas, including V1. However, EEG recordings failed to show any evidence for C1 modulations by spatial attention. Martinez et al. (1999) concluded that the effect of attention on V1 observed in the fMRI data reflects delayed feedback effects, rather than modulations of the initial sweep of activation passing through primary visual cortex.

A similar conclusion was reached by Noesselt et al. (2002), who simultaneously recorded EEG and MEG and obtained fMRI data in a separate recording session. Stimuli and procedure were similar to those employed by Martinez et al. (1999) and again, substantial effects of attention were evident in V1 from the fMRI data. However, neither EEG nor MEG recordings indicated any effects on the earliest components of the respective evoked responses. On the other hand, delayed attentional effects probably reflecting feedback input to V1 were evident in both modalities, further supporting the notion of primary visual cortex being affected by top-down influences only beyond the earliest stages of stimulus-evoked activity.

In summary, these studies instituted the notion that V1 activity in the human is modulated by higher-order influences such as spatial or feature-based attention, but that such modulations only occur at relatively late, re-entrant processing stages. The latter are substantially beyond the peak latency of the C1 and thus considerably later than the first sweep of activity passing through V1. I will now outline indirect evidence from animal experiments and human neuroimaging studies challenging this predominant view.

1.4 Conflicting Results

In this section, I will provide a selective outline, first of animal experiments, then of human neuroimaging studies that challenge the view of primary visual cortex being unaffected by top-down influences. These studies provided an important motivation for the experiments conducted for the present thesis, as they strongly suggest higher-order effects on V1, but do so only indirectly: the results of animal studies may not transfer directly to the human brain; and the hemodynamic and metabolic parameters measured with neuroimaging methods such as fMRI or PET lag behind their underlying neural activity, making inferences about the precise time-course of top-down effects on early sensory processing notoriously difficult.

1.4.1 Animal Experiments

A comprehensive overview of the literature on early sensory processing in non-human primates and other species is beyond the scope of this work (for a recent review, see Gilbert & Sigman, 2007), but I will present some of the most important animal studies suggesting top-down effects at the level of primary sensory cortices. As will become evident, just as in humans the debate on very early modulation of sensory processing is far from resolved in this field, but a substantial body of evidence nevertheless supports the notion that the earliest sweep of activity in V1 may be subject to higher-order influences.

Motter (1993) used a cued attention paradigm (Posner, Snyder, & Davidson, 1980) to direct monkeys' attentional focus either toward or away from the receptive fields of V1, V2, and V4 neurons. Different numbers of stimuli were simultaneously presented and the author observed significant differences in firing rates as a function of focal attention in more than one-third of all neurons recorded in each visual area. Since firing rates differed between conditions from the very onset of neural responses, Motter (1993) concluded that preparatory effects during the cue-target interval must have affected neural responses to the target. Importantly, attentional modulation in most neurons depended on the simultaneous presence of other stimuli in the display. This was the case even in V1 and although distances between stimuli were several times bigger than receptive field diameters, excluding an explanation in terms of suppressive-surround effects. Motter concluded that even the most basic levels of perception are subject to top-down effects, possibly mediated by feedback connections within the visual system (see Section 1.2).

Gilbert and co-workers conducted a series of studies demonstrating the active and dynamic characteristics of primary visual cortex, a notion at odds with the dominant belief that it functions exclusively as a low-level feature detection module (cf. ?, ?). In several studies, Gilbert's group observed powerful modulations of V1 activity as a function of non-classical receptive field stimulation (i.e. modulations of a neuron's activity by stimuli that lie well outside its receptive field center and surround), arguing for a role of early visual cortex in contour integration and figure-background segregation (Gilbert et al., 2000; Ito & Gilbert, 1999; Ito, Westheimer, & Gilbert, 1998). Importantly, these contextual modulations were subject to strong attentional influences, whereas the response to an individual target stimulus (i.e. without flanking stimuli providing context information) remained virtually unchanged across different attentional conditions. The authors concluded that attention most likely acts as a gating mechanism at the level of long-range horizontal interconnections between V1 neurons of similar orientation preference. They specifically note that attentional effects on contextual modulations led to increased firing rates from the very onset of the neural response.

Crist, Li, and Gilbert (2001) examined the neural mechanisms underlying perceptual learning and found no changes in cortical magnification, receptive field size, or orientation tuning for the trained stimuli and locations. However, contextual modulations as described above were strongly shaped by training: neural responses to task-irrelevant bars were increasingly tuned to the task-relevant orientations and this tuning was found to be context-dependent, as it occurred only if the animals were performing the experimental task, but not if they were simply fixating a display containing the same stimuli. As Crist et al. (2001) did not report data on the timing of the attentional modulations observed, their findings could be accounted for either by changes in early V1 activity or by delayed feedback effects. However, Li, Piech, and Gilbert (2004) subsequently demonstrated similar effects in an experiment where the same physical stimuli were employed in two different task contexts (line bisection vs. Vernier tasks; for a similar behavioral approach in humans, see Ahissar & Hochstein, 1993). As in the study of Ito and Gilbert (1999), the effects of task context were evident virtually from the first spike following stimulus presentation, providing strong evidence for the notion that top-down mechanisms can shape even the initial stages of sensory processing in the cortex.

Hupé and co-workers (Hupé, James, Girard, Lomber, et al., 2001; Hupé et al., 1998) used reversible inactivation by cooling to study the role of feedback connections on activity in early visual cortex in the anesthetized monkey. Recording from neurons in V1, V2, and V3, they demonstrated that V5/MT inactivation reduced the response of these neurons, particularly under conditions of low visibility (Hupé et al., 1998). However, since data were aggregated over 50-ms bins, the precise time-course of these effects remained unclear. In a subsequent study using the same stimuli, Hupé, James, Girard, Lomber, et al. (2001) examined this time-course in detail and found that responses in V1 neurons differed as a function of MT inactivation from their earliest detectable activity following stimulus presentation. Since this effect was not related to changes in spontaneous firing rates and was observed in neurons with different onset latencies, the authors concluded that feedback effects may act extremely fast and in a non-linear fashion, shaping the earliest responses in V1 without inducing detectable changes of activity in the absence of a stimulus. (Note that their "feedback effects" thus correspond to top-down modulations as defined above.)

Finally, Shuler and Bear (2006) reported neural activity in V1 neurons in the rat that reflected reward timing more than stimulus characteristics, reminiscent of the well-known activity patterns of midbrain dopamine neurons first reported by Schultz, Dayan, and Montague (1997). This finding is particularly interesting in its relation to recent conceptualisations of early sensory cortex activity in terms of predictive coding (Rao & Ballard, 1999; Summerfield et al., 2006) and will be taken up in the Discussion.

On the other hand, other groups did not report V1 modulations by higher cognitive processes or only observed them at later stages of processing (Mehta, Ulbert, & Schroeder, 2000b, 2000a; Moran & Desimone, 1985; Roelfsema, Lamme, & Spekreijse, 1998; Roelfsema, Tolboom, & Khayat, 2007). In an early study of the subject, Moran and Desimone (1985) recorded neurons in V1 and V4 while monkeys attended to one of two visual stimuli. The authors found that neural responses in V4 were strongly influenced by attention if both stimuli were presented in the neuron's receptive field, but reported no effects of selective attention on V1 activity. This claim was taken up later (e.g. Lange et al., 1998), although closer inspection reveals that *"[w]hen relevant and irrelevant stimuli were in a [V1] receptive field [. . .], the animal could not perform the task"* (Moran & Desimone, 1985, p.784). On the other hand, if one of the stimuli was presented outside the neuron's receptive field, *"as in V4 under this condition, attention had little or no effect on the cells"* (ibd.). It is thus unclear from these data whether V1 and V4 are indeed different in terms of their permeability to selective attention. Similar problems in assessing the characteristics of V1 were reported by Luck, Chelazzi, Hillyard, and Desimone (1997).

Roelfsema et al. (1998) recorded from V1 in monkeys performing a curve-tracing task which required the animals to distinguish between a target and a distracting stimulus. For spatially separated as well as intersecting curves, increased firing rates were observed along the whole extent of the target curve, but this object-based attentional effect had an onset of >200 ms, substantially beyond initial V1 activity elicited by stimulus onset, which occurred with a latency of only 35 ms. In accordance with the interpretations of Gilbert and colleagues (Gilbert et al., 2000; Ito et al., 1998; Ito & Gilbert, 1999), the authors concluded that long-range horizontal interconnections may be the neural substrate of the observed effects, with attention acting as a gate-keeping mechanism, but at longer latencies.

Metha and colleagues (Mehta et al., 2000b, 2000a) used an intermodal attention paradigm while simultaneously recording laminar ERPs in multiple visual areas of the macaque. Although they too observed attentional modulations of V1 activity, these were considerably weaker and occurred substantially later than those recorded in higher visual areas such as V4.

Using a figure-from-motion task, Roelfsema et al. (2007) were able to distinguish different stages of visual processing in the alert monkey, namely feature detection, figure-background segregation, and attentional selection. They showed that each of these processing stages has a distinct neuronal correlate within primary visual cortex: an early burst of activity due to motion onset was seen with a latency of 48 ms; neuronal responses differed between figure and background as early as 57 ms; and target stimuli elicited larger activity than distractors from 137 ms onward. This sequence of events and its approximate timing are in accordance with EEG results reviewed above (e.g. Martinez et al., 1999; Noesselt et al., 2002) in that they suggest attentional modulations of V1 activity only as the result of re-entrant processing and substantially beyond the initial sweep of activation.

In conclusion, the picture emerging from the animal literature is equivocal: very early modulations of sensory processing have been repeatedly observed in both anesthetized (Hupé, James, Girard, Lomber, et al., 2001) and alert non-human primates (Ito et al., 1998; Ito & Gilbert, 1999; Li et al., 2004), whereas such effects were only detected at later processing stages by others (Mehta et al., 2000a, 2000b; Roelfsema et al., 1998, 2007). This discrepancy may partly be explained by the different experimental paradigms used: it seems that early effects of attention were found whenever stimuli and task structure allowed for tonic changes of attentional parameters, such as the block-wise inhibition of one task-set in the experiments of Li et al. (2004). These effects may be similar to the observations of Hupé, James, Girard, Lomber, et al. (2001) in that the consequences of MT suppression on activity in V1 suggest tonic influences of the former on the latter even under anesthesia. On the other hand, if stimuli and task structure offer only a low level of predictability, where no part of the stimulus display can be tonically suppressed without the risk of reduced performance (Roelfsema et al., 1998, 2007), attention seems to act only at the level of recurrent processing in V1. In other words, attention may act as a gate-keeper at the level of V1 only if this early gate in the processing sequence can be closed without substantial loss of information.

In any case, the notion of primary visual cortex as an active processor (Gilbert, Sigman, & Crist, 2001; Gilbert & Sigman, 2007) is supported by these and other, similar findings (Schoups, Vogels, Qian, & Orban, 2001; Vanduffel, Tootell, & Orban, 2000) and is incompatible with a previously dominant view of V1 as a simple and inflexible feature detection module. In the following, I will provide an overview of human neuroimaging studies that underline this relative flexibility of early visual cortex.

1.4.2 Studies in Humans

In humans, a large body of neuroimaging research has described top-down effects on metabolic and hemodynamic indicators of neural activity in early sensory cortices across a wide range of experimental paradigms.

Using spatial attention paradigms similar to those employed in numerous EEG studies (Clark & Hillyard, 1996; Gomez Gonzalez et al., 1994; Johannes et al., 1995), Tootell et al. (1998) as well as Gandhi, Heeger, and Boynton (1999) examined the effects of selective attention on V1 activity using fMRI. Both groups observed attentional modulations in primary visual cortex; in the study of Gandhi and colleagues, these modulations were on the order of 25% of stimulus-evoked activity.

Ress, Backus, and Heeger (2000) used a simple contrast-detection paradigm with auditory cueing to examine BOLD responses of retinotopically organized visual cortex as a function of stimulus presence or absence. They observed significant responses in V1 through V3 which were virtually the same whether a stimulus was presented or not. This 'base response' was systematically linked to behavioral performance, with larger base responses in all three areas predicting better performance. Importantly, the base response was retinotopically specific in that it was observed only in visual cortex regions representing the experimental stimulus. Strikingly, these responses were absent at higher contrast levels, where behavioral performance was at ceiling. The authors interpreted trial-to-trial fluctuations in the base response as correlates of fluctuations of attention which in turn affect performance. While its neurophysiological origins remain to be clarified, the base response probably reflects a specific biasing signal recruited during difficult perceptual judgements and thus suggests the operation of top-down effects at the level of early visual cortex. However, as the authors point out themselves, it is impossible from their data to conclude whether the base response originated in V1 and was passed on to higher visual areas or vice versa.

Mirroring the results of animal studies (Ito et al., 1998), it has been demonstrated that perceptual learning in a texture discrimination task (Karni & Sagi, 1991) selectively increases neural activity at the representation of the trained stimulus in human V1 (Schwartz, Maquet, & Frith, 2002). Importantly, additional analyses of functional connectivity patterns suggested no involvement of other brain regions in mediating this effect. Similar results have been reported by other groups (Furmanski, Schluppeck, & Engel, 2004; Sigman et al., 2005). In another study, Schwartz et al. (2005) varied attentional load (Lavie, 2005) at fixation and found reduced BOLD responses to irrelevant peripheral distractors under increased attentional demands. This increased attentional filtering was seen even at the level of V1, with patterns of reduced activity conforming to a surround-suppression profile (Bahcall & Kowler, 1999). In both cases, long-range horizontal connections recruited during learning or gated as a function of attentional demands could conceivably mediate the suppression of task-irrelevant stimuli, in accordance with the proposals of Gilbert and co-workers (e.g. Gilbert & Sigman, 2007).

Using concurrent transcranial magnetic stimulation (TMS) and fMRI, Ruff et al. (2006) provided direct causal evidence for top-down modulations of early visual cortex activity. In their study, frontal eye-field TMS led to a characteristic pattern of increased BOLD responses throughout V1 to V4 for regions representing the peripheral visual field. Activity in central regions, on the other hand, was reduced by TMS and this pattern of results was observed both in the presence and the absence of visual stimulation. Importantly, a separate psychophysical experiment showed behavioral effects in the same direction, i.e. contrast thresholds were decreased for peripherally presented stimuli (Gabor patches) during TMS. Thus, changes in higher cortical areas can modulate neuronal responses in early sensory cortices and these modulations can in turn modify conscious perception even of very simple stimuli. Similar results have also been reported by Taylor, Nobre, and Rushworth (2006) using combined EEG and TMS .

While these studies strongly suggest high-level influences on activity in V1, the delay of the hemodynamic response does not permit to draw strong conclusions about the time-course of many of the reported effects. However, numerous studies have also demonstrated effects of selective attention on pre-stimulus activity in early sensory cortices, suggesting that top-down mechanisms may exert relatively long-lasting influences on early sensory cortices and thereby influence the latter's response characteristics.

Kastner, Pinsk, De Weerd, Desimone, and Ungerleider (1999) observed BOLD signal modulations in terms of both baseline shifts and attentional modulations of visually evoked responses in retinotopic visual areas. Both classes of effects differed as a function of simultaneous or sequential presentation of visual stimuli, as described previously by the same group (Kastner, De Weerd, Desimone, & Ungerleider, 1998). Importantly, retinotopically specific increases of neural activity in preparation for peripherally presented stimuli was observed even at the level of V1, although this effect was less reliable than in higher visual areas (see also Schwartz et al., 2005). Stimulus-evoked responses were modulated by attention only from V2 onwards, although this may be linked to the large extent of the stimuli, potentially reducing the involvement of V1 with its small receptive fields in attentional biasing.

O'Connor, Fukui, Pinsk, and Kastner (2002) observed attentional modulations of both stimulus-evoked responses and baseline activity in the lateral geniculate nucleus (LGN), the principal thalamic relay of the visual pathway connecting the retinae to visual cortex. Thus, selective attention could conceivably gate information processing even at subcortical stages (Crick, 1984), indicating a possible physiological mechanism for attentional modulations of early stimulus-evoked activity in primary sensory cortices.

Muckli, Kohler, Kriegeskorte, and Singer (2005) used an apparent motion paradigm, real motion stimuli, and retinotopic mapping to examine the neural representations of apparent motion paths. They observed equivalent activity patterns in V1 both for apparent and real motion. Just as the findings of Shuler and Bear (2006) reviewed in the preceding section, these results are related to the idea that activity in early sensory cortices may reflect the matching of dynamic predictions and actual stimulus patterns (Rao & Ballard, 1999). Similar results have been reported by Summerfield et al. (2006), and Bahrami, Lavie, and Rees (2007) later demonstrated that V1 activity in response to invisible stimuli is itself subject to attentional effects.

Ruff and Driver (2006) showed that attentional modulations in visual cortex can be observed not only for target stimuli, but also for irrelevant distractors. In a psychophysical experiment, they found that advance knowledge reduced the behavioral costs associated with distractor occurrence. In a subsequent fMRI experiment, they observed changes in early visual cortex activity contralateral to cued distractors, and these changes were already present during the cue-target interval. Their results suggest that top-down influences on sensory processing may not only bias competition in favor of relevant stimuli, but may also serve to suppress neural processing of predictable distracting information, similar to the findings of Schwartz et al. (2005). However, since Ruff and Driver (2006) did not acquire retinotopic maps in their subjects, the involvement of V1 in these effects remains unclear.

Even more recently, Bestmann, Ruff, Blakemore, Driver, and Thilo (2007) observed enhanced phosphene perception following TMS over visual cortex if subjects paid attention to the stimulated quadrant. Although the specificity of TMS stimulation is limited, these findings suggest that attention can enhance levels of excitability in sensory cortices independent of the source of information, i.e. even if visual cortex is stimulated directly rather than via the retino-thalamic pathway.

The preparatory effects reported in these studies may correspond to non-linear interactions between top-down signals and sensory processing as postulated by Hupé, James, Girard, Lomber, et al. (2001). Although in the latter study, differences in baseline activity were specifically excluded as mediators of the observed modulations of early visual cortex activity following MT inactivation, baseline shifts as a consequence of selective attention have been reported in the awake monkey (Luck et al., 1997). The BOLD signal as a complex, cumulative indicator of neural activity (Logothetis, 2002; Logothetis et al., 2001) could conceivably capture large-scale preparatory processes which may have gone unnoticed in single-cell or multi-unit studies in non-humans.

1.5 A Paradigm Shift?

In this section, I will review the relatively small number of human EEG and MEG studies that suggested top-down effects on the earliest cortical levels of sensory processing until a few years ago. I will also suggest reasons for the prevalence of null-findings and propose methodological improvements to better address the question of top-down influences on early visual processing.

1.5.1 Recent EEG Studies

Over the last few years, several experiments have provided evidence against the long-held view that early visual cortex activity in humans is not affected by top-down factors. I will provide an exhaustive review of these studies in order to allow for a detailed assessment of why their results are different from those reviewed in section 1.3.2.

Some of the earliest indications of early visual cortex activity being affected by higher cognitive processes were reported by Skrandies and co-workers (Skrandies & Fahle, 1994; Skrandies, Jedynak, & Fahle, 2001; Ludwig & Skrandies, 2002). Focussing on topographical changes and overall electrical field strength (global field power, GFP), their analyses indicated that neural activity measured over occipital scalp regions may be modulated by perceptual learning within the first 100 ms post-stimulus. However, due to the small stimuli used and the restricted coverage of the electrode montage employed, it is unclear whether these measurements reflect the C1 component.

Measuring EEG in a dot-probe task, Pourtois and colleagues studied exogenous orienting towards emotional cues (Pourtois, Thut, Peralta, Michel, & Vuilleumier, 2005; Pourtois et al., 2004). Facilitatory effects on the P1 component were observed for stimuli presented at locations previously occupied by fearful, but not happy or neutral, faces. In addition to this cueing effect, the authors also examined early visual responses to the emotional cues themselves and found a significant modulation of the C1 component for fearful as compared to neutral or happy faces. Importantly, C1 modulations were correlated with P1 effects on the probe stimuli, suggesting a facilitatory effect of primary visual cortex responses to emotionally significant information on extrastriate processing of subsequent stimuli. Since behavioral performance was also increased for emotionally cued probe stimuli, increased V1 responses to emotional stimuli could conceivably serve an alerting function that translates into behavioral advantages. Alternatively, rapid feedback from subcortical structures involved in coarse emotional processing such as the amygdala (Morris, Ohman, & Dolan, 1999) could have mediated emotional effects on both cue and probe processing.

Khoe, Mitchell, Reynolds, and Hillyard (2005) examined the effects of exogenous cueing in a transparent motion paradigm. Superimposed random-dot patterns rotated in opposite directions, creating the illusion of two transparent surfaces. A brief translation of one pattern was used to direct attention to one of the surfaces; a second translation could either occur for the cued or the uncued surface. Surprisingly, the authors observed not only a modulation of the N1 component as found in previous studies (Lopez, Rodriguez, & Valdes-Sosa, 2004; Pinilla, Cobo, Torres, & Valdes-Sosa, 2001), but also increased C1 amplitudes if the second translation occurred for the previously cued surface. They suggested saturation effects on the C1 in previous studies as a possible reason for this novel result and argue that preferential treatment of the cued surface results from object-based attentional mechanisms. The effects of exogenous cueing on the C1 thus suggest short-term top-down effects on early activity in primary visual cortex.

Stolarova, Keil, and Moratti (2006) examined emotional effects on early visual processing using an emotional conditioning paradigm. In their study, subjects underwent high-density EEG recording during baseline, conditioning, and extinction of the association between peripherally presented gratings as conditioned stimuli (CSs) and centrally presented affective images as unconditioned stimuli (USs). It was found that CSs elicited significantly higher C1 amplitudes during conditioning blocks when compared to baseline or extinction periods. This extends the findings of Pourtois et al. (2004) by demonstrating that emotional significance acquired on a relatively short time-scale can induce changes at the earliest levels of sensory processing in the cortex. Thus, as has been shown for attentional mechanisms (Gilbert et al., 2000), the effects of emotion on perception seem to be subject to learning, and such learning is evident very early in the visual cortex hierarchy.

In summary, several recent studies report effects of attention, emotion, and learning on the C1 component, in accordance with a large number of animal experiments suggesting that V1 is more than an inflexible stimulus detection module. It is interesting in this respect that recent clinical research has suggested low-level, potentially subcortical visual processing deficits in schizophrenia (Brand, Kopmann, Marbach, Heinze, & Herzog, 2005; P. D. Butler et al., 2005; P. D. Butler & Javitt, 2005), a disease previously thought to involve mainly high-level cortical dysfunction. These findings may contribute to our understanding of interactions between bottom-up activation and top-down modulations in early sensory cortices by highlighting the effects of disruptions in low-level stimulus characterisation.

I will now turn to possible reasons for why the results of recent EEG studies systematically differ from those reviewed in section 1.3.2 which suggested no top-down modulations of early visual cortex activity.

1.5.2 Prerequisites for Observing Top-down Effects on Early Visual Processing

Possible reasons for the discrepancies between studies which did and did not indicate higher-order influences on V1 activity in humans include the combination of two factors:

First, presentation conditions were usually not well-adapted to the functional characteristics of V1. Thus, stimuli have frequently been presented on the horizontal meridian which may not be an ideal location for eliciting a clear C1 component in many subjects; if peripheral stimulus patterns were used, they were often small, activating only correspondingly small portions of V1 unlikely to produce equivalent EEG patterns in different subjects; conversely, the size of task-relevant stimulus elements often extended well beyond the size of the small receptive fields in V1, effectively minimizing possible contributions of early visual cortex to task performance. In other words, if the extraction of task-relevant information from a visual display can only be accomplished by neurons possessing relatively large receptive fields, it seems likely that the influence of early visual cortex on the performance of such a task would be reduced.

Secondly, the large individual variability of early visual cortex observed in previous anatomical (Amunts et al., 2000) and functional (Dougherty et al., 2003; Hasnain et al., 1998) studies was usually not taken into account during either experimental design or data analyses.

Future studies examining top-down effects on early visual cortex activity should take into account at least one of these two fundamental issues: either experimental stimuli and tasks should be designed with a focus on whether the functional characteristics of V1 (i.e. small receptive fields, high degree of retinotopic organisation, high orientation sensitivity) allow it to substantially contribute to task performance; or steps should be taken to appropriately consider individual variability in visual cortex anatomy. Ideally, both issued should be addressed at the same time.

1.6 Questions and Hypotheses

Based on the studies reviewed in the preceding sections, we wanted to address the following questions, each in a separate experiment:

Does perceptual learning in the human visual system involve the earliest stages of visual cortex activity? This question was based, first, on animal literature suggesting profound effects of perceptual learning on early activity in the visual system (Gilbert et al., 2001; Ito et al., 1998; Schoups et al., 2001); secondly, on behavioural evidence in humans suggesting that retinotopically organised visual areas may be implicated in perceptual learning (Censor, Karni, & Sagi, 2006; Karni & Sagi, 1991; Karni, Tanne, Rubenstein, Askenasy, & Sagi, 1994); and third, on previous fMRI studies

(Furmanski et al., 2004; Schwartz et al., 2002) indicating changes in V1 activity following training on the texture discrimination task developed by Karni and Sagi (1991). We expected to observe retinotopically specific changes in C1 amplitudes which, within the limits of precision afforded by this component (see Foxe & Simpson, 2002), would indicate modulation of the first sweep of activation passing through primary visual cortex as a result of prior task exposure. Note that although perceptual learning may appear as a very simple form of learning, it cannot be explained in terms of pure bottom-up processes but requires substantial top-down input (Herzog & Fahle, 1998; Li et al., 2004).

Can endogenous attention induce filtering effects involving the earliest stages of visual cortex activity? This question directly relates to a previous fMRI study (Schwartz et al., 2005) which assessed the effects of attentional load (Lavie, 1995, 2005) on the processing of peripheral, irrelevant distractors. The load theory suggests that attentional selection does not generally occur early (Treisman, 1969) or late (Deutsch & Deutsch, 1963) during perception, but is adapted to the attentional demands of the current task. As previous studies had overwhelmingly reported no effects of endogenous attention on early visual cortex activity, we wanted to test this assertion using a task that would require attentional suppression rather than enhancement of stimuli. Again, we hypothesized that changes in attentional task demands would affect early visual cortex activity as indexed by the C1 component. Pilot studies for this second experiment suggested a third important question:

Do endogenous and exogenous attentional task demands interact at the earliest stages of visual cortex activity? We observed that slight changes of stimulation parameters induced large differences in attentional effects on early visual cortex activity and decided to test this observation in a separate experiment. Again using an attentional load paradigm, we hypothesized that higher demands on exogenous attentional mechanisms would disrupt any effects of endogenous attention on the C1 component, in accordance with exogenous attention serving the role of a 'circuit breaker' (Beck & Kastner, 2005; Connor, Egeth, & Yantis, 2004; Corbetta & Shulman, 2002; Serences et al., 2005). Previous studies had failed to demonstrate interaction effects this early in the visual hierarchy (Doherty, Rao, Mesulam, & Nobre, 2005; Hopfinger & West, 2006). Stronger recruitment of exogenous attention was operationalized by simultaneous presentation of target and distractor stimuli, as previous studies had indicated strong effects of synchrony on exogenous attention systems (Fournier, 1994; Kahneman, Treisman, & Burkell, 1983; Burg, Olivers, Bronkhorst, & Theeuwes, 2008; Wilson & Singer, 1981), possibly linked to the Gestalt law of common fate (Blake & Lee, 2005).

Chapter 2

Methods

This chapter will give an overview of the experimental methods employed to study the questions and hypotheses detailed in Section 1.6. I will first describe the behavioral tasks used in each of the three experiments and then provide details on data acquisition and analysis procedures. All experiments were conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee. Subjects provided informed consent and received a small payment for their participation. For details of the respective subject groups, please see the individual papers in the Appendix.

2.1 Experimental Stimuli and Tasks

Experiment 1 addressed the neural underpinnings of perceptual learning and employed an experimental task well-established in this field of research: the so-called texture discrimination task (TDT; Karni & Sagi, 1991). As shown in Figure 2.1, this is a dual task in which subjects are required to fixate a stream of rapidly presented letters while covertly monitoring peripherally presented stimuli containing a target texture, i.e. a small part of the overall stimulus that differs in its orientation from the background elements.

In our study, the letters presented were either an uppercase ‘L’ or an uppercase ‘T’ in varying orientations. Subjects indicated the identity of the letter with their right index and middle finger, respectively. Peripheral textures consisted of white horizontal line elements, with three diagonal elements hidden in the array. Here, participants indicated the overall orientation of the diagonal elements (i.e. whether they were arranged horizontally or vertically) with their right ring finger and pinky. Due to the high presentation rate and the fact that central letters and peripheral textures were simultaneously presented, this task is extremely difficult. In addition, a mask of randomly oriented ‘V’ shapes immediately followed this display in order to exclude any effects of retinal after-images.

Adequate performance on this task requires extensive training, which was provided during a first experimental session where target textures were selectively presented in one visual quadrant. It has been shown that initial training on most perceptual learning

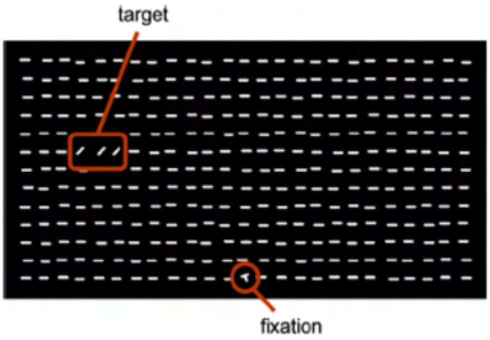

Figure 2.1: The texture discrimination task used in Experiment 1. Participants had to detect the identity of a letter presented at fixation while covertly monitoring the periphery for three diagonal bars which could be presented either in a horizontal or vertical arrangement.

task requires sleep for consolidation of learning effects (Karni et al., 1994; Karni & Sagi, 1991; Mednick, Nakayama, & Stickgold, 2003). We therefore asked subjects to return the following day after a night of normal sleep and recorded EEG while stimuli were presented either in the trained quadrant or the opposite quadrant of the same visual hemifield. Two groups of subjects were trained and tested in either the upper or the lower visual hemifield. In order to exclude task difficulty as a confounding factor, stimuli in both quadrants were presented well above threshold during the EEG testing session. A comparison of visual evoked potentials between trained and untrained quadrants should thus yield an indication of the effects of perceptual learning on early visual processing.

Experiment 2 examined the effects of attentional load (Lavie, 1995; Lavie & Tsal, 1994; Lavie, 2005) on early visual processing. As shown in Figure 2.2, stimuli consisted of T-shapes rapidly presented at fixation, which differed in colour and orientation. In the periphery, textures similar to those used in Experiment 1 were shown with a variable stimulus onset asynchrony (SOA) with respect to the central task stimuli. However, in this experiment, peripheral textures were completely irrelevant and subjects were asked to ignore them as best as possible. Again, separate groups of subjects were tested in either the upper or the lower visual field.

On different experimental blocks, participants performed either an easy pop-out detection task, responding to the colour of the T-shapes independently of their orientation, or a difficult conjunction detection, where both the colour and the orientation of the T-shapes had to be monitored. According to the load theory of selective attention (Lavie, 2005), higher demands on attentional resources lead to increased filtering of irrelevant stimuli. Comparison of visual evoked potentials from experimental blocks with low vs. high attentional load should thus allow for an assessment of the temporal characteristics of such increased attentional filtering.

For *Experiment 3*, we used essentially the same task and stimuli as for Experiment 2, with one important modification: central task stimuli and peripheral distractors were now presented simultaneously, based on psychophysical evidence that this would increase demands on exogenous attention (Fournier, 1994; Kahneman et al., 1983; Wilson &

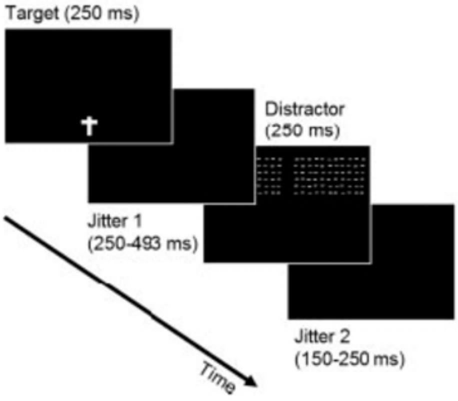

Figure 2.2: Stimuli and task structure used in Experiment 2. T-shapes of different colour and orientation were presented at fixation, followed by task-irrelevant peripheral distractors. Subjects either monitored only the colour or both colour and orientation of T-shapes, yielding different degrees of attentional load which were expected to affect processing of the peripheral distractors.

Singer, 1981). As exogenous attention has previously been shown to affect early visual processing (Khoe et al., 2005), effects of attentional filtering under high load should be reduced if distractors are presented simultaneously.

2.2 Data Acquisition

All data were continuously acquired at a sampling rate of 500 Hz using Neuroscan hard- and software, with 62 EEG channels referenced to the nose and two bipolar EOG channels for monitoring blinks and eye movements. All recordings were done in an acoustically and electrically shielded room and generally lasted between 60 and 90 minutes including breaks.

2.3 Data Analysis

For preprocessing and ERP analyses, we generally used BrainVision Analyzer version 1.05 (BrainProducts, Munich, Germany); parts of the analyses for Experiments 1 and 2 were verified using Neuroscan's Scan 4.3 software. Topographic analyses were conducted in Cartool (Functional Brain Mapping Laboratory, University of Geneva) and distributed source localization analyses were based on a local autoregressive average (LAURA; Peralta Menendez, Murray, Michel, Martuzzi, & Gonzalez Andino, 2004) procedure implemented as a Cartool plugin.

2.3.1 Preprocessing

In order to avoid habituation effects, the number of relevant peripheral stimuli was kept relatively low in all three experiments. We therefore chose to correct eye-blink artifacts using the regression-based approach proposed by Gratton, Coles, and Donchin (1983), as implemented in BrainVision Analyzer. If necessary, an initial high-pass filter was applied in order to reduce slow signal drifts, e.g. due to perspiration. Stimulus-locked epochs including at least the interval of from 100 ms before (-100) to 300 ms after (+300) stimulus onset were then extracted from the data, baseline-corrected, and submitted to semi-automatic artifact rejection as detailed in the individual papers in the Appendix.

2.3.2 Event-related Potentials

Visual evoked potentials were calculated for each subject and condition and low-pass filtered at 30 Hz. Care was taken to avoid filtering artifacts by re-extracting shorter epochs from the filtered data where appropriate. Individual subject VEPs were then used to semi-automatically extract peak amplitude and latency information on which statistical analyses were based. Grand averages across subjects were used for display purposes, topographical analyses, and source localization (see below). They were also employed to define electrodes and time-windows for peak extraction. Where distinction between ERP components based on visual inspection was ambiguous, topographic analyses were used to define the duration of each component.

2.3.3 Topographic Analyses

Topographic microstate segmentation (Michel, Seeck, & Landis, 1999; Pasqual-Marqui, Michel, & Lehmann, 1995; Pourtois et al., 2005)was used to objectively identify differences between experimental conditions in overall electrical activity and voltage distribution across the whole scalp. The underlying concept assumes that while a particular distribution of electrical activity (i.e., a voltage topography) observed at the scalp may be the result of a virtually unlimited number and combination of neural sources, differences in topography necessarily indicate differences in neural sources. In order to statistically distinguish between periods of topographical stability and dissimilarity, a spatio-temporal cluster analysis is applied across all time-frames of a particular recording. Usually, grand-average evoked potentials are used for initial identification of microstates and the latter are then fit to individual subjects' evoked potentials to verify any differences between experimental conditions observed at the level of grand averages. All these analyses steps were conducted in the dedicated software Cartool (Denis Brunet, Functional Brain Mapping Lab, University of Geneva).

2.3.4 Source Localization

While topographic analyses can detect changes in voltage distribution and thus distinguish intervals during which the same neural sources dominate EEG activity from moments when the configuration of sources changes, they do not permit to pinpoint the actual generators of the observed topographies. As a particular distribution of voltage values across the scalp can be the result of neural activity in a virtually unlimited number of brain areas, finding the most likely neural sources of any given topography requires additional processing to solve this so-called inverse problem. Two general approaches to this problem can be distinguished: equivalent current dipole (ECD) approaches already mentioned in the Introduction (Scherg & Berg, 1991), and distributed inverse solutions (Peralta Menendez et al., 2004).

The former assume that activity in circumscribed neural ensembles can be modeled by a single dipole reflecting the summation of dipolar electric fields elicited by synaptic input to the apical dendrites of pyramidal neurons in the cortex which are thought to underlie the EEG signal (Birbaumer & Schmidt, 1999; Westbrook, 2000). These approaches usually require the incorporation of advance knowledge regarding the number and approximate locations of neural sources to be modeled. The quality of inverse solutions is assessed as the fit between original and reconstructed voltage topographies.

Distributed source localisation procedures such the LAURA approach (Peralta Menendez et al., 2004) also require a large number of parameters to be defined a priori, but they subsequently allow for the calculation of the most likely distribution of activity in a large number generators (usually several thousands). The latter are equally distributed throughout the gray matter of either a template brain or an individual subject's anatomical MRI scan.

We opted for the second class of solutions (specifically, a LAURA solution implemented as a Cartool plugin, courtesy of S. Gonzalez and R. Grave, Electrical Neuroimaging Group, Geneva University Hospital), as the large extent of our peripheral stimuli should yield activity in correspondingly large patches of visual cortex, which may not be adequately modeled by a single dipole.

Chapter 3

Results

This section will provide a brief overview of the experimental results detailed in the papers in the Appendix.

3.1 Perceptual Learning Modulates Early Visual Cortex Activity

The results of Experiment 1 corroborated our hypothesis of modulations of early V1 activity, with one important exception: amplitudes of the C1 component differed between trained and untrained conditions only for the group of subjects trained and tested in the upper visual field; no effects of perceptual learning were observed in the lower visual field group.

Behavioral results of the training session clearly indicated effects of perceptual learning, with significantly reduced 80% texture detection thresholds across the three training blocks. This within-session effect was present in both the upper and lower visual field groups, as indicated by a non-significant interaction effect between the group and SOA factors. Performance variables measured during the EEG session the next day also failed to indicate differences between the visual field groups, with the number of misses and false alarms closely matched. However, post-EEG threshold measurements did indicate differences between groups, with significantly lower thresholds for the trained quadrant found only in the upper visual field group (Fig. 3.1).

Interestingly, similar group differences were observed at the electrophysiological level, with significant effects of perceptual learning on VEPs present only in the upper visual field group (Fig. 3.2): a measure of overall electrical activity across all electrodes (GFP) indicated significant differences between trained and untrained quadrants starting at 44 ms and lasting until after the peak of the C1; subsequent running t-tests indicated that these GFP differences were due to learning effects at central parieto-occipital electrode locations, in accordance with the usual topography of the C1 (cf. Fig. 1.2); finally, repeated measures ANOVAs across nine parieto-occipital leads (CP1, CPz, CP2, P1, Pz, P2, PO3, POz, PO4) revealed significant differences in peak amplitude, with lower values

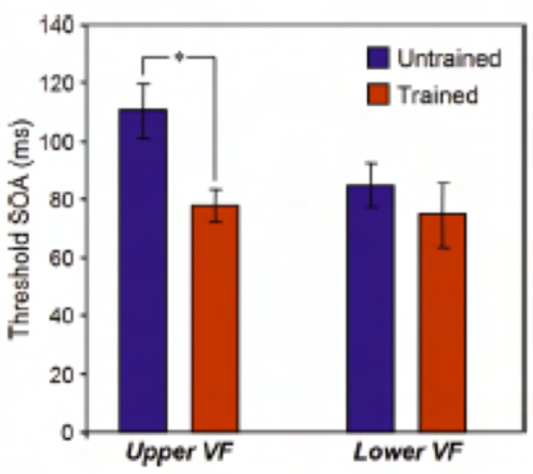

Figure 3.1: Effects of perceptual learning on texture detection thresholds on the following day. Data were acquired following EEG recordings, following the same procedure used during the initial training sessions. Results indicate significant improvements for subjects trained in upper visual field, but not for the lower visual field group.

observed in the trained quadrant. As can be seen in Figure 3.2B, the respective data from the lower visual field group failed to indicate any such effects. Possible reasons for this discrepancy are discussed in the papers in the Appendix. Notwithstanding this issue, our results corroborate and extend the earlier findings of Skrandies and co-workers (Ludwig & Skrandies, 2002; Skrandies & Fahle, 1994; Skrandies et al., 2001), who demonstrated very early effects of perceptual learning on ERP topographies. Later, extrastriate VEP components P1 and N1 were also analysed, but no effects of perceptual learning were observed at these processing levels.

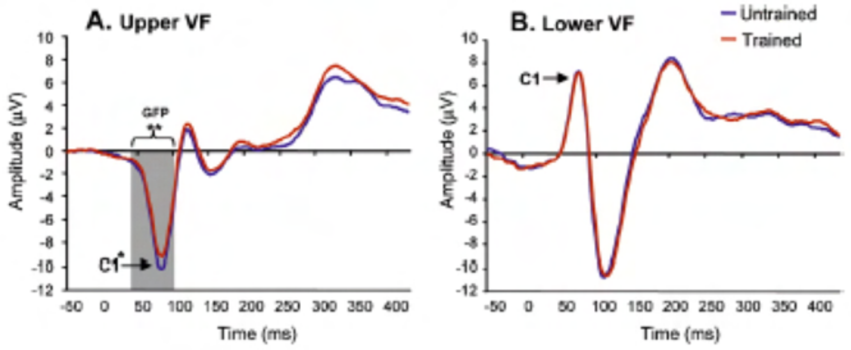

Figure 3.2: Effects of perceptual learning on visual evoked potentials. C1 amplitudes were selectively reduced following training in the upper visual field, but not in the lower visual field. Both global field power and standard peak amplitude analyses indicated that differences were significant only at central parieto-occipital locations.

Finally, distributed source localisation analyses were conducted to verify the likely neural sources of the C1. Their results indicated maximal activity during the C1 period near the occipital pole, in accordance with early visual cortex generators (data not shown; cf. Appendix). However, probably due to the limited spatial resolution offered by our method and the known anatomical variability of early visual cortex, we were unable to clearly distinguish between upper and lower visual field sources with these analyses.

Reference Pourtois, Rauss, Vuilleumier, and Schwartz (2008). Effects of perceptual learning on primary visual cortex activity in humans. *Vision Research*, 48, 55-62.

Contributions Gilles Pourtois and Sophie Schwartz conceived experiment; Sophie Schwartz programmed experiment; Gilles Pourtois and Karsten Rauss analysed data; Gilles Pourtois, Karsten Rauss, Sophie Schwartz, and Patrik Vuilleumier wrote manuscript.

3.2 Attentional Load Modulates Early Visual Cortex Activity

In Experiment 2, we found visual field asymmetries similar to those observed in Experiment 1: our hypothesis of increased attentional filtering during the earliest stages of visual processing in the cortex were corroborated in a group of subjects tested in the upper visual field, but the expected pattern of results was not obtained the lower visual field group.

Behavioural results indicated significant effects of attentional load: although overall error rates were low, subjects performed significantly worse and were significantly slower under high attentional load, where the task-stimulus stream had to be monitored for a conjunction of colour and orientation, rather than for colour only.

Analysis of VEPs elicited by the central task-stimuli (data not shown, cf. Appendix) indicated significantly increased N1 amplitudes, in accordance with previous reports of this component's role in difficult stimulus discriminations (Hopfinger & West, 2006; Luck, 1995). No effects of attentional load were observed on the preceding P1 component, and no C1 was observed for these centrally presented stimuli (Clark et al., 1995; Jeffreys & Axford, 1972a). In addition, no differences between upper and lower visual field groups were evident in the VEP traces, suggesting that results were not affected by differences in fixation accuracy or eye movements towards the respective distractor locations.

Analysis of peripherally presented, task-irrelevant distractors indicated significantly reduced C1 amplitudes under high attentional load in the upper visual field group, in accordance with our hypothesis and the predictions of the load theory of selective attention (Lavie, 2005). However, no such effect was observed for subjects tested in the lower visual field, reproducing the asymmetries observed in Experiment 1 (Fig. 3.3).

No effects of attentional load on later components of distractor-elicited VEPs were observed either in the upper or the lower visual field group. Additional topographic microstate segmentation analyses suggested very early (0-100 ms post-stimulus) differences in voltage topography between load conditions in the upper visual field group (data not shown), indicative of changes in the neural sources active during this time period. We

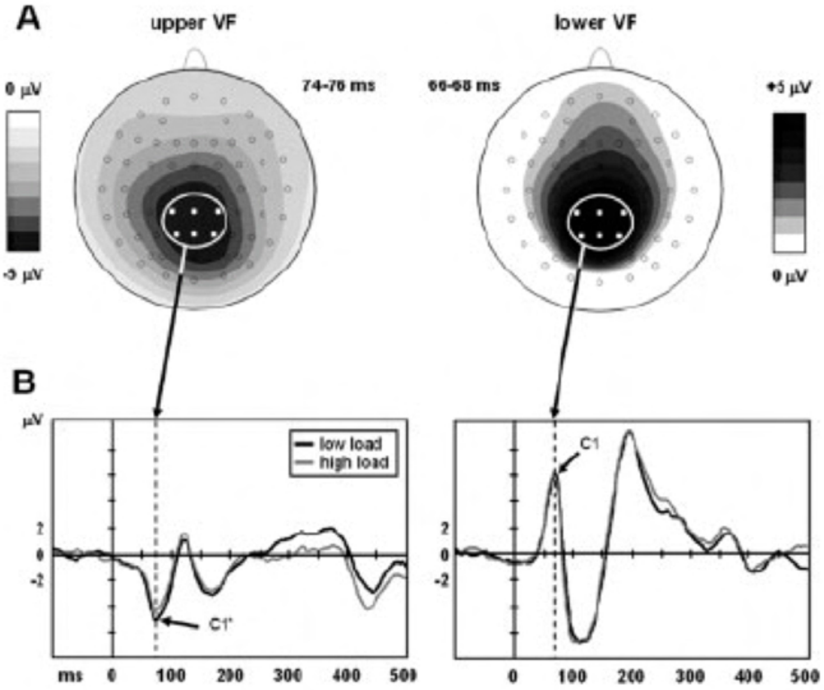

Figure 3.3: As in Experiment 1, visual evoked potentials from Experiment 2 indicated top-down modulations of the C1 component only in upper visual field. Traces shown as well as all analyses were calculated across the highlighted electrodes.

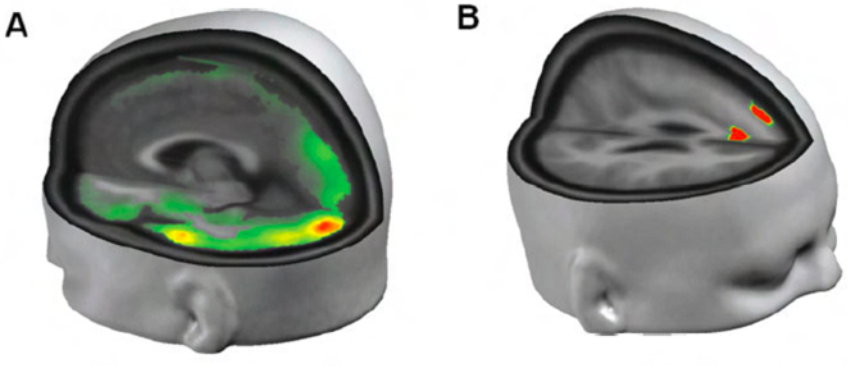

Figure 3.4: Distributed inverse solutions for the C1 interval (60-100 ms post-stimulus) in upper visual field subjects. Solutions based on data from all conditions indicate dominant activity around the occipital pole, in accordance with early visual cortex generators of the C1 (A). Activity between between load conditions was then compared across all subjects and sources by paired t-tests (B), with results indicating early differences in medial frontal regions as possible sources of the attentional effects observed at the VEP level.

therefore conducted detailed source localization analyses by comparing reconstructed neural activity between load conditions in each subject. Subsequent analysis of these differences across subjects yielded activity differences in medial frontal regions, possibly corresponding to the sources of top-down modulations evident at the VEP level (Fig. 3.4). However, we did not observe such early differences in early visual cortex, possibly due to the limited spatial resolution of our approach, as discussed above. Thus, Figure 3.4A depicts an inverse solution based on raw data for illustrative purposes only.

Reference Rauss, Pourtois, Vuilleumier, and Schwartz (2009). Attentional load modifies early activity in human primary visual cortex. *Human Brain Mapping*, 30, 1723-1733.

Contributions Sophie Schwartz and Gilles Pourtois conceived experiment; Sophie Schwartz programmed experiment; Gilles Pourtois and Karsten Rauss acquired data; Karsten Rauss and Gilles Pourtois analysed data; Karsten Rauss, Gilles Pourtois, Sophie Schwartz, and Patrik Vuilleumier wrote manuscript.

3.3 Exogenous and Endogenous Attention Interact During Early Visual Cortex Activity

Experiment 3 was based on pilot studies for Experiment 2 suggesting that changes in stimulus timing could have a profound effect on early visual cortex activity. We examined this issue in a separate experiment, this time with only one group of subjects tested in the upper visual field. The most important change with respect to Experiment 2 was that the elimination of the variable stimulus onset asynchrony (SOA) between central task stimuli and peripheral distractors, such that on distractor trials, both stimuli appeared simultaneously.

Behavioral results were comparable to those obtained in Experiment 2, i.e. performance was lower and reaction times higher under high attentional load. There was no general increase in task difficulty compared to the asynchronous presentation in Experiment 2: analysing behavioral data were across both experiments, neither the experiment factor nor any of its interactions were significant, indicating that performance levels did not differ between the two paradigms. (Note that presentation times were prolonged in Experiment 3 to produce this equivalence in task difficulty.)

Differences between the two experiments were, however, evident at the level of task-only VEPs: even if no distractor was presented, P1 amplitudes differed between high and low load conditions, whereas such an effect was not observed in Experiment 2. Specifically, P1 amplitudes were higher under high load, possibly due to stronger engagement of attentional suppression mechanisms which have been linked to the P1 component (Freunberger et al., 2008; Luck, 1995). As in Experiment 2, N1 amplitudes were significantly increased under high attentional load, in accordance with higher demands on stimulus discrimination mechanisms in this condition.

The most striking effect observed in this follow-up study, however, was a complete reversal of the effects of attentional load on the C1 component elicited by trials on which a distractor was presented (Fig. 3.5): that is, attentional effects on the C1 were again evident, but this time the component was augmented under high attentional load. Although a direct comparison of these results with those obtained in Experiment 2 is complicated by the fact that visual responses were elicited by simultaneously presented central task stimuli and peripheral distractors in the present paradigm, the basic characteristics of the C1 argue against any contribution of the foveally presented task stimuli to this effect. Corroborating this interpretation, no trace of a C1 was evident in the task-only VEPs (cf. figures in the Appendix).

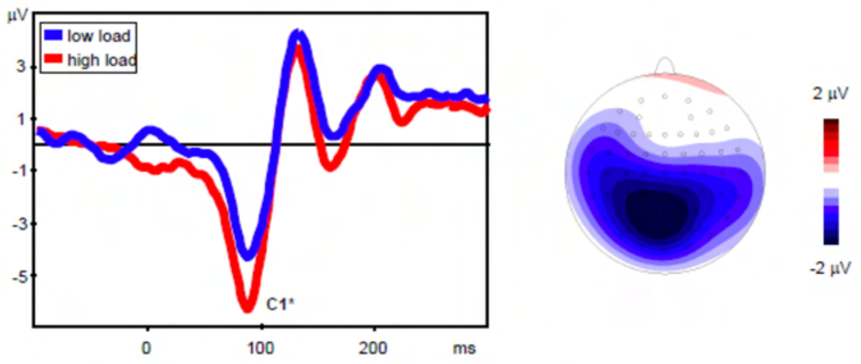

Figure 3.5: Attentional modulations of C1 amplitudes were observed in Experiment 3, but they were opposite in direction compared to Experiment 2. This striking finding was predicted on the basis that simultaneous presentation of central task-stimuli and peripheral distractors should engage exogenous attentional mechanisms that may override endogenous attentional filtering effects as observed for non-simultaneous presentation conditions in Experiment 2. The topography of the difference (high minus low load) shown on the right is highly similar to the standard C1 topography expected for upper visual field stimulation and thus supports the notion that the effect has its origins in early visual cortex.

The pattern of results for the subsequent P1 and N1 components was more complex: modulations of the P1 component were only if contributions from the peripheral distractors were explicitly considered in the analysis. On the other hand, N1 amplitudes were generally higher in the presence of distractors, but modulated by attentional load only in the absence of distractors. The latter finding could be due to a simple ceiling effect on N1 amplitudes on distractor trials. Alternatively, it may indicate a functional interaction of exogenous and endogenous attentional mechanisms at processing stages corresponding to this component, as has been suggested previously (Hopfinger & West, 2006).

Considering this proposed role of the N1 component, we asked whether it might relate to early visual cortex activity. Indeed, N1 modulations in task-only trials correlated significantly with C1 modulations on task-plus-distractor VEPs, such that stronger C1 modulations predicted stronger N1 effects (Fig. 3.6A). Strikingly, a significant correlation of opposite direction was observed when the same analysis was conducted on the data from Experiment 2 (Fig. 3.6B).

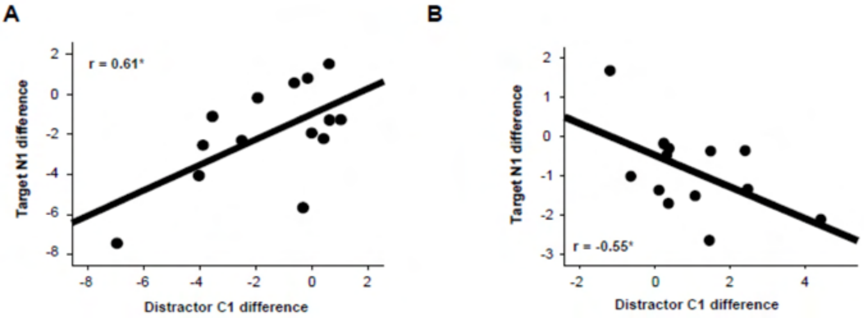

Figure 3.6: Correlations between attentional effects (high minus low load) on distractor-elicted C1 amplitudes and task-elicited N1 amplitudes. (A) Data from Experiment 3 indicate that *increases* in C1 amplitude under high load are correlated with increases in N1 amplitude on task-only trials. (B) Equivalent analyses conducted on the data from Experiment 2 show that *decreases* in C1 amplitude correlate with increases in N1 amplitude.

Reference Rauss, Pourtois, Vuilleumier & Schwartz (submitted). Stimulus synchrony modulates effects of endogenous attention on early visual processing.

Contributions Sophie Schwartz and Gilles Pourtois conceived experiment; Sophie Schwartz programmed experiment; Gilles Pourtois acquired data; Karsten Rauss analysed data; Karsten Rauss, Gilles Pourtois, Sophie Schwartz, and Patrik Vuilleumier wrote manuscript.

Chapter 4

Discussion

In summary, the results of our experiments strongly suggest that top-down modulations of early activity in human primary visual cortex can be detected using EEG, albeit under closely controlled conditions. These results are in accordance with recent evidence in both animals (Hupé, James, Girard, Lomber, et al., 2001; Li et al., 2004; Motter, 1993) and humans (Khoe et al., 2005; Pourtois et al., 2004; Stolarova et al., 2006), but they challenge the long-standing view of V1 as an inflexible stimulus-detection module, unaffected by attentional influences in particular (e.g. Hillyard et al., 1998).

While the experiments for this thesis were conducted, several studies not described in the Introduction have been published whose results further corroborate this conclusion. I will briefly review them below, before outlining an ecological framework placing the reviewed literature and our experiments within the context of natural viewing, in the hope of providing a unified picture of the importance of top-down effects on early visual cortex activity. I will then address the limitations of our experiments and indicate directions for future research.

4.1 Recent Studies of the C1

I will first consider new studies that systematically mapped early visual cortex activity in humans over the last three years; I will then describe experiments published during the same interval whose results corroborate our findings of top-down modulations evident at the level of the C1. To my knowledge, only one study has been published in the last three years claiming the opposite: Yoshor, Ghose, Bosking, Sun, and Maunsell (2007) recorded intracranial EEG in epileptic patients during a spatial attention task and observed comparatively modest attentional modulations at locations near the occipital pole. However, the authors did not provide information about their subjects' medication; effects of selective attention at the behavioural level were verified only in three out of six subjects; and the claim that recording electrodes were localized to early visual areas is not substantiated by figures or anatomical coordinates. Most importantly, as two subjects did show attentional modulations, the authors main claim is that attention does not strongly modulate neuronal responses in early human visual cortex, in accordance with both animal and human studies showing comparatively stronger effects of attention in extrastriate areas. However, their results do not exclude that under optimal task and recording conditions, such effects may be present and functionally important.

4.1.1 Recent Mapping Studies

Foxe et al. (2008) followed up on earlier electrophysiological findings in monkeys (Schroeder, Mehta, & Givre, 1998; Schroeder, Tenke, Givre, Arezzo, & Vaughan Jr, 1991) suggesting different contributions of magno-(M) and parvocellular (P) systems to initial activity in V1 as measured on the scalp. Using high luminance contrast stimuli activating both M- and P-systems, low luminance contrast stimuli isolating the M-system, and isoluminant chromatic contrast stimuli isolating the P-system, they observed a clear C1 component only if the P-pathway was activated. The authors argue that spatial attention may exert its influences mainly via the dorsal visual stream, which is dominated by the M-system and that consequently, a component apparently dominated by the P-system may not be the ideal index of attentional effects on early sensory processing. Relating these findings to our experiments, the high contrast and high spatial frequency of the stimuli employed may effectively have led to predominant activation of the P-pathway, thus facilitating the observation of top-down effects on the C1 component.

The most comprehensive mapping study to date was recently published by Hagler et al. (2009), who used isoeccentric checkerboard patterns while simultaneously measuring EEG and MEG. In addition, the authors acquired structural and functional MRI, including retinotopic mapping data. Combining all modalities, they were able to substantially reduce the complexity of the inverse problem by mapping individual dipoles to the representation of each stimulus patch in early visual areas V1 through V3. Individual anatomical differences thus yielded a characteristic signature of the different visual areas in each subject, effectively reducing cross-talk among the modeled sources. In accordance with the results of Foxe and Simpson (2002), relatively small delays were observed between sources reflecting activity in V1, V2, and V3, with substantial activation being present in extrastriate visual cortex at the peak latency of sources located in V1. Although laborious (data of only 2 subjects were presented by Hagler and colleagues), this technique seems highly promising for future studies of top-down effects on early sensory processing, as it uses individual variability in visual cortex anatomy to increase sensitivity for detecting top-down effects in early visual cortex. A similar approach was suggested even more recently by Ales, Carney, and Klein (in press).

4.1.2 Recent Studies of Top-down Effects

Chaumon, Drouet, and Tallon-Baudry (2008) used a modified contextual cueing paradigm and MEG to examine the effects of unconscious associative memory on the earliest stages of cortical visual processing. Repeatedly presented distractor patterns could be associated with the same target position in a visual search display, thus allowing predictions based on the distractors; in a non-predictive condition, on the other hand, target positions changed for each instance of a particular distractor pattern. Behavioral results suggested rapid learning effects, with mean reaction time differences of 80 ms for the last four of 12 presentations of each distractor pattern. Differences in MEG recordings between conditions were observed as early as 50-100 ms post-stimulus, selectively over posterior scalp regions. Both their earliness as well as their topography suggested that these effects may be linked to differences in early visual cortex activity. Importantly, a battery of debriefing tests showed that contextual memory of distractor patterns and target locations remained completely unconscious. Chaumon et al. (2008) concluded that early stages of processing in the visual cortex may be influenced by implicitly learned contextual associations, possibly via an interaction of rapid feedback mechanisms and contextual memories stored locally in early sensory cortices. It seems plausible that these contextual memories were used to guide attentional selection of the locations to be searched for targets. According to the working definitions provided in the Introduction, the temporal window over which these memories are acquired and employed would qualify them as top-down effects. Chaumon et al. (2008) speculated that effects of memory-based attention may differ from more frequently used attentional paradigms that failed to indicate such early effects (Heinze et al., 1994; Martinez et al., 1999; Noesselt et al., 2002). However, our results on the early effects of attentional load as well as the studies described in the following indicate that classical endogenous cues may also produce attentional modulations at the level of primary visual cortex.

Kelly, Gomez-Ramirez, and Foxe (2008) were the first to publish observations indicating an effect of endogenous attention on C1 amplitudes. They directed the attention of their participants to a particular location in the peripheral visual field using a centrally presented arrowhead and compared responses to peripherally presented gratings with and without attention. Based on the findings and suggestions of Foxe and Simpson (2002), they used a separate mapping procedure to select in each subject the diametrically opposite locations in the upper and lower visual field associated with the biggest difference between positive- and negative going C1 peaks. With this simple adaptation to the large individual differences in functional neuroanatomy of the visual cortex (Amunts et al., 2000; Dougherty et al., 2003; Hasnain et al., 1998) and the resulting variability of C1 topographies (compare Fig. 1.2; Proverbio et al., 2007), they observed significant differences in early visual cortex activity as a function of endogenous attention: the subjects' task was to detect a slight change of contrast in the peripherally presented gratings and C1 amplitudes were found to be increased when subjects were actively attending to the location at which the grating appeared.

Using MEG and a multisensory setup, Poghosyan and Ioannides (2008) observed attentional effects on early activity of auditory and visual cortices, both in their evoked potential data and subsequent distributed source localization analyses. Specifically, spatial attention directed to one ear or one side of the visual field led to increased activity in regions implicated in simple sensory evoked activity (i.e. without attention) in either modality. Importantly, the time-course of attentional effects was highly similar to that observed for sensory activity without attention, arguing against the notion that primary sensory cortices are affected by top-down influences only during later, re-entrant stages of processing (Martinez et al., 1999; Roelfsema et al., 2007). In their discussion, Poghosyan and Ioannides (2008) address the question of why previous studies both in animals and humans using similar paradigms have often reported null findings. They argue that source analyses using ECD approaches are ill-conceived for the study of early effects of attention in the visual domain, as they usually assume a single dipole at the level of V1. In light of the findings of Foxe and Simpson (2002) this assumption seems doubtful. Distributed source localization techniques should provide higher sensitivity for early attentional effects as they include simultaneously active sources (e.g., the sources of putative top-down effects). This was empirically verified by additional ECD analyses, in which single sources used to fit the first component of the evoked magnetic field were either unconstrained or fixed to the locations obtained from the previous distributed source analyses. Results showed that the displacement of dipoles obtained in the unconstrained analyses effectively wiped out early attentional modulations in these sources. Regarding delayed attention effects observed in animal experiments, Poghosyan and Ioannides (2008) argue that neuronal synchrony may play a central role in early attentional modulations (Buehlmann & Deco, 2008; Engel, Fries, & Singer, 2001; Fries, Reynolds, Rorie, & Desimone, 2001), and that both single-unit activity and local current source density may not be sufficiently sensitive to large-scale synchrony to reliably detect attentional effects at very early processing stages.

Given these issues, it is interesting that in a recent EEG study, Karns and Knight (2009) reported a dissociation between evoked gamma-band responses and ERPs for the tactile modality, where they observed early effects of intermodal attention only on the former. Their results also extend the findings of Poghosyan and Ioannides (2008) by demonstrating very early effects of attention on both auditory and visual evoked potentials. In their task, subjects responded to stimuli in one of the three modalities, with attended modalities varied between experimental blocks. Amplitudes of the C1 and N1 components as well as early evoked gamma-band responses were augmented when subjects were attending to visual stimuli. Attentional effects were restricted to the early phase of the C1, arguing against extrastriate contributions (Foxe & Simpson, 2002).

Finally, a recent study by Fu et al. (2009) reported interactive effects of exogenous attention and perceptual load on early visual processing: increased C1 amplitudes for exogenously cued stimuli were observed only under high perceptual load. However, from the published figures it seems difficult to exclude low-level stimulus differences as a possible confound of this effect and control experiments yielded equivocal results. Nevertheless, these data may reflect mechanisms similar to those that produced the results of Experiment 3 in that exogenously cued stimuli under high perceptual load elicited higher C1 amplitudes, although increased attentional filtering would actually be required for these stimuli.

4.2 An Ecological Framework for Top-down Effects on Early Visual Processing

The studies conducted for this thesis as well as those reviewed in the Introduction and the preceding section suggest two conclusions: First, V1 in the human is not as inflexible and as impermeable to top-down effects as was previously believed. Secondly, these effects are less pervasive than those observed for later VEP components. In particular, the detection of top-down modulations of the C1 seems to require highly specific experimental setups, such as individual mapping of the component's topography (Kelly et al., 2008), stimuli adapted to the characteristics of V1 (Foxe et al., 2008), including differences across the visual field (Experiments 1 and 2), and close monitoring of stimulus timing (Experiments 2 and 3).

This specificity suggests that the underlying neural mechanisms are less widely recruited and less pervasive compared to those forming the basis of top-down effects on higher levels of the visual hierarchy. Thus, on the empirical level, recent findings showing very early modulations of sensory processing extend, rather than contradict, the large body of literature on the effects of attention on visual evoked potentials in particular (Hillyard & Anllo-Vento, 1998; Hillyard et al., 1998): they show that under particular conditions, well-characterised gain control mechanisms of selective attention may operate even at the level of primary sensory cortices. On a conceptual level, however, the consequences of the emerging view of V1 as an adaptive processor (Gilbert & Sigman, 2007) are far-reaching: for example, it has been suggested that theories on the attentional functions of the thalamus (Crick, 1984; McAlonan et al., 2006) are invalidated by experimental findings showing no influence of attention on initial processing in V1 (Martinez et al., 1999). The evidence reviewed above suggests otherwise: there is no primary-secondary barrier separating V1 from extrastriate visual areas in terms of attentional or other top-down influences. Rather, it is the functional characteristics of different cortical areas and their relation to stimulus characteristics and task demands that determine the type and strength of top-down modulations observable at any particular level of processing.

It is noteworthy in this respect that some of the earliest reports of higher-level effects on the C1 were obtained with stimuli of high ecological and evolutionary importance: thus, the original report of an emotional effect on C1 amplitudes (Pourtois et al., 2004) was obtained by contrasting fearful with neutral faces and such an effect was absent for a similar comparison involving happy facial expressions; and Stolarova et al. (2006) used highly unpleasant emotional images as unconditioned stimuli. Although it is still debated whether emotional stimuli can be processed in the complete absence of attention (Bishop, Jenkins, & Lawrence, 2007; Pessoa, McKenna, Gutierrez, & Ungerleider, 2002; Vuilleumier, Armony, Driver, & Dolan, 2001), there seems to be agreement that due to their ecological and evolutionary importance, they require comparatively less attention to be processed and perceived than comparable stimuli without emotional content. At the neural level, this relative predominance of emotional information may be implemented via connections from the amygdala to early as well as object-specific visual areas, with the amygdala receiving advance information on emotional content via subcortical pathways (LeDoux, 2007; Morris et al., 1999; Vuilleumier & Pourtois, 2007).

As reviewed above, other ecologically important stimulus characteristics have been shown to profoundly affect early visual processing: thus, the studies of Hupé and colleagues (Hupé, James, Girard, & Bullier, 2001; Hupé, James, Girard, Lomber, et al.,

2001) demonstrating effects of input from motion-sensitive area MT into lower visual areas V1 through V3 underline the importance of movement information for the integration of the fragmented image coded at the level of primary visual cortex. The recent study by Fu et al. (2009) as well as Experiments 2 and 3 of the present thesis show that under appropriate conditions, involuntary attentional orienting can induce changes at the level of the C1, in accordance with the importance of pop-out stimuli and synchrony between visual events.

While the neurophysiological implementation of such rapid effects on the earliest cortical stages of visual processing requires further investigation, these findings suggest that specialised feature detectors such as the amygdala or MT impinge on all stages of visual processing. This is not surprising considering the general-purpose architecture of primary visual cortex and its associated relative blindness to all but the most simple stimulus characteristics. However, it leads to a paradoxical situation in which higher visual areas need V1 input in order to detect relevant stimulus attributes and V1 needs input from higher visual areas in order to efficiently enhance or filter information at the earliest stage of cortical processing.

This paradox is likely to be less pronounced under conditions of natural viewing, where the influence of higher-order areas on early sensory processing would most frequently be based on previous stimulation and act on neural activity related to subsequent stimuli as the visual environment changes continuously. According to the definitions outlined in the Introduction, natural viewing of non-stationary environments would thus mainly involve top-down effects, in the sense that stimulus history is used to frame processing of the current stimulus episode. This constitutes an obvious shortcoming of the proposed definition of top-down and feedback effects: it seems intuitively implausible (and may be empirically impossible) to split perception of a coherent visual scene into categories of "current" stimuli producing feedback and "previous" stimuli inducing top-down effects.

On a conceptual level, the issue may be resolved by extending the definition of the "current stimulus" to encompass coherent visual scenes as a whole (Gibson, 1986). Depending on the context, the latter may be anything from a static stimulus pattern to a complete visual environment changing coherently and with a high degree of predictability. I will not discuss these conceptual issues further, but it is worth noting that such an extended definition of what constitutes a visual stimulus would allow for the inclusion of eye movements as an important factor in natural vision into current models of visual perception (Rajkai et al., 2008).

On the physiological level, the properties of the visual system as a whole must certainly reflect the fact that visual input changes constantly under natural conditions. Thus, early visual areas can be expected to adapt their processing characteristics in such a way as to preferentially retain or enhance those stimulus representations most likely to be affected by positive feedback; and to inhibit or filter those representations that are least likely to be processed further. This notion is related to recent conceptualisations of primary visual cortex activity as an instance of predictive coding (Muckli et al., 2005; Rao & Ballard, 1999; Summerfield, Trittschuh, Monti, Mesulam, & Egner, 2008), where neural signals are related less to a stimulus per se than to its congruence with internal predictions calculated on the basis of previous input to the system.

As reviewed by Rao and Ballard (1999), early studies in this direction were motivated mainly by the question of how the central nervous system achieves efficient (i.e. non-redundant) coding of perceptual input. Basic neurophysiological characteristics of primary visual cortex neurons such as end-stopping have been successfully reproduced in predictive-coding models (Rao & Ballard, 1999), and it has been shown that illusory contours elicit activity along the representation of equivalent real contours in early visual cortex (Muckli et al., 2005). As reviewed in the Introduction, Shuler and Bear (2006) found that a substantial proportion of V1 neurons in the rat exhibit reward timing after a period of learning in a simple operant conditioning paradigm. More recently, Dambacher, Rolfs, Göllner, Kliegl, and Jacobs (2009) have shown that during sentence reading, visual evoked potentials differ within the first 100 ms post-stimulus between conditions in which predictable vs. unpredictable words were presented. This indicates a rapid comparison between expected and actual input to the visual language system probably involving the earliest stages of cortical visual processing. Instances of predictive coding have also been reported at the other end of the cortex, with medial frontal regions encoding predictive templates against which perceptual input is presumably matched (Summerfield et al., 2006). Furthermore, it has been proposed that predictive coding might be a fundamental property not only of sensory processing, but of brain function in general (Bar, 2007). Even supposedly low-level adaptation phenomena such as repetition suppression in fMRI have been re-interpreted in terms of predictive coding (Summerfield et al., 2008).

Consequently, the properties of early visual processing as assessed in most of the studies described in the preceding sections (including our own experiments) may reflect, not hard-wired properties of visual cortex, but contingencies learned by a flexible system exhibited to our usual environment. The strenuousness of perceptual learning (Fahle, 2005; Herzog & Fahle, 1998; Karni & Sagi, 1991; Schwartz et al., 2002) underlines this fact, as do a host of early studies on the effects of sensory deprivation in newborn animals (Wiesel, 1982). I propose that learned contingencies in a perceptual system are most clearly expressed in predictions about forthcoming sensory input and I believe that future studies will benefit from explicitly considering to what extent predictive mechanisms at early visual processing stages may contribute to task performance before concluding that top-down effects are or are not observable at the level of V1. The strongest possible test of these proposals would be to show that experimentally induced top-down predictions affect the earliest stages of cortical visual processing even in the absence of visual stimulation. This would extend previous neuroimaging findings on preparatory effects in visual cortex (Chawla, Rees, & Friston, 1999; Kastner et al., 1999; Ruff & Driver, 2006) by showing that the latter can affect subsequent processing very early along the visual hierarchy.

In such a predictive-coding framework, selective attention is best understood as a mechanism allowing for moment-to-moment flexibility in the relatively stable network of learned associations on which predictive coding is based. Depending on the stability of learned associations recruited by a particular task, attentional mechanisms may have to exert a relatively strong influence in order to adapt processing to current task demands, which may be one of the reasons why it has been difficult to observe their effects on early vision in trial-by-trial (as opposed to blocked) designs. On the other hand, the strength of learned predictions may also help to uncover contributions of early visual cortex to high-level tasks, as demonstrated in the sentence-reading experiment of Dambacher et al. (2009). A question of particular interest will be whether very early effects of emotional stimuli are based on separate, subcortical predictive mechanisms that employ cruder template-matching algorithms. The limits of moment-to-moment flexibility in early visual cortex could in turn be defined by tasks which require extensive perceptual learning before changes in neural activity can be observed. When interpreted in this light, our results may reflect how the visual system handles different degrees of interference depending on their ecological importance:

- Irrelevant information separated both spatially and temporally from relevant information can be suppressed at the earliest levels of cortical processing (Experiment 2). Here, task stimulus and distractor do not share any central features and the visual system can rapidly suppress distractors without risking loss of crucial information. Even though SOAs were jittered, stimulation parameters may have offered a relatively high degree of predictability due to the fact that task stimuli and distractors were always interleaved in time.

- In contrast, irrelevant information sharing temporal characteristics with a relevant stimulus cannot be filtered at such early processing levels and may actually be enhanced the more attention is required by the relevant stimulus (Experiment 3). Abrupt onsets in general (Egeth & Yantis, 1997; Yantis & Jonides, 1990) and simultaneous onsets in particular (Fournier, 1994; Kahneman et al., 1983; Wilson & Singer, 1981) have been shown to capture attention in an automatic, exogenous fashion and this may be linked to the Gestalt law of common fate (Blake & Lee, 2005). I propose that simultaneity acts as an important indicator of relevance in our visual environment, so that it cannot be ignored at the earliest levels of cortical processing. Thus, top-down knowledge about the irrelevance of one of two simultaneous events could only act at later stages of processing.

- Finally, irrelevant information that is both spatially and temporally coincident with relevant information can be suppressed at early visual processing stages only after extensive training (Experiment 1).

In the future, it would be interesting to test whether an initial period of learning may be present even in comparatively simple suppression paradigms such as the one used in Experiment 2. Furthermore, one could hypothesize that training on the simultaneous paradigm used in Experiment 3 would lead to a reversal of the observed effects of exogenous attention on the C1. In a similar vein, comparison of VEPs acquired during and after perceptual learning in a paradigm similar to Experiment 1 could yield important clues as to the time-course of the observed ERP effects. Such studies may provide important information on the relationship between attention and learning in early sensory processing: it has been proposed that both depend on similar mechanisms at the cellular level (Mehta et al., 2000b) and, although speculative, it may turn out that our three paradigms simply differ in terms of the extent of re-wiring of early sensory cortex networks required to efficiently suppress distracting information.

The view outlined above is related to the Reverse Hierarchy Theory of visual learning and perception proposed by Ahissar and Hochstein (Ahissar & Hochstein, 2004; Hochstein & Ahissar, 2002), which states that both perceptual learning and visual perception itself are the product of two interactive mechanisms: first, a crude-and-fast first guess corresponding to the representation of the initial sweep of activity arriving in higher cortical areas; and second, a subsequent reverse-hierarchy resolution of perceptual conflicts and difficult tasks, where higher areas guide in-depth processing by recursing onto the still-activated representations in lower areas. The framework suggested here extends this theory in three aspects: first, by explicitly considering natural viewing as the basis of the characteristics of the visual system as assessed in the laboratory; secondly, by indicating a process mediating these characteristics, namely predictive coding; and finally, by showing that under appropriate conditions, top-down (or reverse-hierarchy) processing can affect the earliest stages of the initial feedforward sweep of activity in the visual system.

4.3 Limitations

The interpretation of the experimental results reported above is subject to several limitations. I will first consider problems related to experimental design and analysis techniques and then address theoretical issues.

A limitation of Experiment 1 is the psychophysical procedure we used during training and for threshold detection following EEG acquisition: in both cases, we did not use adaptive staircase procedures, but simply presented a fixed number of trials at a particular SOA before diminishing the latter. This method can be questioned on several grounds, but it does have the advantage of equating stimulus exposure across subjects. Additionally, the fact that learning clearly occurred throughout the training session and that learning effects were present following EEG acquisition indicate that the procedure achieved its goal. Finally, although the precision of the measured thresholds may be limited, this does not affect the interpretation of our electrophysiological results, as the latter were acquired with suprathreshold stimulation in all conditions.

A limitation of Experiments 2 and 3 is the use of a blocked design rather than trial-by-trial modulations of attention. Thus, from our data, it is not possible to say whether similar effects would be observed if attentional demands vary on a shorter time-scale. The rationale for choosing a blocked design was to maximize the possible effects of attention, as previous studies (many of which used trial-by-trial designs) overwhelmingly failed to observe C1 modulations. However, the recent report of Kelly et al. (2008) clearly indicates that attentional effects on the C1 can also be observed in event-related experimental designs if individual differences in the component's topography are appropriately considered.

The results of Experiment 3 were interpreted in terms of direct and indirect comparisons of those obtained in Experiment 2. I already mentioned that the C1 effects observed in Experiment 3 might be questioned as they relate to trials in which central task-stimuli and peripheral distractors are presented simultaneously. As outlined above, the retinotopic characteristics of the C1 make any contribution of the central task stimulus unlikely; however, it is impossible to definitely exclude such an effect. Unfortunately, any study comparing simultaneous vs. non-simultaneous interference effects would be affected by this problem. An additional issue relates to the fact that different distractors were used in the two experiments (see Appendix). One way to verify that exogenous and endogenous attention indeed interact very early in the visual system would be to assess interference effects across several SOAs so as to map them in time. More generally, our findings could be tested in a paradigm using non-temporal stimulus characteristics to recruit exogenous attentional mechanisms, for example by using emotional vs. non-emotional distractors.

In all three experiments, we observed initial activity in early visual cortex using distributed inverse solution techniques. However, the effects of attention observed in Experiments 2 and 3 mapped onto differences in source activity in predominantly frontal areas and no significant differences were observed in the occipital lobe. This finding seems to contradict the differences observed at the ERP level. However, as pointed out above and in the papers in the Appendix, these results may primarily reflect a lack of spatial resolution of the LAURA procedure, particularly at the level of early visual cortex, whose anatomical variability may not be effectively captured by the template brain used. As shown recently (Hagler et al., 2009; Im et al., 2007), source reconstruction based on individual functional anatomy could yield better results; a fourth experiment is currently underway which will make use of these techniques (see below).

On the results level, it is obvious that the visual field asymmetries observed in Experiments 1 and 2 require further detailed study. Although we have outlined physiological differences between upper and lower hemiretina systems as a possible reason for our disparate findings in upper and lower visual field, a detailed examination of these differences in the same group of subjects is needed to corroborate this hypothesis. Subsequently, stimuli adapted to upper and lower visual field characteristics could be used to test whether there is after all a general difference in attentional permeability between visual hemifields.

A more general limitation of all three experiments is the uncertain degree of correspondence between the C1 component and V1 activity. As mentioned in the Introduction, it has been suggested that only the initial phase of the component corresponds to activity limited to V1 and that the component's peak might already contain substantial contributions both from higher visual regions and feedback effects originating from as far away as prefrontal cortex (Foxe & Simpson, 2002; Vanni, Warnking, et al., 2004). From a strictly empirical point of view, this does not invalidate our findings, as they still address the important issue of how early on in the sequence of VEP components one may observe top-down effects. On the other hand, this issue makes it difficult to infer top-down modulations of activity specifically and exclusively in V1 from surface EEG recordings. I have tried to take this problem into account by describing as "early visual cortex activity" the processing stages corresponding to the C1 component, most notably in the thesis title. I hope that the reader will nevertheless be convinced by the review of both animal and human literature that top-down effects are at least likely to occur at the level of V1. However, given the numerous studies describing comparatively larger effects of spatial attention at higher levels in the visual cortex hierarchy and the fact that we did not acquire retinotopic mapping data in our subjects, I cannot exclude that the differences in C1 peak amplitude observed in our experiments may be partly caused by differential activity in, for example, V2. As for rapid feedback from higher structures such as prefrontal cortex suggested by earlier reports (Foxe & Simpson, 2002), I am not aware that they have been conclusively demonstrated for strictly non-emotional stimuli as employed here. That is, while neurophysiological correlates of very early feedback effects from the amygdala onto visual cortex have been described (Morris et al., 1999), equally rapid effects of endogenous attention would most likely be achieved via sustained top-down modulations originating in higher cortical areas and gating information processing in sensory cortices (Gilbert & Sigman, 2007), rather than by a trial-to-trial feedback mechanism involving crude-and-fast subcortical processes.

4.4 Future Directions

Several proposals for future studies have already been outlined in the two preceding sections. In the following, I will focus on a study closely related to Experiments 1-3 that we are currently conducting. The goals of this study were twofold:

First, as described in the Introduction, some of the original findings of C1 modulations as a function of higher cognitive processes were obtained in studies using emotional stimuli (Pourtois et al., 2004; Stolarova et al., 2006). However, in the study of Pourtois et al. (2004), a certain amount of attention may have been focussed at the locations where task-irrelevant emotional stimuli were presented, as the same locations were subsequently occupied by relevant probe stimuli. Thus, the effects observed at the level of the C1 cannot be unequivocally attributed to the emotional content of the stimuli as the latter may have interacted with attentional mechanisms. Similarly, Stolarova et al. (2006)used a conditioning paradigm to produce C1 modulations, thus assessing the combined effects of learning and attention on early visual processing. We therefore wanted to test whether emotion by itself can modulate early visual processing, even if both the emotional stimuli and their spatial locations are completely task-irrelevant.

Secondly, we wanted to design an experiment that would allow us to adequately test the predictions of the biased-competition theory of attention, which was developed mainly on the basis of electrophysiological recordings in animals (Desimone, 1998; Luck et al., 1997; Moran & Desimone, 1985). Based on the finding that when two stimuli are simultaneously present in a neuron's receptive field, the neuron's response will depend on which of the two is attended, this theory has been highly influential in shaping our current understanding of basic attentional processes. However, previous attempts to reproduce these findings in humans (Kastner et al., 1998, 2001) have methodological limitations due to the fact that electrophysiological recordings at the level of individual receptive fields in early visual cortex are practically impossible in humans. Kastner et al. (1998) therefore operationalized different levels of competition by presenting visual stimuli either simultaneously or in sequence and compared BOLD responses of early visual areas in the two conditions. They found decreased activity under simultaneous presentation conditions. Importantly, this suppressive effect could be partially overcome by subjects' paying attention to the originally irrelevant stimuli, in accordance with the predictions of the biased-competition theory. However, due to the limited temporal resolution of BOLD-fMRI, it is difficult to exclude alternative explanations such as response summation in the sequential presentation condition. Moreover, as shown by the results of Experiment 3 of the present thesis, visual responses elicited by synchronously and asynchronously presented stimuli may differ in a number of ways and may selectively interact with attentional task-demands.

In order to overcome these problems, we adapted an experimental task from the visual search literature: Watson and Humphreys (1997) first described the phenomenon of visual marking, where distractors presented slightly earlier than the rest of a search display containing a target stimulus seem to be actively suppressed and do not affect search times. These findings were replicated and extended in several studies, including EEG and fMRI experiments (Han, Jiang, Mao, Humphreys, & Qin, 2005; Han, Jiang, Mao, Humphreys, & Gu, 2005; Humphreys, Stalmann, & Olivers, 2004; Jacobsen, Humphreys, Schröger, & Roeber, 2002; Pollmann et al., 2003). Mounts and Tomaselli (2005) later described a similar phenomenon. While this manipulation also involves the comparison of simultaneous and non-simultaneous visual events, it permits a more finely graded approach to attentional competition, as target stimuli can be flanked by different numbers of previously presented (i.e., suppressed) and simultaneously presented (i.e. non-suppressed) stimuli.

In our experiment, we presented five circular stimuli in the upper left visual quadrant: one human face which could be either fearful or neutral, and four scrambled faces of the same average luminance as the face. Subjects performed an easy fixation task and were asked to ignore the peripheral stimuli. On each trial, two scrambled faces were first presented, followed by the remaining two scrambled stimuli and the complete face after a variable SOA of 600-900 ms. We reasoned that (i) neural responses to the peripheral stimulation should be dominated by the face stimuli as they were the only ones containing ecologically important information, although irrelevant to the experimental task; (ii) neural responses to human faces would be diminished as a function of attentional competition with simultaneously presented scrambled stimuli; and (iii) attentional competition should be biased in favour of emotional faces, making them more resistant to interference by simultaneously presented scrambled stimuli than neutral faces.

So far, we have simultaneously recorded EEG and fMRI in 16 healthy subjects using this task. While the technical difficulties associated with combining the two imaging modalities are not entirely resolved (Leclercq et al., 2009; Srivastava, Crottaz-Herbette, Lau, Glover, & Menon, 2005; Sun, Rieger, & Hinrichs, 2009), preliminary analyses indicate that basic visual responses both in EEG and fMRI correspond to our expectations. Thus, Figure 4.1 shows the comparison of fearful vs. neutral facial expressions for an array of eight posterior electrodes displaying maximal C1 activity and for eight electrodes at which N170 amplitudes were maximal. It is evident in both cases that peristimulus differences between the two conditions complicate the interpretation of any effects, but we are confident that improved preprocessing will yield clearer results on which statistical analyses can subsequently be conducted.

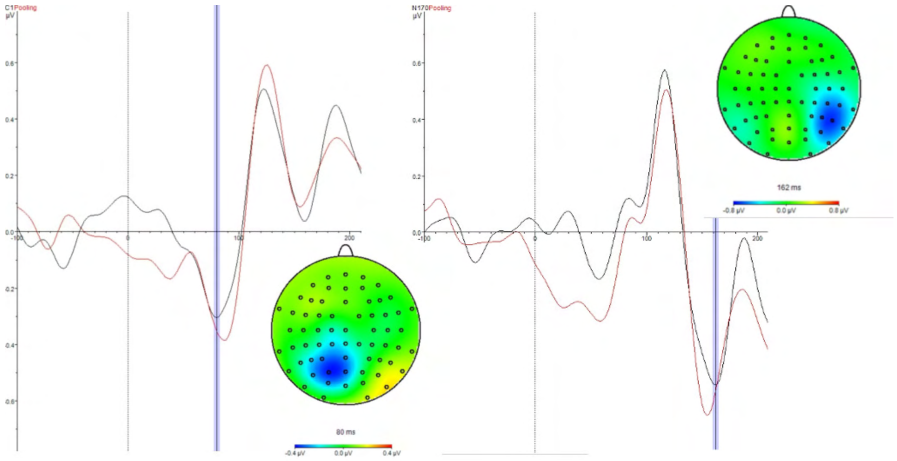

Figure 4.1: ERPs and topographic maps for neutral (black) and fearful (red) facial expressions presented at time 0. Traces show averages across eight electrodes capturing the maximum of the C1 (left) and N170 (right) components. In both cases, fearful stimuli appear to elicit higher component amplitudes, although peristimulus differences between conditions do not permit clear conclusions for the time being.

As noted above, distributed inverse solutions based on template brains failed to indicate top-down effects in occipital cortex in our experiments. A methodological aim of this study was therefore to construct individually tailored inverse solutions which would allow for a detailed assessment of the effects of attention and emotion on early visual cortex activity. This problem has been the focus of several recent publications (Ales et al., in press; Hagler et al., 2009; Im et al., 2007) and we plan to adapt these published methods for our analyses. Importantly, the fact that we acquired EEG and fMRI data simultaneously should then allow us to compare the results of individual inverse solutions with BOLD responses acquired under exactly the same conditions. While this work is still in progress, preliminary fMRI results suggest that basic effects of the experimental manipulations conform to our expectations, with, for example, stronger activity elicited in the vicinity of the fusiform face area (FFA) when subjects saw fearful rather than neutral facial expressions (Fig. 4.2).

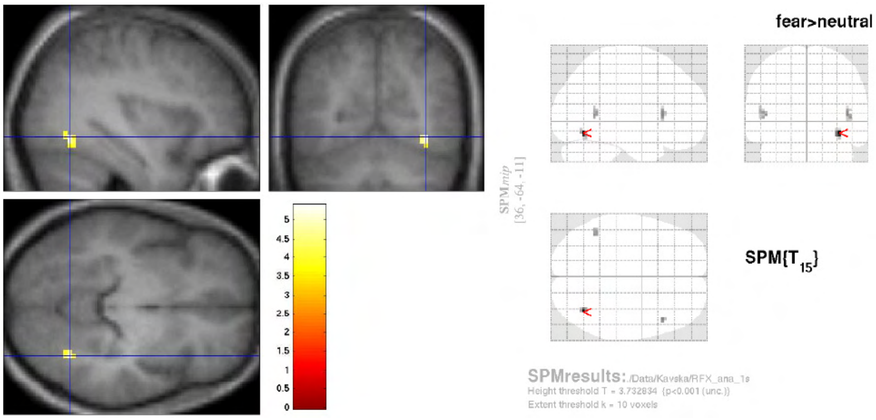

Figure 4.2: Preliminary fMRI results (N=16 subjects) for the comparison of fearful and neutral facial expressions. Short blocks of 15 seconds in which only one emotion was presented were compared to each other ($p>0.001$, uncorrected; cluster-threshold=10). Maximal differences were observed at an inferior occipital location in the vicinity of the FFA. The reverse contrast (neutral>fear) did not yield any significant activations.

4.5 Conclusions

Recent evidence from human EEG and MEG studies suggests that the traditional view of V1 as an inflexible module for low-level stimulus characterisation needs to be revised. Under appropriate conditions, effects of attention, emotion, and learning on the earliest components of visually evoked electro- and magnetoencephalographic responses can be detected. The notion that V1 acts as an adaptive and flexible processor, based mainly on animal studies, is thus gaining support from the human literature. We have proposed and applied methodological improvements in order to better characterise the conditions under which the earliest stages of cortical visual processing may and may not be affected by top-down influences. These efforts should help create a framework for assessing the top-down permeability of early visual cortex and may eventually help to determine whether very early effects of attention, emotion, and learning on cortical processing play a role outside the artificial stimulus conditions created in the laboratory. I believe that consideration of the constraints and affordances of natural vision (Gibson, 1986) will lead to a conceptual enrichment of research into early visual processing and that the notion of predictive coding, in particular, will help generate novel hypotheses allowing for a better characterisation of the C1 component.

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Appendix A

Pourtois G., Rauss, K. S., Vuilleumier, P. & Schwartz, S. (2008). Effects of perceptual learning on primary visual cortex activity in humans. *Vision Research* 48, 55-62.

Available online at www.sciencedirect.com

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Vision Research 48 (2008) 55–62

Vision Research

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Effects of perceptual learning on primary visual cortex activity in humans

Gilles Pourtois [a,b], Karsten S. Rauss [a], Patrik Vuilleumier [a,b,c], Sophie Schwartz [a,b,c,*]

[a] *Laboratory for Neurology and Imaging of Cognition, Department of Neurosciences, University of Geneva, Switzerland*
[b] *Swiss Centre for Affective Sciences, University of Geneva, Switzerland*
[c] *Department of Clinical Neurology, University Hospital of Geneva, Switzerland*

Received 27 August 2007; received in revised form 16 October 2007

Abstract

Psychophysical and neuroimaging studies suggest that perceptual learning may affect activity in primary visual cortex (V1). Yet, it remains unclear whether such changes involve intrinsic V1 plasticity or feedback from later processing stages. Here we recorded high-density electro-encephalography in 24 volunteers, 24-h after training on a visual texture discrimination task in the upper or lower visual-field. Post-training improvement in upper visual-field was associated with changes in early visual responses, starting 40 ms post-stimulus, with reduced amplitude of retinotopic C1, known to reflect V1 activity. No behavioral or neurophysiological effect was found after training in lower visual-field, suggesting retinotopic constraints on perceptual learning. Our results demonstrate that successful acquisition of a perceptual skill can produce long-lasting changes for initial sensory inputs in the adult human visual system.

Keywords: Perceptual learning; C1; EEG; Visual field asymmetry; Visual texture discrimination

1. Introduction

Through perceptual experience, the human brain learns to recognize the visual world and to distinguish fine sensory features that would remain undetected without practice. The specificity of improvement in some tasks (Karni & Sagi, 1991) suggests an involvement of the primary visual cortex (V1), as recently confirmed by functional magnetic resonance imaging (fMRI) studies in humans (Furmanski, Schluppeck, & Engel, 2004; Schwartz, Maquet, & Frith, 2002). However, it is still debated whether these post-training changes in fMRI responses in V1 arise primarily from local plasticity, or instead reflect feedback mechanisms exerted on V1 by top-down influences from later visual processing stages (Hupe et al., 1998; Mehta, Ulbert, & Schroeder, 2000) or fronto-parietal attentional networks (Schwartz et al., 2004).

To address this issue, we examined the precise time-course of perceptual learning using high-density electro-encephalography (EEG)[1] in human volunteers who were intensively trained on a classic visual texture discrimination task (TDT). Previous work has shown that training on such tasks may lead to long-lasting improvement in performance that is specific to the trained retinal location (Karni & Sagi, 1991; Stickgold, James, & Hobson, 2000) and associated with corresponding changes of fMRI responses within retinotopic V1 (Schwartz et al., 2002; Walker, Stickgold, Jolesz, & Yoo, 2005). Based on the hypothesis that TDT learning might involve local plasticity at the earliest

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* Corresponding author. Address: Department of Neurosciences, University Medical Centre, 1 Michel-Servet, 1211 Geneva, Switzerland. Fax: +41 22 379 5402.
E-mail address: sophie.schwartz@medecine.unige.ch (S. Schwartz).

[1] *Abbreviations used:* EEG, electro-encephalography; EOG, electro-oculogram; fMRI, functional magnetic resonance imaging; GFP, global field power; SOA, stimulus-to-mask onset asynchrony; TDT, texture discrimination task; V1, primary visual cortex; VEP, visual evoked potential, VF, visual field.

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doi:10.1016/j.visres.2007.10.027

cortical stages of visual processing, we predicted that visual stimuli presented at a trained location (relative to similar stimuli at an untrained location) should modify the initial cortical response imputable to V1 activity, as recorded by EEG (Clark, Fan, & Hillyard, 1995; Foxe & Simpson, 2002). Unlike EEG recordings, previous fMRI studies (Furmanski et al., 2004; Schwartz et al., 2002) did not have sufficient temporal resolution to establish the exact latency of V1 effects observed after TDT learning.

An extensive body of work has established that exogenous visual stimuli produce a characteristic sequence of electric potentials recorded by scalp EEG. Here, we tested for the effects of perceptual learning on the first of these visual evoked-potentials (VEP), the so-called C1 component (Jeffreys & Axford, 1972). C1 represents an evoked response in V1 (Clark et al., 1995) whose earliest portion reflects the initial volley of sensory afference in the visual system (Foxe & Simpson, 2002), prior to subsequent feedback from later stages of neural processing (Di Russo, Martinez, & Hillyard, 2003; Martinez et al., 1999; Noesselt et al., 2002). C1 polarity is typically reversed when stimuli are presented in the upper versus lower visual field, consistent with the cruciform organization of V1 around the calcarine fissure.

We exploited this electrophysiological property in our study by training two groups of participants with visual textures presented in either the upper or lower visual field. Post-training EEG was recorded 24 h later. During recording sessions, our participants performed TDT on targets presented at either the trained location or an untrained location in the opposite quadrant (Fig. 1A and B). All visual targets and their locations were thus physically similar but differed in terms of the previous training experience. Our results show for the first time that TDT learning can modify the earliest sensory response evoked within visual cortex for stimuli presented at the trained location, and that such effects may arise in the upper but not the lower visual field, indicating retinotopically specific constraints on TDT learning.

2. Methods

2.1. Participants

Twenty-four volunteers (12 male; 25.2 ± 3.5 years) without neurological or psychiatric history gave informed consent to participate in our study, which was conducted in accordance with the Declaration of Helsinki and approved by the local Ethics Committee. All subjects had normal vision. Half of the subjects were trained and tested in the upper visual field (upper VF group), the others in the lower visual field (lower VF group), with equal numbers of males and females in each group.

2.2. Stimuli and behavioral task

We used the same task and stimulus parameters as described in previous work (Karni & Sagi, 1991). Texture displays were made of 13 × 25 high-contrast horizontal line-elements, presented either in the upper or lower visual fields (Fig. 1A). Targets consisted of three adjacent diagonal lines presented at varying positions (13–19° from fixation) and forming either a horizontal or a vertical array. A randomly rotated ‘L’ or ‘T’ also appeared at the bottom (top) of the display for the upper (lower) VF group, in order to impose fixation. The whole display covered 21 × 41 degrees of visual angle (1024 × 768 pixel screen resolution, 60 Hz refresh rate).

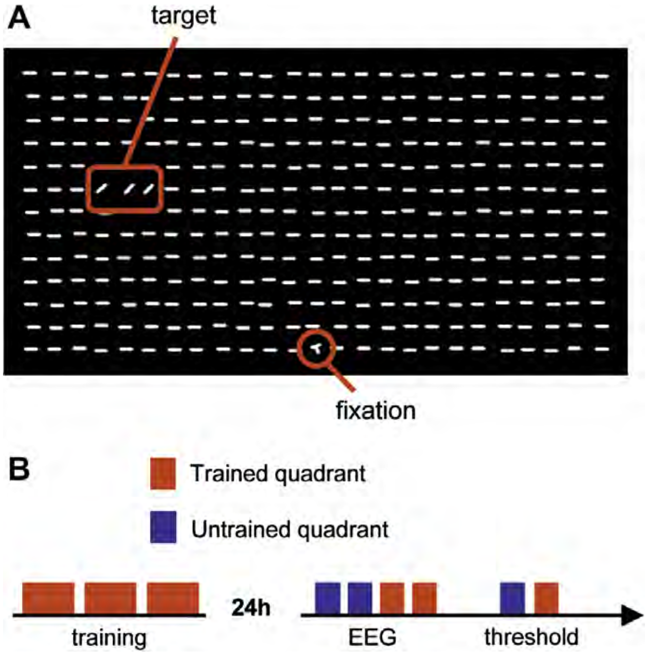

Fig. 1. Experimental paradigm. (A) TDT targets were three adjacent diagonal lines (vertically or horizontally aligned) presented in upper (or in lower) visual field. Participants had to discriminate target orientation, while fixating and reporting a central letter at the bottom (or top) of the display. (B) During training, targets always appeared within the same quadrant. During EEG recording (24 h later), targets appeared in the trained or, symmetrically, in the untrained quadrant across successive blocks. Performance threshold was then assessed for each quadrant separately.

On each trial, a texture display was briefly flashed (16 ms), followed by a blank interval (stimulus-to-mask onset asynchrony, SOA), and then by a mask (100 ms) in which randomly rotated V-shaped elements replaced all line-segments (Karni & Sagi, 1991; Schwartz et al., 2002). New visual displays were generated on each trial, using a Matlab toolbox allowing precise presentation timing and synchronization with the EEG recording (www.vislab.ucl.ac.uk/Cogent2000). On each trial, participants first reported the central letter at fixation (T or L), and then judged the orientation of target-lines (horizontal or vertical), using four predefined keys (two for each task).

The training session was given 24 h prior to EEG recordings. During this session, participants performed TDT for three consecutive blocks (total 1260 trials, duration ~90 min; Fig. 1B), in which targets were always presented in the same quadrant (either right or left, counterbalanced across participants). The SOA between target display and mask was progressively reduced from 460 to 100 ms to establish learning (Karni & Sagi, 1991).

The EEG test session was recorded 24 h later, while participants performed the same task (4 blocks of 100 TDT trials each), but now with the targets shown in either the trained or the untrained quadrant (in AABB or BBAA order, counterbalanced across participants). During EEG recording, SOA duration was fixed at 500 ms so as to avoid any contamination of early VEPs by the mask presentation, and to rule out any spurious EEG effects due to mere differences in task difficulty or effort between the trained and untrained conditions.

Immediately following EEG recordings, a behavioral test phase was given to measure target discrimination thresholds for the trained and untrained quadrants (80% correct responses), during which two series of 9 successive blocks (10 trials each) were presented in the trained and untrained hemifield with progressively decreasing SOAs (from 260 to 60 ms).

2.3. EEG recording and analyses

Scalp-EEG was recorded from 62 Ag/AgCl electrodes (Neuroscan, Synamps, El Paso, TX) positioned according to the extended international 10–20 EEG system; 30 K amplification, 0.01–100 Hz bandpass filter, and 50 Hz notch filter were used. Horizontal and vertical electro-oculograms (EOG) were monitored using 4 bipolar electrodes. EEG and EOG were acquired continuously at 500 Hz. Offline data processing included reduction of eye-blinks according to the procedure described by Gratton, Coles, and Donchin 1983; epoching from −50 to +450 ms around stimulus-onset; removal of epochs with EEG or residual EOG exceeding ±70 μV; and baseline correction over 50 ms pre-stimulus. Individual VEPs were then averaged and digitally low-pass filtered at 30 Hz.

Differences between conditions were first examined using the global field power (GFP) of EEG responses evoked by trained and untrained visual stimuli. GFP measures the strength of electric potentials concurrently recorded at all electrodes (rather than effects at a single electrode). We retained as significant any time-period during which GFP differed for 10 consecutive time-points ($\geqslant$20 ms) between trained and untrained conditions (paired t-tests, $p < .05$; cf. Guthrie & Buchwald, 1991).

We then identified the C1, P1, and N1 components based on their distinctive polarities, latencies, and topographic properties, and quantified their peak amplitude and latency in each participant. Because of the polarity inversion between upper and lower VF stimulation, we first computed learning-related changes by subtracting trained from untrained measures at each electrode for each subject before submitting them to standard ANOVAs (SPSS 15).

Finally, we tested for any topography differences between trained and untrained conditions during the C1 time-window (in addition to differences in amplitude or latency of this component), by using a microstate segmentation analysis (Pasqual-Marqui, Michel, & Lehmann, 1995). We also applied a Local Auto-Regressive Average (LAURA) procedure to estimate electric sources in the brain volume corresponding to the C1 scalp topography (Grave de Peralta Menendez, Murray, Michel, Martuzzi, & Gonzalez Andino, 2004). This distributed source localization method emulates the properties of neural generators by computing simultaneously active sources within the brain without any a-priori assumption on the number and position of generators.

3. Results

3.1. Behavioral data

During the training sessions, letter identification was high across the three successive blocks (>80%, >90%, >90%, respectively), for both the upper and lower VF groups, indicating that participants were able to maintain fixation equally well at all stages of training.

In contrast, texture detection thresholds (SOA at 80% correct) revealed a significant effect of training blocks [mean = 353 ms ± 131, 197 ms ± 49, and 184 ms ± 32 for blocks 1, 2 and 3, respectively; $F(2,44) = 43.7$, $p < .001$]. These results indicate that a significant familiarization with the task was already established after block 1 (420 trials), with no further difference between blocks 2 and 3, consistent with previous reports using the same task (Karni & Sagi, 1991; Schwartz et al., 2002; Stickgold et al., 2000). There was no main effect or interaction involving the visual field factor (training in upper vs. lower VF). Note that in all our analyses, data were collapsed across the two training sides (left or right, randomized across subjects), as there were no relevant differences between these stimuli (Fig. 1A) and no differences in task performance.

During EEG recording on the second day (post-training), behavioral results confirmed that the 500 ms SOA allowed us to obtain equal task difficulty across experimental conditions for both the letter identification ($\geqslant$98% correct across all blocks) and texture discrimination ($\geqslant$95%), in both the upper and lower VF groups. Non-parametric statistical analyses of performance on each task did not disclose any difference between groups (upper vs. lower VF, all $p > .10$; performance difference <1%) or between conditions (trained vs. untrained quadrant, all $p > .10$; performance difference <1.5%).

Critically, however, TDT thresholds measured on the testing day (24 h after training) clearly demonstrated location-specific perceptual learning (Karni & Sagi, 1991; Schwartz et al., 2002; Stickgold et al., 2000). These threshold values were submitted to an ANOVA with one within-subject factor (trained vs. untrained quadrant) and one between-subject factor (upper vs. lower VF group). This revealed a highly significant main effect of learning [$F(1,21) = 9.22$, $p = .006$; mean threshold = 98 ± 30 vs. 76 ± 31 ms for untrained vs. trained quadrants]. Although the interaction was not significant [$F(1,21) = 2.65$, $p = .12$], we performed planned comparisons to better characterize the learning effect in each group using paired t-tests. We found a significant effect of learning for upper VF subjects [$t(11) = 3.28$, $p = .007$; mean threshold = 78 ± 20 vs. 111 ± 32 ms for trained vs. untrained quadrants], whereas this effect was not significant in the lower VF [mean thresholds = 75 ms ± 38 vs. 85 ms ± 27 for trained vs. untrained quadrants, $t(11) = 1.00$, n.s.; see Fig. 2].

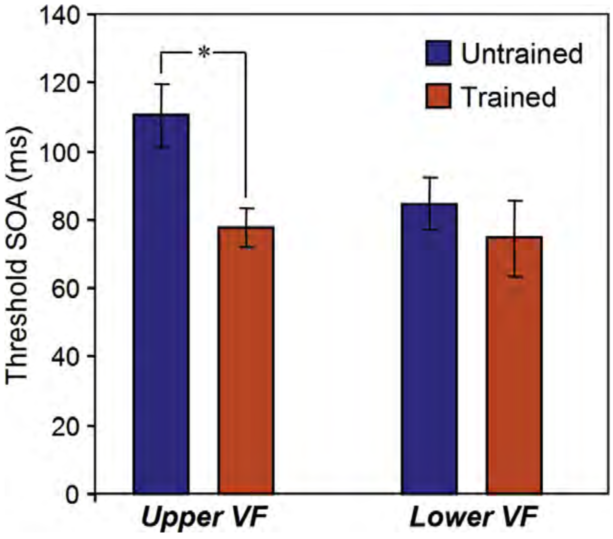

Fig. 2. Texture detection in trained and untrained quadrants on the testing day. Thresholds were computed for each individual as the SOA value for 80% correct texture detection; $^*p < .05$.

Taken together, these behavioral data demonstrate a long-lasting benefit on TDT performance for the trained quadrant 24 h after intensive practice in upper VF, but no effect after practice in lower VF.

3.2. EEG data

In line with the behavioral results, perceptual learning produced robust changes in early cortical responses for subjects trained in the *upper VF*. First, GFP analysis revealed a significant reduction in the electric field strength evoked by targets in the trained versus untrained quadrant, arising from 44 to 102 ms post-onset [$t(11) = 2.35$, $p = .022$ (one-tailed); Fig. 3A]. Such GFP changes suggest robust effects on EEG activity, with a substantial extent across different electrodes over the scalp. We also submitted voltage differences between the trained and untrained conditions to an electrode-by-electrode paired *t*-test for each time-point during this period of significant GFP difference. This revealed that the training-induced changes were significant only for posterior electrodes over occipito-parietal sites, in keeping with the typical topographic distribution of C1. On the other hand, subjects trained in the *lower VF* showed no significant differences in GFP between the trained and untrained quadrants (Fig. 3B).

A typical C1 waveform with a large amplitude (Fig. 3) was reliably obtained during the same time-window for every participant, in both the upper and lower VF groups, consistent with a strong response of V1 to peripheral visual arrays of high-contrast line-elements (Clark et al., 1995). The polarity inversion (negative vs. positive activity over posterior midline electrodes) and slight peak-latency difference between the upper and lower VF (~85 ms vs. ~75 ms post-stimulus, respectively; $F(1,22) = 6.7$, $p = .017$) are also consistent with previous reports on C1 (Jeffreys & Axford, 1972; Lehmann & Skrandies, 1979). We tested for any learning-dependent changes in this component using repeated-measure ANOVAs on amplitude differences between conditions (targets at trained minus untrained locations), with electrode locations (Anterior-Central-Posterior and Left-Central-Right for electrodes CP1, CPz, CP2; P1, Pz, P2; PO3, POz, PO4) as within-subject factors and VF position (Upper-Lower) as between-subject factor. Results showed a significant interaction between learning and position in the upper versus lower VF [$F(1,22) = 7.8$, $p = .011$]. This was due to reduced C1 amplitude for trained targets in the upper VF (Fig. 3A), but no such effect for trained targets in the lower VF (Fig. 3B). Indeed, separate ANOVAs in each VF group confirmed a significant reduction of C1 amplitude following training in upper VF [$F(1,11) = 5.3$, $p = .042$], but indicated no reduction in lower VF subjects. In each group, peak latency differences between trained and untrained conditions were smaller than our 2 ms sampling period and therefore not followed up.

Taken together, these data indicate that similar visual targets in TDT displays could produce different cortical responses in the early C1 time-range when presented at a previously trained location relative to an untrained location (in upper VF), resulting in retinotopically selective changes in amplitude (but not in latency). We also tested for any topographic differences associated with these early cortical responses. Voltage maps covering the C1 time-window for each group were submitted to a standard microstate analysis (Pasqual-Marqui et al., 1995). This analysis did not reveal any significant differences in scalp topographies between training conditions, indicating that neural generators underlying the C1 component were the same in the trained and untrained conditions in both groups. Distributed source localization analyses showed that these generators were primarily located in early visual cortices, in accordance with the known properties of the C1 (Fig. 4; Clark et al., 1995; Foxe & Simpson, 2002).

Next, we examined whether learning could also modulate the subsequent VEPs that are typically affected by top-down attention, namely P1 and N1 (Heinze et al.,

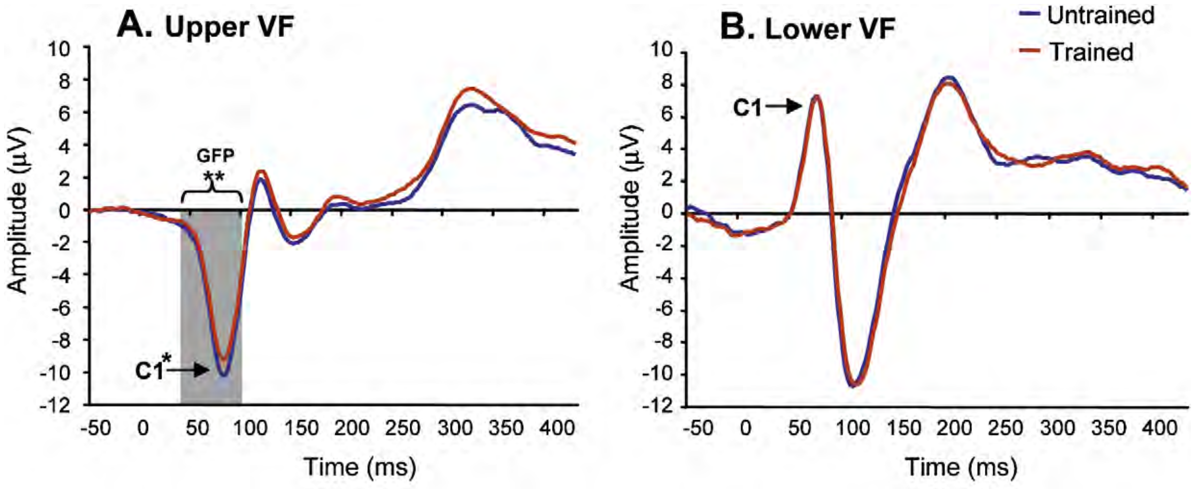

Fig. 3. Averaged C1 illustrated here at electrode Pz for trained and untrained quadrants. (A) Subjects trained in upper visual field, with time-window of learning-related GFP difference shown in light gray; (B) subjects trained in lower visual field; $^{*}p < .05$; $^{**}p < .01$.

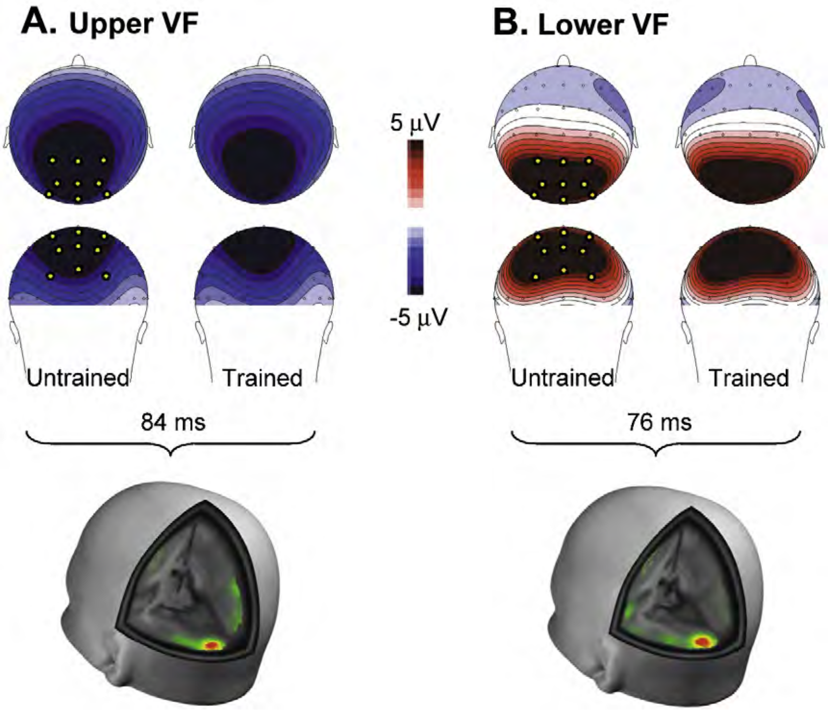

Fig. 4. Scalp current density maps at C1 peaks and retinotopic V1 sources for stimuli presented in (A) upper and (B) lower visual field. Positions of the 9 relevant electrodes used for C1 analyses are shown in yellow. Data for the distributed source localization are averaged across training conditions, because microstate analyses demonstrated equivalent topographies for trained and untrained conditions within each group (see text).

1994; Martinez et al., 1999). An ANOVA with the factors Training, Hemisphere, and Electrode (PO8/PO6/P8/P6 and symmetrically PO7/PO5/P7/P5) was performed on P1 peak amplitude (maximal ~130 ms post-onset) in upper VF subjects, but showed no significant effects of interest. In lower VF subjects, we did not observe a reliable P1 (presumably because it was generally cancelled out by the large positive C1 evoked in this condition); instead we observed a centrally distributed negative component (maximal at ~105 ms; Fig. 3B), with characteristics similar to a N90op (occipito-parietal; cf. Clark et al., 1995). As for P1 in upper VF, there was no significant effect of Training on the amplitude of this component (Pz, POz, Oz). No effect was found on latency measures for either P1 or N90op. Finally, training did not reliably modulate the amplitude of the N1 component (peak at ~160 ms) in any of the groups, and analyses of peak latencies for this component did not show any training-related effects either (cf. Fig. 3).

4. Discussion

By selectively training and testing visual quadrants at symmetrical retinal locations during TDT, and comparing targets at trained versus untrained positions, we were able to show for the first time that perceptual experience may result in a modulation of the retinotopic C1 component, associated with an early and sustained change in global field power from 44 to 102 ms post-stimulus onset. Critically, the behavioral improvement in TDT as well as the neural changes indexed by EEG activity were observed 24 h after training took place. Furthermore, both behavioral and EEG effects were found only in subjects who were trained in the upper visual field and not in those trained in the lower visual field.

Our findings reveal that perceptual learning may influence specific components in the sequence of neuronal events associated with the processing of trained visual configurations. The learning-related modulation of C1 contrasts with a lack of modulation of this early retinotopic component by other task-related factors, such as selective attention, as previously shown by numerous EEG studies (Clark et al., 1995; Di Russo et al., 2003; Fu, Greenwood, & Parasuraman, 2005; Martinez et al., 1999; Noesselt et al., 2002). Changes in C1 amplitude as a function of higher-level stimulus attributes have been reported during rapid presentation of emotional stimuli (Pourtois, Grandjean, Sander, & Vuilleumier, 2004) and following emotional conditioning (Stolarova, Keil, & Moratti, 2006). Previous work examining the effects of perceptual learning on early visual processing, on the other hand, did not specifically look for changes in the C1 component and is thus not directly comparable to our study due to differences in experimental setups. Skrandies and co-workers examined the effects of perceptual learning on ERP topography in Vernier acuity tasks (Ludwig & Skrandies, 2002; Shoji & Skrandies, 2006; Skrandies & Fahle, 1994; Skrandies, Jedynak, & Fahle, 2001). They observed topographic and latency effects of learning (starting from around 90 ms) when using stimuli presented either at central locations

(Skrandies & Fahle, 1994; Skrandies et al., 2001), or along the horizontal meridian (Ludwig & Skrandies, 2002), or simultaneously in all four quadrants (Shoji & Skrandies, 2006). No component matching the characteristics of the C1 is reported in any of theses studies. To our knowledge, long-lasting and retinotopically-specific effects of non-emotional stimuli on this earliest component of the visual evoked potential have not been demonstrated before. The use of large displays with high contrast elements eliciting a sizable C1 was necessary for detecting these subtle effects, as they are overlaid by large individual differences in the functional anatomy of early visual cortex (Dougherty et al., 2003). Our results therefore suggest that intrinsic plasticity in primary sensory cortices may underlie the consolidation of a newly acquired perceptual skill, and shape the initial volley of sensory inputs through the visual system (Foxe & Simpson, 2002).

A second important finding of our study is the spatial selectivity of these learning effects, with both behavioral improvement and neurophysiological changes arising only after training in the upper visual field. Taken together, our data provide new insights into the nature of learning-related changes in sensory responses of human V1, and constrain recent theoretical models of neural plasticity, as we discuss below in more detail.

4.1. Neural bases of perceptual learning

A plausible neural mechanism for perceptual learning in TDT involves strengthening of intrinsic connectivity between V1 neurons, in the absence of changes in basic receptive-field properties (Tsodyks & Gilbert, 2004). Top-down or reentrant influences operate on V1 to produce retinotopic increases in sensory response following the initial volley of visual inputs (Martinez et al., 1999; Noesselt et al., 2002). However, early reductions of GFP and C1 amplitude for trained stimuli (in upper VF), as observed in our study, suggest local changes within V1 after TDT learning, rather than later, reentrant influences. Importantly, any sustained top-down mechanisms would imply an interaction with local plasticity within V1 for the trained location (Li, Piech, & Gilbert, 2004), because the behavioral task and target-textures were identical for trained and untrained conditions, and because any training-related differences in attention orienting towards the target side were cancelled by using blocked presentations for each hemifield.

The observed significant *reduction* of early electrical activity for trained visual configurations provides new empirical support for recent computational models (Tsodyks & Gilbert, 2004) according to which learning biases intracortical inputs in favor of inhibitory activity to increase the discrimination of trained targets relative to background flankers (Herzog & Fahle, 1998; Tsodyks & Gilbert, 2004). Such interactions between excitatory and inhibitory processes in TDT learning may explain why discrimination of learned targets is impaired when background flankers are changed (Karni & Sagi, 1991).

These models may also account for the fact that trained stimuli produce an increase of BOLD signal in V1, as shown by previous fMRI studies of TDT (Schwartz et al., 2002; Walker et al., 2005) and other perceptual learning tasks (Furmanski et al., 2004; Sigman et al., 2005). Because BOLD signal is strongly modulated by the temporal structure rather than the total amount of synchronous neuronal discharges (Niessing et al., 2005), enhanced suppression of non-target background stimuli might increase BOLD signal, while reducing GFP and C1 amplitude at the scalp.

Critically, previous neuroimaging studies using fMRI could not unambiguously attribute learning-related V1 changes to early rather than later, reentrant stages of visual processing (Noesselt et al., 2002; Schwartz et al., 2002). In contrast, here we show neurophysiological changes implicating specific components associated with early sensory responses in striate cortex.

4.2. Visual field asymmetries in perceptual learning

Although we found clear behavioral and neurophysiological effects of learning for subjects trained in the upper visual field, we did not observe corresponding effects in the lower visual field. Asymmetries between upper and lower VF have been reported in many previous studies, including a latency shift of VEPs in favor of lower VF that corresponds well with our own results (Lehmann & Skrandies, 1979). Such differences have often been attributed to environmental constraints favoring the processing of complex textures in lower VF (Rubin, Nakayama, & Shapley, 1996; Skrandies, 1987). In contrast, we found no performance advantage prior to training and a lack of learning benefits in lower VF.

To our knowledge, no studies using the TDT have directly compared learning effects in the upper and lower VF. Moreover, some studies where subjects were only presented with lower VF stimuli have reported an initial deterioration of performance in TDT after training (Censor, Karni, & Sagi, 2006; Mednick, Arman, & Boynton, 2005). Thus, a reduction of performance due to intensive training sessions (Ofen, Moran, & Sagi, 2007) may occur more rapidly in lower VF and subsequently interfere with long-term consolidation processes (Censor et al., 2006). An alternative account of upper vs. lower VF asymmetries in TDT is suggested by Carrasco and co-workers (Talgar & Carrasco, 2002; Yeshurun & Carrasco, 1998) who demonstrated that higher spatial resolution close to the fovea may interfere with visual texture processing, and that such effects are stronger in lower VF due to its higher contrast sensitivity. Thus, higher spatial resolution in lower VF may interfere with effective learning in our task. However, more research is needed to fully elucidate the perceptual mechanisms underlying these asymmetries and their neural correlates.

5. Conclusions

Our results show that intrinsic plasticity in adult primary visual cortex may underlie the consolidation of a learned perceptual skill, leading to durable changes (>24 h) at early stages (<85 ms) of the visual cortical response to trained stimuli, presumably involving the very first cortical relay of inputs within V1. The observed asymmetry between upper and lower visual field may indicate differences in perceptual learning efficacy depending on retinotopic location and should be addressed more systematically in future research.

Acknowledgments

We thank C. Michel and two anonymous reviewers for helpful comments. This work was supported by grants from the Swiss National Science Foundation (#3100A0-102133; #632-65935; #51A240-104897), and by a grant from the Geneva Neuroscience Center.

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Appendix B

Rauss K. S., Pourtois, G., Vuilleumier, P. & Schwartz, S. (2009). Attentional load modifies early activity in human primary visual cortex. *Human Brain Mapping*, 30, 1723-1733.

◆ **Human Brain Mapping 30:1723–1733 (2009)** ◆

Attentional Load Modifies Early Activity in Human Primary Visual Cortex

Karsten S. Rauss,[1,2]* Gilles Pourtois,[1,2,3] Patrik Vuilleumier,[1,2,3,4] and Sophie Schwartz[1,2,3,4]

[1]*Department of Neurosciences, Laboratory for Neurology and Imaging of Cognition, University of Geneva, Geneva, Switzerland*
[2]*Geneva Neuroscience Center, University of Geneva, Switzerland*
[3]*Swiss Centre for Affective Sciences, University of Geneva, Geneva, Switzerland*
[4]*Department of Clinical Neurology, University Hospital of Geneva, Geneva, Switzerland*

Abstract: Recent theories of selective attention assume that the more attention is required by a task, the earlier are irrelevant stimuli filtered during perceptual processing. Previous functional MRI studies have demonstrated that primary visual cortex (V1) activation by peripheral distractors is reduced by higher task difficulty at fixation, but it remains unknown whether such changes affect initial processing in V1 or subsequent feedback. Here we manipulated attentional load at fixation while recording peripheral visual responses with high-density EEG in 28 healthy volunteers, which allowed us to track the exact time course of attention-related effects on V1. Our results show a modulation of the earliest component of the visual evoked potential (C1) as a function of attentional load. Additional topographic and source localization analyses corroborated this finding, with significant load-related differences observed throughout the first 100 ms post-stimulus. However, this effect was observed only when stimuli were presented in the upper visual field (VF), but not for symmetrical positions in the lower VF. Our findings demonstrate early filtering of irrelevant information under increased attentional demands, thus supporting models that assume a flexible mechanism of attentional selection, but reveal important functional asymmetries across the VF. *Hum Brain Mapp 30:1723–1733, 2009.* **© 2008 Wiley-Liss, Inc.**

Key words: attention; C1; EEG; V1; vision

INTRODUCTION

One of the most long-standing discussions in cognitive psychology and cognitive neuroscience concerns the locus of attentional selection during perception [Broadbent, 1958; Mangun, 1995; Treisman, 1969]. Over the last decade, the load theory of selective attention, as proposed by Lavie [1995; Lavie et al., 2004; Lavie and Tsal, 1994], has received increasing research interest, as it integrates a range of disparate findings obtained with different experimental paradigms. According to this model, the locus of selection of perceptual information is not fixed at either early or late stages of perception, but varies depending on the amount of concurrently presented information and the cognitive demands associated with its processing. The bottleneck of attentional selection is thus thought of as an adaptive

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Contract grant sponsor: Swiss National Science Foundation; Contract grant numbers: 3200B0-114014, 3100A0-102133, 310000-114008; Contract grant sponsor: Geneva Neuroscience Center PhD fellowship.

*Correspondence to: Karsten Rauss, Department of Neuroscience, Laboratory of Neurology and Imaging of Cognition, University of Geneva, rue Michel-Servet 1, 1211 Geneva, Switzerland.
E-mail: karsten.rauss@medecine.unige.ch

Received for publication 21 April 2008; Revised 9 June 2008; Accepted 14 June 2008

DOI: 10.1002/hbm.20636

filtering mechanism which prevents cognitive resources from being overburdened, while at the same time ensuring a maximum intake of information under varying conditions.

Although Lavie's [1995] original concept of perceptual load was tested using either stimulus displays containing different amounts of information or the same stimulus displays with different amounts of cognitive processing, the latter type of manipulation is now commonly referred to as attentional load [Bahrami et al., 2007; Rees et al., 1997; Schwartz et al., 2005]. Results from previous fMRI studies [Bahrami et al., 2007; O'Connor et al., 2002; Pinsk et al., 2004; Schwartz et al., 2005] suggest that manipulations of attentional load may affect activity in several regions of the human visual cortex, including primary visual cortex (V1). Although these findings provide strong evidence for flexible mechanisms of attentional selection, it is still debated whether top-down influences impact on information processing from the earliest stages in the cortex, as reported in a number of animal studies [Crist et al., 2001; for review, see Gilbert and Sigman, 2007], or whether modulations of early sensory cortex activity are the result of feedback influences from later stages of processing, which may operate on and reshape the still-activated representations in lower-level areas [Foxe and Simpson, 2002; Hupe et al., 1998; Lamme and Roelfsema, 2000; Martinez et al., 1999].

Evidence for the latter view comes from a large number of studies in which the earliest part of the visual evoked potential (VEP) was shown to be influenced only by physical stimulus characteristics, but not by manipulations of spatial attention [Handy et al., 2001; Heinze et al., 1994; Martinez et al., 1999; Noesselt et al. 2002]. Nevertheless, several recent studies have demonstrated that even the earliest cortical stages of visual processing as measured with EEG may be affected by factors other than simple visual features. For instance, the amplitude of the earliest component of the VEP, the C1 [Clark et al., 1995; Jeffreys and Axford, 1972], can be modified by emotional content [Halgren et al., 2000; Pourtois et al., 2004] and emotional associations [Stolarova et al., 2006] of visual stimuli, as well as following perceptual learning [Pourtois et al., 2008b]. In addition, one recent study suggested that the C1 component may be modulated by spatial attention [Kelly et al., 2008], unlike previously assumed [Martinez et al., 1999]. So far, this single study stands out as a striking exception to the lack of attentional effects typically reported for C1 responses.

In the present study, we sought to test the hypothesis that early visual cortex activity, as indexed by the retinotopic C1 component, may be affected by attentional load. This hypothesis was based on the combined evidence from previous fMRI studies in humans [Bahrami et al., 2007; O'Connor et al., 2002; Pinsk et al., 2004; Schwartz et al., 2005] demonstrating an influence of attentional load on V1 activity (but not whether attention affected early or late visual processing in V1), and animal electrophysiology [Crist et al., 2001; Gilbert et al., 2000; Ito and Gilbert, 1999] showing that attention can affect the earliest stages of visual information processing. Taking advantage of the high temporal resolution offered by EEG, we aimed to test whether early effects of attention on V1 activity predicted from the load theory of selective attention can also be observed in humans. We reasoned that previous failures to find such an effect may have been due to the high variability of visual cortex functional anatomy [Amunts et al., 2000; Dougherty et al., 2003] combined with stimulation protocols not optimized for eliciting clear V1 responses. We therefore adapted the paradigm employed by Schwartz et al. [2005] and recorded EEG responses to large-scale, high-contrast distractors presented at different locations in the peripheral visual field (VF) while subjects performed either an easy or a highly demanding task at fixation. Subjects were tested either in the upper or the lower VF. Our results reveal that attentional load modulates C1 amplitude for irrelevant visual distractors. However, these effects differed as a function of the part of the VF tested, suggesting asymmetries in attentional influences across the VF.

MATERIALS AND METHODS

Subjects

A total of 28 subjects (between 22 and 40 years old) were tested, 14 in the upper VF (11 male) and 14 in the lower VF (11 female). All of them had normal or corrected-to-normal vision and provided written informed consent. None of them reported any previous neurological or psychiatric disease. The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethics committee.

Stimuli

Stimuli were created using Cogent (www.vislab.ucl.ac.uk/Cogent2000), a MATLAB toolbox allowing precise timing and synchronization with the EEG system, and presented on a 17″ CRT screen (viewing distance 40 cm, refresh cycle 60 Hz). A rapid serial visual presentation task consisting of differently colored (six colors) and differently oriented (two orientations) T-shapes was presented at fixation (stimulus duration 250 ms; interstimulus interval 900–1243 ms), either at the bottom (upper VF group) or at the top of the screen (lower VF group). Task-irrelevant arrays of white horizontal line elements were flashed in the periphery for 250 ms ($8.7^\circ \times 37.8^\circ$ of visual angle; Fig. 1A), either close to fixation or further away (vertical distance to the center of distractor 7.3° and 17.6°, respectively). These distractors followed targets after 250–493 ms. The screen background remained black throughout the experiment (Fig. 1B).

The manipulation of distractor location was introduced to replicate the findings of Schwartz et al. [2005], who

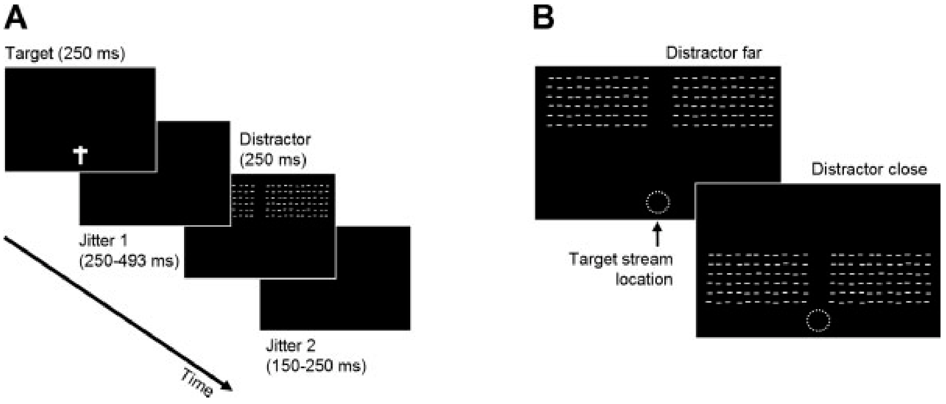

Figure 1.

Experimental stimuli. **A:** Time-course of a single trial. On each trial, subjects had to detect either a single feature (color) or a feature conjunction (color and orientation of the T-shape) at fixation while distractors were presented unpredictably. A jitter was introduced between onsets of the central task stimuli and peripheral distractors in order to distinguish between neural responses elicited by each type of event. **B:** Distractors were presented in the periphery, either close to or far from fixation (denoted by a white dotted circle which was not shown in the experiment). Distractors were always irrelevant to the task and subjects were instructed to ignore them. Distractors for upper VF are shown; for subjects tested in lower VF, the display was inverted.

observed suppression of activity elicited by a distracting stimulus close to fixation, but less suppression in more eccentric areas of the VF. However, ERPs elicited by more eccentric distractors turned out to be difficult to interpret, with only two subjects in the upper and six subjects in the lower VF group showing a clear C1. We therefore limited our analyses of distractor-related activity to stimuli presented close to fixation, which elicited a clear C1 in all subjects and conditions.

Procedure

Subjects were placed in a quiet, dimly lit, and electrically shielded recording booth. Four blocks of 410 trials each were presented. At the beginning of alternating blocks, participants were instructed to press the space-bar of a standard computer keyboard only if they saw either (i) an upright or upside-down red T-shape (pop-out detection, low attentional load) or (ii) an upright yellow or an upside-down green T-shape (conjunction discrimination, high attentional load). The two tasks alternated between blocks, with the starting condition counterbalanced across participants. Subjects were instructed to respond as correctly and as rapidly as possible. Pseudo-random trains of stimuli were created for each block of 410 trials; about 32 of these trials were target trials requiring a motor response. In each block, 62 distractors were presented in each eccentricity condition, 46 of which were uncontaminated by target-related motor activity. The large number of nondistractor trials was required to generate a strong and stable attentional set from to the central load task, ensuring a valid measurement of attentional load, and also to avoid visual adaptation/habituation to the distractors. Instructions stressed that randomly occurring distractors in the periphery were task-irrelevant and to be ignored. Each block lasted approximately 10 min, including a short break after half of the trials had been completed. Figure 1B depicts the sequence of visual events forming a single trial.

Data Recording and Analysis

Scalp-EEG was recorded from 62 Ag/AgCl electrodes (Neuroscan, Synamps, El Paso, TX) positioned according to the extended international 10–20 EEG system [Oostenveld and Praamstra, 2001]. Signals were amplified at 30 K and band-pass filtered between 0.01 and 100 Hz; a 50 Hz notch-filter was applied to filter line noise. Horizontal and vertical electro-oculograms (EOG) were monitored using four bipolar electrodes. Both EEG and EOG were acquired continuously at 500 Hz.

Using Brain Vision Analyzer 1.05 (Brain Products, Munich, Germany), eye-blink artifacts were semiautomatically corrected using the procedure described by Gratton et al. [1983] and a 0.5 Hz high-pass filter was applied. Epochs from −100 ms to +600 ms around stimulus-onset were extracted and baseline-corrected for the 100 ms preceding stimulus-onset. Epochs with EEG or residual EOG exceeding ±80 μV were rejected. Single-trial VEPs were then averaged and low-pass filtered at 30 Hz and the C1, P1, and N1 components were semiautomatically identified based on their distinctive polarities, latencies, and topographic properties. Their peak amplitudes and latencies were measured in each participant at electrode sites determined from the grand averages.

We then tested for topographical differences between load conditions during these components, using a microstate segmentation analysis [Pasqual-Marqui et al., 1995] as implemented in the software Cartool (www.brainmapping.unige.ch). This analysis is based on the assumption that while a given distribution of voltage values across the scalp may reflect any combination of distributed neural generators, different distributions necessarily imply different neural generators [Lehmann and Skrandies, 1980]. It has been demonstrated that voltage distributions (or voltage maps) do not change randomly over the course of an ERP but remain stable for several milliseconds, reflecting so-called EEG microstates which in turn are assumed to reflect different stages of information processing [Michel et al., 2001; Pourtois et al., 2005, 2008a]. To detect such microstates, voltage maps corresponding to each time-frame of a grand-average ERP are subjected to a K-means spatio-temporal cluster analysis which segments the data into periods of stable topographical patterns, varying only in intensity over time [Pasqual-Marqui et al., 1995]. Voltage maps obtained from the grand averages are then fitted back to the data of individual subjects, to allow for statistical comparison between conditions based on several fit indices, such as the duration and onset time of a dominant map as well as the global explained variance (GEV), the latter being an estimate of the goodness of fit. We used the following standard settings [cf. Michel et al., 2001; Pasqual-Marqui et al., 1995]: A K-Means algorithm was run on the first 300 ms poststimulus of grand averages from both load conditions, separately for upper and lower VF groups. Individual microstates were considered as reliable if they persisted for at least three time-frames (i.e., 6 ms). Analyses were calculated using 5–25 initial clusters and the optimal number of clusters was determined objectively using both cross-validation [Pasqual-Marqui et al., 1995] and Krzanowski-Lai [Tibshirani and Walther, 2005] criteria. Fitting onto individual subject data was then performed for periods showing significant effects of task conditions.

Finally, a local auto-regressive average (LAURA) procedure was employed to estimate electrical sources in the brain volume corresponding to the scalp topographies identified by the segmentation procedure [Grave de Peralta Menendez et al., 2004]. This distributed source localization analysis does not use any a priori assumption on the number and position of neural generators, but determines the most likely configuration of activity simultaneously in a large number of solution points (4,024 in our case) placed throughout the cortical grey matter. We opted for this method because it allows for a flexible spatial distribution of activations, as elicited by the large-scale peripheral distractors used.

RESULTS

Behavioral Performance

Accuracy data were analyzed using nonparametric Friedman Analysis of Variance [Friedman, 1937], as absolute numbers of errors were low, with none of the participants committing more than five misses or more than seven false alarms per block of 410 trials (~32 of which were true targets requiring a motor response). Results demonstrated a significant effect of Attentional Load. Both misses [$\chi^2(3) = 10.4$, $P = 0.014$] and false alarms [$\chi^2(3) = 48.2$, $P < 0.001$] were more frequent under high load, underlining the increased difficulty of this condition. On the other hand, Bonferroni-corrected Mann-Whitney tests did not uncover any significant differences on either of the two accuracy measures between the upper (0.93 misses/1.20 false alarms on average) and lower VF (1.14/2.21) groups.

Reaction times (RTs) for correctly detected targets were analyzed using repeated-measures ANOVAs with Attentional Load (high/low) and Block (first/second) as within-subjects factors and VF (upper/lower) as between-subjects factor. Again, significant main effects were found for Attentional Load [low (mean ± SE): 478 ± 10 ms, high: 623 ± 11 ms; $F(1, 26) = 367.6$, $P < 0.001$, partial $\eta^2 = 0.934$] and Block [first: 546 ± 11, second: 556 ± 10 ms; $F(1, 26) = 4.6$, $P = 0.042$, partial $\eta^2 = 0.150$]. The effect of Block may reflect fatigue, but note that this effect is based on a very small difference in RTs (~10 ms) compared with the effect of Attentional Load (~150 ms).

Although the error rate was low (as required by the task instructions), it is remarkable that both error rates and RT measurements showed significant effects of attentional load, thus confirming that task instructions successfully modulated demands on attentional resources.

Central Target VEPs

To characterize activity induced by the task at fixation, we first analyzed trials where the central task did not require a motor response and was not followed by a peripheral distractor. There were approximately 390 such trials in each load condition, 25–33% of which were excluded during data preprocessing. (Note that ERPs to imperative target stimuli were not computed due to the small number of trials).

Grand-averaged data for the central stimulus did not show a C1 component, as would be expected following central presentation in the VF [Clark et al., 1995; Jeffreys and Axford, 1972]. Based on the grand-average topographies, we selected electrodes P3-P8 and P05-PO8 for analysis of the P1 component. Peak amplitude data were entered into a repeated-measures ANOVA with Attentional Load (low/high) as within-subjects factor and VF (upper/lower) as between-subjects factor. In all peak analyses, data were collapsed across the two hemispheres (because hemispheric asymmetries were not relevant for our study) as well as across electrodes (because changes in voltage topographies were examined separately, see Topographic Analyses). Results indicated no differences between peak amplitudes of P1 under low versus high load ($P = 0.19$) or for lower versus upper VF groups

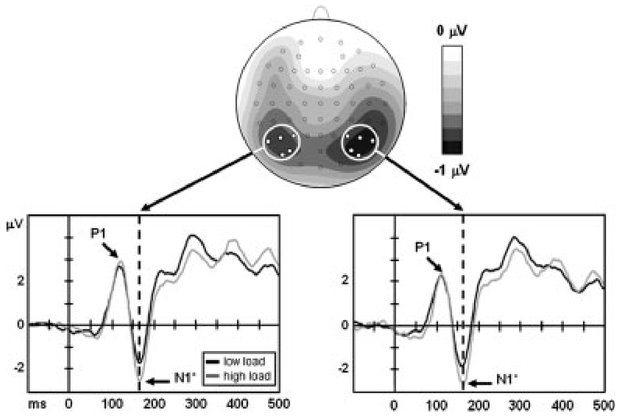

Figure 2.

Grand averages elicited by central stimuli (task-relevant but nontargets), for subjects tested in upper VF. Top: Difference topography (high minus low load) at the time of the N1 peak (~165 ms). Electrode sites included in statistical analyses of P1 and N1 components are highlighted. Bottom: Grand averages across the indicated electrodes over left and right hemispheres, respectively. *$P < 0.05$.

($F < 1$). P1 peak latencies were also unaffected by these experimental factors (both $F < 1$).

Analyses of the N1 component were conducted on the same electrodes as for P1, that is, P3-P8 and PO5-PO8, and with the same factors. Peak amplitudes were modulated by Attentional Load, as expected due to changes in visual discrimination demands [Hopfinger and West, 2006], with more negative voltages observed under high load [−3.5 ± 0.7] than under low load [−3.0 ± 0.68 µV; $F(1, 26) = 5.94$, $P = 0.022$, partial $\eta^2 = 0.186$]. There was no effect of VF group on peak amplitudes and no effect of Attentional Load or VF on N1 latencies (all $F < 1$).

Figure 2 illustrates the grand averages under low- and high-load conditions for upper VF subjects. The main effect of Attentional Load on peak amplitudes was qualitatively similar in the lower VF group. Additional analysis using peak-to-peak measurements (N1 minus P1 amplitudes [cf. Picton et al., 2000]) as the dependent variable confirmed these results, with the main effect of Attentional Load even more significant ($P = 0.001$) than when simple peak amplitude measurements were used, and again no interaction between load and VF group.

Peripheral Distractor VEPs

As the C1 reverses polarity with upper versus lower VF stimulation [Clark et al., 1995; Jeffreys and Axford, 1972], a difference score was computed between the two load conditions and then used for combined analyses in the two groups of subjects (with scores from lower VF subjects sign-inverted). Based on the grand-average topographies, we selected a 3 × 2 electrode grid for C1 peak analyses: CP1, CPz, CP2, P1, Pz, and P2. Although topographies for upper and lower VF stimulation were not perfectly equivalent, the maximum of the C1 component was captured well with these leads in both groups (see Fig. 3).

A clear C1 was evoked in all 28 subjects by distractors close to fixation (see Materials and Methods). Again, we performed an ANOVA with Attentional Load (low/high) as within-subjects and VF (upper/lower) as between-subjects factor. Results showed a significant Attentional Load × VF interaction [mean differences: 0.95 ± 0.40 (upper VF) and −0.26 ± 0.40 µV (lower VF); $F(1, 26) = 4.72$, $P = 0.039$, partial $\eta^2 = 0.154$]. Additional analyses conducted separately for each group showed that C1 peak amplitudes were significantly reduced under high attentional load following distractors in upper VF [$F(1, 13) = 6.17$, $P = 0.027$, partial $\eta^2 = 0.322$], but not for distractors in lower VF ($F < 1$). Peak latencies of the C1 were not affected either by Attentional Load ($P = 0.20$) or by its interaction with VF ($F < 1$). The VF factor itself was also nonsignificant ($F < 1$).

Subsequent VEP components were analyzed separately for upper and lower VF groups. No clear P1 was observed following lower VF stimulation [see also Clark et al., 1995], in line with previous findings with similar stimulus parameters [Pourtois et al., 2008b] and probably due to the overlap between C1 and P1. Instead, in lower VF subjects, we observed a centrally distributed negative component reminiscent of what Clark et al. [1995] termed the N90op. Neither peak amplitudes nor latencies of this component

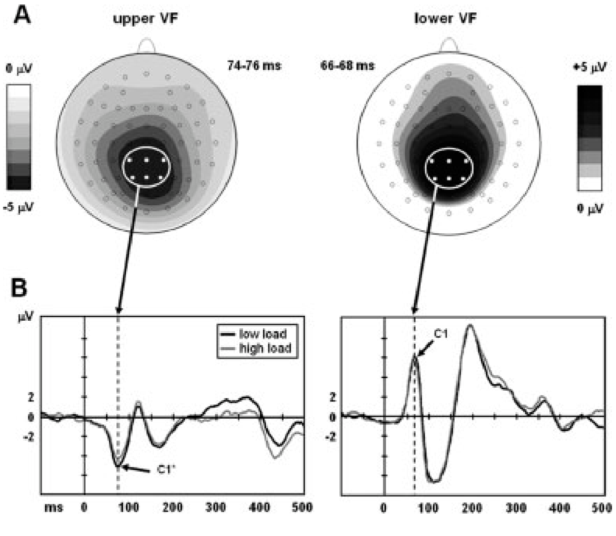

Figure 3.

C1 grand average topographies (**A**) and ERPs (**B**) in response to distractors close to fixation. Data from subjects tested in upper VF are shown on the left, and those tested in lower VF on the right. Topographies are shown for low attentional load. ERPs in (B) are averages across the electrodes indicated in (A). *$P < 0.05$.

(as measured at electrodes CP1, CPz, CP3, P1, Pz, P2, PO3, POz, and PO4) were influenced by Attentional Load (all $F < 1$). Likewise, no significant effects were obtained for the P1 component in upper VF subjects (measured at electrodes P1, Pz, P2, PO3, POz, PO4, O1, Oz, and O2, in keeping with a more posterior distribution than N90op; all $F < 1$).

The N1 response to peripheral stimuli was observed bilaterally, in both lower and upper VF subjects, with its peak situated over lateral centro-parietal electrode sites. For the upper VF group, electrodes CP1-CP6 and P1-P6 were selected to analyze the N1 voltage and latency, with Attentional Load as within-subjects factor, but this showed no significant modulation for either measure of this component (both $P > 0.37$). Likewise, for the lower VF group, no effects of Attentional Load on N1 amplitude or latency (as measured at electrodes CP3-CP6 and P3-P6) were observed (all $F < 1$). In the latter group, however, evaluation of the N1 was complicated by its partial overlap in time and space with the aforementioned N90op, and we therefore confirmed these results using a microstate segmentation analyses (see later) that allowed us to better disentangle these two negative-going components.

Topographic Analyses

To complement the peak analyses described above, we investigated scalp voltage distributions in the different experimental conditions across time using a microstate segmentation analysis (see Materials and Methods) as implemented in Cartool (www.brainmapping.unige.ch). Spatio-temporal K-means cluster analyses [Pasqual-Marqui et al., 1995] were first conducted on the grand averages of ERPs to central target stimuli in both load conditions, with the lower and upper VF groups analyzed separately. Results demonstrated a high degree of similarity for the successive microstates between low- and high-load conditions in both groups; with the earliest indication of topographic differences between load conditions arising at ~250 ms poststimulus. Combined with the peak measures, this topographic analysis suggests that the significant differences in N1 amplitude (peak ~150 ms) evoked by the central stimuli (see above) was the result of differing strength of activity within the same set of neural generators.

We then tested for differences in voltage topography in response to the peripheral distractors. Based on the results of the peak analyses reported in the preceding section, we conducted separate analyses for upper and lower VF subjects. The segmentations showed a high degree of topographic similarity between low- and high-load conditions, particularly in the lower VF group, where the first indication of topographical differences were present at ~240 ms poststimulus. In the lower VF group, however, different maps were already observed during the first 100 ms following distractor presentation, in addition to differences at later stages of processing (see Fig. 4). The first difference was seen during the initial period after distractor onset (Maps 1 vs. 2, 0–50 ms), while another difference was also present later (Maps 4 vs. 5, 70–100 ms).

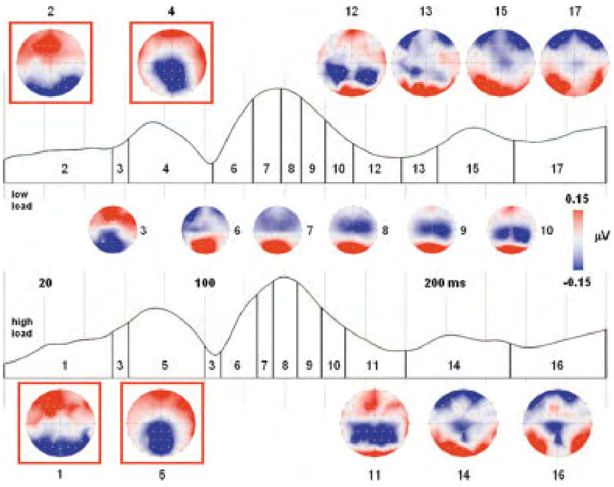

Figure 4.

Microstate segmentation (first 300 ms poststimulus) of grand averages elicited by distractors in upper VF. Map numbers are superimposed on global field power traces of low- and high-load conditions. Topographic maps differing between load conditions are displayed at the top and bottom, respectively. For the highlighted maps, a significant Load × Map interaction ($P < 0.05$) was observed after fitting onto single-subject ERPs (backfitting was done only for the first 100 ms poststimulus). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

We tested these differences by fitting the respective maps obtained by segmentation of the grand-average data onto individual subject ERPs from each load condition, and then compared the number of time-frames during which each map was present (TF criterion), as well as the amount of topographical variance explained by each map (GEV criterion). When examining the early succession of topographical maps in the first 100 ms poststimulus onset, we found a significant Load×Map interaction for the TF criterion [$F(1, 13) = 9.39$, $P = 0.009$], indicating that Map 1 was present significantly longer under high than low load ($P = 0.02$, paired t-test) and vice versa for Map 2 ($P = 0.03$). The same pattern of results was observed for the GEV criterion, although the interaction term did not quite reach significance ($P = 0.057$). Analysis of Maps 4 and 5 yielded similar results, with a significant Load × Map interaction for the TF criterion [$F(1, 13) = 5.73$, $P = 0.032$] and a marginally significant effect for the GEV criterion ($P = 0.09$). However, post-hoc t-tests indicated that differences between load conditions were significant only for Map 5 (TF criterion, $P = 0.02$; GEV criterion, $P = 0.03$).

Taken together, these results suggest very early differences in the configuration of neural generators implicated in the processing of task-irrelevant distractors as a function of attentional load. Importantly, these differences were most pronounced before C1 or during its rising phase, suggesting that these changes may reflect a possible source of the attentional influences on C1 peak amplitude as reported earlier. Again, no such difference between low- and high-load conditions was observed in lower VF subjects.

Source Localization

Finally, we applied a Local Autoregressive Average [LAURA; cf. Grave de Peralta Menendez et al., 2004] distributed source localization algorithm on the VEPs elicited by distractors in upper VF. Using the approximate time-windows for which significant topographic differences were observed (0–60 and 60–100 ms poststimulus), we calculated inverse solutions for each subject and condition and subsequently averaged them. As expected, distractor-related neural activity common to both load-conditions was primarily observed in early visual areas, with a clear maximum located near the occipital pole (Fig. 5A), although weaker source activity was also found in higher areas along the temporal visual stream. This was the case for both time-windows of interest, although overall activity was stronger during the 60–100 ms interval than during the first 60 ms (data not shown).

To pinpoint the neural correlates of load-induced differences observed in both waveform and microstate analyses, we then compared the activity of each of the 4,024 cortical generators between the two load-conditions and across subjects, using a paired *t*-test with a significance criterion of $\alpha = 0.005$ and an extent threshold of ≥ 3 contiguous generators.

As shown in Figure 5B, significant differences were observed for the second time-window from 60 to 100 ms, where activity in medial and dorsal prefrontal cortex in the left hemisphere was reduced under high attentional load. Considering the extent of these areas as well as their distance from the electrodes used for C1 measurements, it seems unlikely that the observed differences in source activity can explain the amplitude and topographic effects reported earlier. We therefore assume that higher attentional load did not induce differences in the configuration of neural activity in occipital cortex (but amplitude differences only) or that the head model used did not offer sufficient spatial resolution to detect any subtle load-related differences in early visual cortex. By contrast, differential activity in prefrontal cortex might indicate the recruitment of cognitive resources under high attentional load and a concomitant reduction of activity in default- or resting-state-networks.

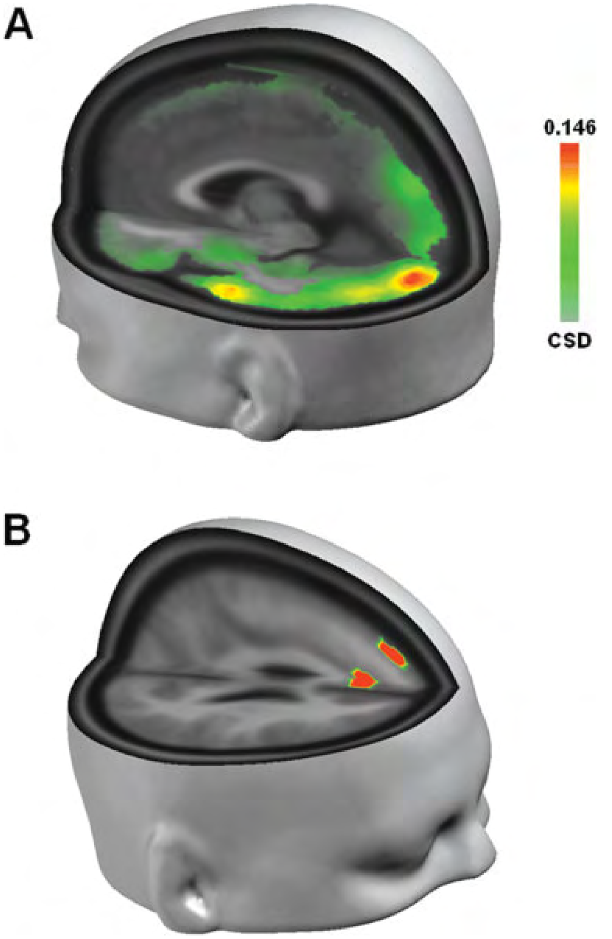

Figure 5.

A: Distributed inverse solution results for distractors in upper VF across subjects and conditions. Maximum activity was observed near the occipital pole. Data are for the time-window during which C1 topography persisted (60–100 ms, see Fig. 4). A similar pattern of activity was observed for the first 60 ms poststimulus, although at lower levels of overall activity. **B:** Results of paired *t*-test on distributed inverse solutions. Activity was compared between load conditions across all cortical generators, and those exceeding a significance criterion of 0.005 and an extent threshold of ≥ 3 are shown. The same time-window as in Figure 5 is displayed (no significant differences were observed during the first 60 ms poststimulus). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

DISCUSSION

Using a well-established experimental paradigm that induces different degrees of attentional load at fixation [Bahrami et al., 2007; Lavie, 2006; Schwartz et al., 2005], we demonstrate a modulation of visual responses to peripheral distractors involving the very early stages of visual cortex activity in humans. To our knowledge, only a single ERP study [Kelly et al., 2008] recently described an effect of spatial attention on the C1, which is the earliest component of the VEP and is considered to reflect the first volley of sensory information reaching V1 [Foxe and Simpson, 2002; Jeffreys and Axford, 1972]. Here, we show for the first time that C1 can be modulated by attentional load, providing new support for the view that even initial inputs associated with C1 are sensitive to attentional influences. In addition, in our study, topographical analyses suggest that load-induced changes in C1 amplitude are related to subtle shifts in neural generators even before the component's peak. We note that feedback effects have not been reported on the rising phase of the C1 [Foxe and Simpson, 2002; Vanni et al., 2004], arguing against the notion that our observations are linked to recurrent processing in V1. Finally, distributed source localization results indicate disengagement of medial and dorsal prefrontal cortex with increasing task demands, pointing to possible sources of top-down effects modulating the processing of task-irrelevant distractors due to changes in activity in executive frontal networks.

These data go beyond many previous EEG studies suggesting that attention does not affect primary visual cortex activity as indexed by the C1 [Handy et al., 2001; Heinze et al., 1994; Martinez et al., 1999; Noesselt et al., 2002], but are in agreement with a number of animal studies showing early attentional effects on V1 activity that may be unrelated to feedback influences from later stages of processing [Gilbert and Sigman, 2007]. Our findings also converge with previous behavioral [McAnany and Levine, 2007; Rubin et al., 1996; Yeshurun and Carrasco, 1998], electrophysiological [Pourtois et al., 2008b], and fMRI [Liu et al., 2006] evidence suggesting major functional asymmetries across the upper and lower VF, since a significant effect of attentional load was detectable only following peripheral stimulation above the horizontal meridian.

Modulation of Early Visual Processing by Attention

Top-down attentional modulations of early visual cortex activity, including V1, have been consistently observed in animal studies [Crist et al., 2001; Li et al., 2004] before feedback from later stages of visual processing. Our results provide important evidence that similar effects of attention may be observed in human primary visual cortex. By contrast, previous studies examining primary visual cortex activity in the context of manipulations of attention in humans have usually emphasized effects on P1 and N1, but reported an absence of effects on the C1 [Fu et al., 2008; Handy et al., 2001; Heinze et al., 1994; Martinez et al., 1999; Noesselt et al., 2002]. Possible reasons for these negative findings include the use of relatively small-scale stimuli [e.g., Handy et al., 2001], ineffective stimulus presentation on the horizontal midline [Martinez et al., 1999], or confounding stimulus differences between attentional conditions [e.g., Fu et al., 2008].

On the other hand, several recent studies reported that early visual cortex activity may be influenced by factors not directly related to attention or physical characteristics of the stimuli. For example, Halgren et al. [2000] as well as Pourtois et al. [2004] observed C1 modulations as a function of the emotional content of rapidly presented faces. Similarly, using an emotional conditioning procedure, Stolarova et al. [2006] found that C1 amplitude was increased for grating patterns previously associated with threat-related cues. Moreover, we [Pourtois et al., 2008b] previously showed that perceptual learning can also influence C1 amplitude and even more recently, Kelly et al. [2008] elegantly demonstrated an effect of spatial attention on C1 amplitudes using an individualized mapping procedure to account for large individual differences in the component's topography. Considering the high variability of human visual cortex functional anatomy [Amunts et al., 2000; Dougherty et al., 2003], these studies suggest that stimulation protocols tuned to the receptive field characteristics of V1 [Pourtois et al., 2004, 2008b; Stolarova et al., 2006] and/or individual mapping procedures such as employed by Kelly et al. [2008] are necessary to uncover subtle effects of higher cognitive processes on initial processing in V1.

In the present study, we used large-scale, high-contrast stimuli in the peripheral VF to demonstrate that increased attentional load at fixation leads to stronger filtering of distractors and an associated *reduction* of C1 amplitudes. Our results thus support the load theory of attentional selection [Lavie et al., 2004], according to which increased attentional demands for the central task may lead to a diversion of resources away from peripheral distractors and reduce their processing at early cortical stages. By contrast, previous ERP studies on attentional demands [Heinze et al., 1994; Martinez et al., 1999; Noesselt et al., 2002] often used tasks with a comparatively low impact on processing resources, which could in turn explain the comparatively late stages at which attentional filtering was observed.

Interestingly, Kelly et al. [2008] observed *increases* in C1 amplitude with spatial attention, presumably linked to enhanced contrast perception [cf. Talgar and Carrasco, 2002; Yeshurun and Carrasco, 1998]. Whether C1 amplitude increases or decreases might thus depend on the task-relevance of the stimuli used to trigger the C1. In the present experiment, as well as in our previous study of perceptual learning [Pourtois et al., 2008b], peripheral stimuli were task-irrelevant and thus suppressing neural processing of these distractors at early stages—as reflected in reduced C1 amplitudes—would benefit task performance on stimuli presented at fixation. By contrast, in the study of Kelly et al. [2008], subtle changes in contrast had to be detected in the peripheral stimuli used to elicit C1 responses. An enhanced representation of these stimuli would aid task performance, in accordance with their finding of higher C1 amplitudes under increased spatial attention. It thus seems that the interaction of visual cortex functional anatomy, experimental stimulus characteristics, and attentional task demands determines whether or not modulations of early primary visual cortex activity can be detected, and whether such modulations are reflected in increased or decreased EEG signals.

From a more general viewpoint, it seems unlikely that attentional effects should be observed across the whole visual cortex except V1. In natural situations, where stimulation does not occur within short and clearly separated time-windows, information extracted in higher-order visual cortex is presumably crucial to shape or refine the processing of subsequent stimuli from the earliest cortical stages onwards [Hupe et al., 2001]. The demonstration by Hupe et al. [2001] of transient MT/V5 inactivation leading to changes in firing frequency of V1 neurons from the very first time-bin of activation underlines the functional importance of ongoing top-down input to early visual cortex [see also Foxe and Simpson, 2002]. The fact that neuronal activity in V1 elicited by the same visual stimuli may change as a function of task demands [Crist et al., 2001] indicates that top-down influences can affect V1 excitability [see also Bestmann et al., 2007; Ruff et al., 2006]. Although both animal [Mehta et al., 2000] and human studies [Schwartz et al., 2005] suggest that attentional effects are less pronounced at lower levels of the visual cortex hierarchy, it is thus highly plausible that top-down control plays an important role in shaping sensory processing within early visual areas [Hupe et al., 1998], and our results add an important piece of evidence to the emerging view of primary visual cortex as an adaptive processor [Gilbert and Sigman, 2007; Gilbert et al., 2001] rather than a specialized and inflexible module for the treatment of low-level visual information.

Recent studies have demonstrated modulations of prestimulus α oscillations by spatial attention, linking them to an active, retinotopically specific process of distractor suppression [Kelly et al., 2006; Rihs et al., 2007]. Future research will have to test whether a similar mechanism may explain distractor suppression in paradigms where spatial attention is fixed but other attentional parameters are manipulated, as in the present study.

Differences in Attentional Effects Across the Visual Field

Manipulation of attentional load in the task performed at fixation elicited the expected pattern of behavioral and electrophysiological effects. Subjects were slower to react and committed more errors under high load, in accordance with earlier reports [Bahrami et al., 2007; Lavie, 1995]; and VEPs elicited by central target stimuli (see Fig. 2) showed enhanced occipito-parietal N1 amplitudes in this condition, in agreement with numerous studies demonstrating effects of endogenous attention on this component [Doallo et al., 2006; Eimer, 1998; Hillyard and Anllo-Vento, 1998; Hopfinger and West, 2006; Mangun, 1995; Vogel and Luck, 2000]. Importantly, this attentional modulation of VEPs to central stimuli was similar in upper and lower VF groups, whereas attentional effects on VEPs to the peripheral distractors revealed a clear asymmetry between upper and lower VF, with significant reductions of C1 amplitude only in the former group.

We have previously reported a similar asymmetry in C1 modulation [Pourtois et al., 2008b] and discussed possible sources of this effect. In particular, physiological differences along the upper versus lower hemiretina systems [Lehmann and Skrandies, 1979; Previc, 1990; for review, see Skrandies, 1987] may interact with attentional states in such a way as to produce seemingly contradictory results if the same stimuli are presented in different parts of the VF. This has been elegantly demonstrated by Carrasco and coworkers [Talgar and Carrasco, 2002; Yeshurun and Carrasco, 1998], who found that the same attentional manipulation may lead to performance increases or decreases depending on the eccentricity of stimulation. They interpreted this effect as a consequence of differences in spatial resolution and contrast sensitivity across the retina, with spatial attention being applied to areas of high spatial resolution resulting in reduced perception of low-resolution stimuli. However, this hypothesis cannot readily explain the asymmetries observed in the present paradigm, where peripheral stimuli were completely irrelevant and thus ignored by the subjects.

Nevertheless, psychophysically relevant differences between upper and lower VF seem a likely explanation for the differential effects observed. We surmise that differences in several physiological properties such as contrast sensitivity, spatial resolution, and conduction velocity may give rise to different degrees of load-sensitivity in upper and lower VF. This hypothesis is in accordance with the proposal that in humans, ecological constraints should favor higher spatial resolution in lower VF [Previc, 1990; Skrandies, 1987]. Furthermore, given the predominant projections of the upper VF to the ventral temporal stream, and the major role of attention for gating visual processing along object recognition pathways [Chelazzi, 1995], it is possible that attentional filtering might have a stronger impact on the upper than lower VF. Conversely, therefore, stimuli presented in the lower VF may be more resistant to modulation by attentional load, as found in the present study. The fact that Kelly et al. [2008] found effects of spatial attention on C1 amplitudes in both upper and lower VF is probably linked to stimulus differences: As noted by Previc [1990], asymmetries between upper and lower VF are most pronounced at low spatial frequencies and when large stimuli are used (as in the present study), whereas such asymmetries are much reduced at high spatial frequencies and for smaller stimuli [as employed by Kelly et al., 2008].

CONCLUSION

We have demonstrated a modulation of the first component of the VEP in response to peripheral distractors as a function of attentional load of a task at fixation. The effect was selectively observed in the upper VF. This is the first demonstration of attentional load effects on the very early stages of visual processing in humans, corresponding to the initial inputs into V1. We suspect that previous results showing the C1 to be unaffected by attentional manipulations are related to insufficient load being imposed on the attentional domain under study, differences in physical stimulation between experimental conditions, or individual differences in functional anatomy precluding reliable assessment of C1.

ACKNOWLEDGMENTS

The authors would like to thank Christoph Michel and Gregor Thut of the Functional Brain Mapping Lab for helpful discussions; and Rolando Grave de Peralta and Sara Gonzalez of the Electrical Neuroimaging Group for the realistic head model and the inverse solutions used in this work.

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Appendix C

Rauss K. S., Pourtois, G., Vuilleumier, P. & Schwartz, S. (submitted). Stimulus synchrony modulates effects of endogenous attention on early visual processing.

Stimulus Synchrony Modulates Effects of Endogenous Attention on Early Visual Processing

Karsten S. Rauss[1,2], Gilles Pourtois[3], Patrik Vuilleumier[1,2,4], & Sophie Schwartz[1,2,4]

[1] *Department of Neuroscience, University Medical School, University of Geneva, Switzerland*
[2] *Geneva Neuroscience Center, University of Geneva, Switzerland*
[3] *Department of Experimental Clinical and Health Psychology, Ghent University, Belgium*
[4] *Department of Neurology, Geneva University Hospital, Switzerland*

Corresponding author:
Sophie Schwartz, Laboratory of Neurology and Imaging of Cognition, Department of Neuroscience, University Medical School, University of Geneva, rue Michel-Servet 1, 1211 Geneva, Switzerland
phone: +41-22-37 95 376
fax: +41-22-37 95 402
e-mail: sophie.schwartz@unige.ch

Keywords:
attentional load, C1, EEG, V1, early vision

Running head:
Exogenous vs. Endogenous Attention in Early Visual Processing

Abstract

A growing number of studies suggest that early visual processing is not only affected by low-level perceptual attributes, but also modified by higher-order cognitive factors such as attention or emotion. Using high-density electroencephalography, we recently demonstrated that attentional load of a task at fixation reduces the response of primary visual cortex to peripheral distractors, as indexed by the C1 component. Here, we used a similar paradigm to examine the role of competing demands on exogenous attention by synchronizing task and distractor stimuli. Results show that rather than suppressing distractor responses, high attentional load elicits higher C1 amplitudes if task and distractor stimuli are presented simultaneously. This suggests that endogenous attentional processes underlying early attentional filtering may be overridden by the presentation of a highly salient exogenous cue. Thus, exogenous and endogenous attentional demands may interact at the earliest levels of processing in human visual cortex.

Introduction

A growing body of evidence indicates that even the earliest stages of cortical visual processing in humans may be modified by higher-level factors such as emotion (Pourtois, Grandjean, Sander, & Vuilleumier, 2004; Stolarova, Keil, & Moratti, 2006), learning (Pourtois, Rauss, Vuilleumier, & Schwartz, 2008; Schwartz, Maquet, & Frith, 2002), or attention (Kelly, Gomez-Ramirez, & Foxe, 2008; Rauss, Pourtois, Vuilleumier, & Schwartz, 2009; Schwartz et al., 2005). While early attentional effects are in accordance with results from animal experiments (Crist, Li, & Gilbert, 2001; C. Gilbert, Ito, Kapadia, & Westheimer, 2000; C. D. Gilbert & Sigman, 2007), previous electroencephalography (EEG) studies could identify only later effects of attention in human primary visual cortex (V1) (Di Russo, Martinez, & Hillyard, 2003; Heinze et al., 1994; Hillyard, Vogel, & Luck, 1998; Martinez et al., 1999; Noesselt et al., 2002). Reasons for this discrepancy may lie in the large variability of human visual cortex anatomy (Amunts, Malikovic, Mohlberg, Schormann, & Zilles, 2000; Dougherty et al., 2003; Hasnain, Fox, & Woldorff, 1998) that potentially precludes adequate overlap of individual EEG topographies (Kelly et al., 2008), as well as stimulation parameters not adequately adapted to V1 characteristics (for detailed discussions, see Pourtois, Rauss et al., 2008; Rauss et al., 2009).

On the other hand, true functional differences may exist between the effects of different attentional parameters on early sensory processing, particularly if different attentional demands associated with an experimental task compete with each other (Schreij, Owens, & Theeuwes, 2008). A distinction is often made between endogenous and exogenous attention (Corbetta & Shulman, 2002; Posner, 1980; Yantis & Jonides, 1990), with the former being under the voluntary control of the subject and the latter reflecting an automatic and non-voluntary capture of attention by salient (but not necessarily relevant) stimuli. Both exogenous (Khoe, Mitchell, Reynolds, & Hillyard, 2005; Pourtois et al., 2004) and endogenous attention (Kelly et al., 2008; Poghosyan & Ioannides, 2008; Rauss et al., 2009) have recently been shown to influence the earliest stage of visual processing within human visual cortex, as indexed by the C1 component which is principally generated in V1 (Clark, Fan, & Hillyard, 1995; Foxe & Simpson, 2002; Jeffreys & Axford, 1972). However, their interactive influence on these early cortical stages remains debated (see Hopfinger & West, 2006).

In a previously published experiment (Rauss et al., 2009), we manipulated the attentional load (Lavie, 1995, 2005; Lavie, Hirst, de Fockert, & Viding, 2004) of a central task while presenting irrelevant distractors in either the upper or the lower visual field. Using high-density EEG, we observed that the C1 component elicited by distractors in the upper visual field was reduced under conditions of high attentional load, suggesting very early filtering of distractors as a function of retinal location and task demands on endogenous attention. Inasmuch as our large-scale, high-contrast distractors attracted exogenous attention due to their sudden, unpredictable onset (Egeth & Yantis, 1997; Yantis & Jonides, 1984), this result indicates that endogenous attentional mechanisms can attenuate effects of exogenous attentional capture (Handy, Soltani, & Mangun, 2001; Hillyard et al., 1998; Ruff & Driver, 2006) at the earliest level of cortical visual processing in V1.

In the present study, we were interested in the boundary conditions of such early endogenous attentional filtering: We asked whether filtering effects on distractor processing as a result of load manipulations would persist in the presence of even more salient distractors, capturing exogenous attention to a greater degree. In order to increase distractor saliency while keeping basic stimulus and task characteristics constant, we changed the timing of the previously used protocol by eliminating the stimulus onset asynchrony (SOA) between central task stimuli and peripheral distractors. Since foveally presented stimuli do not elicit a C1 component (Jeffreys & Axford, 1972), synchronous or asynchronous presentation of central task stimuli and peripheral distractors should not *per se* affect the earliest parts of the visual evoked potential (VEP). On the other hand, exogenous attention should be engaged to a higher degree with simultaneous presentation of task stimuli and distractors: Although attentional capture by simultaneous events has mostly been examined in bi- or multimodal contexts (Santangelo & Spence, 2007; Van der Burg, Olivers, Bronkhorst, & Theeuwes, 2008a, 2008b), it also occurs with exclusively visual stimuli (Fournier, 1994; Kahneman, Treisman, & Burkell, 1983; Wilson & Singer, 1981). As reviewed and replicated by Fournier (1994), simultaneously presented noise interferes with the processing of target stimuli in both search- and non-search tasks, even if target and noise are highly distinct and presented relatively far apart. Kahneman et al. (1983) conducted a series of experiments in which they examined the effects of target-distractor similarity, display-size, cueing, and timing on visual filtering. One of their experiments specifically tested the influence of different distractor time-courses and better performance was observed in conditions where distractors were presented prior to, rather than simultaneously with, target stimuli. The authors concluded that:

“[…] the cost of filtering should be attributed, at least in part, to competition between events rather than between objects.” (Kahneman et al., 1983, p.519)

Specifically, Kahneman and colleagues argued that events competed for limited attentional resources. Similar arguments have been put forward within the framework of the biased-competition theory of attention (Sabine Kastner, De Weerd, Desimone, & Ungerleider, 1998; Steven J. Luck, Chelazzi, Hillyard, & Desimone, 1997).

Based on these studies, we assumed that simultaneous presentation of task and distractor stimuli should engage exogenous attentional mechanisms to a greater degree than asynchronous presentation. Exogenous attentional capture in turn has been shown to enhance C1 amplitudes (Khoe et al., 2005). We thus predicted that effects of endogenous attentional filtering on early visual cortex activity as observed in our previous experiment (Rauss et al., 2009) would be reduced if task and distractor stimuli were presented simultaneously. Our results indicate that this is indeed the case: Simultaneous task-distractor presentation inverted the previously reported effect of attentional load on C1, with higher V1 activity observed under high load. These findings demonstrate that relatively innocuous changes in stimulation parameters can have profound effects on top-down effects observed at the earliest stages of visual processing. More importantly, they suggest that exogenous and endogenous attentional mechanisms can interact during initial stimulus-evoked activity in V1 and thus at an earlier stage of visual processing than previously thought (Stigchel et al., 2009).

Methods

Subject selection, experimental stimuli and procedure as well as data recording and analysis were made as similar as possible to those used in our previous study (Rauss et al., 2009).

Subjects

Nineteen healthy, right-handed participants without neurological or psychiatric history gave written informed consent to participate in the study, which was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee. Data from five subjects had to be excluded due to poor behavioral performance (i.e., error rates were two standard deviations above the mean of all participants) and/or excessive artifacts on the EEG recordings. The remaining 14 participants (11 females) were aged between 21 and 31 (median: 26). Our previous experiment was also based on the data of 14 participants (three females, age range 22-40, median 26) using the same inclusion and exclusion criteria (Rauss et al., 2009).

Stimuli

Visual stimuli were created online using Cogent (www.vislab.ucl.ac.uk/Cogent2000), a MATLAB toolbox allowing precise timing and synchronization with the EEG system, and presented on a 17” CRT screen (viewing distance 40 cm, refresh cycle 60 Hz). T-shapes of different colors and orientation were rapidly presented at the bottom of the screen (1.35×1.90° of visual angle; Fig. 1A). Task-irrelevant arrays of white horizontal line elements were flashed in the periphery (~41×18°, distance from upper edge of task stimuli ~3.8°) on 22% of central events. Distractors were presented in synchrony with the T-shaped central task stimuli, i.e., unlike our previous study in which distractors were interleaved with task stimuli (Rauss et al., 2009). The screen background remained black throughout the whole experiment.

Figure 1 shows the trial time-course for both the present (B) and previous experiment (C). As poorer performance was expected for synchronous task-distractor presentation (Kahneman et al., 1983), we adapted stimulus duration so as to equate difficulty across the two experiments: Central task stimuli (and thus distractors) were presented for 500 ms in the present study while they were each presented for 250 ms in our previous experiment. In addition, we used distractors covering the whole vertical extent of the screen, whereas different eccentricities were tested with smaller distractors in our previous study. We will come back to this issue in the discussion section.

Insert Figure 1 around here

Procedure

Subjects were placed in a quiet, dimly lit and electrically shielded recording booth. Four blocks of 410 trials were presented yielding 60 distractor trials of interest per load condition. At the beginning of each block, participants were instructed to press the space-bar of a standard computer keyboard either (i) if they saw an upright or upside-down red T-shape (pop-out detection, low attentional load); or (ii) if they saw an upright yellow or an upside-down green T-shape (conjunction discrimination, high attentional load). The two tasks were alternated across blocks, with the starting condition randomized across subjects. Pseudo-random trains of stimuli were created for each block, with an equal number of imperative central task stimuli requiring motor responses (~30) in the low and high load conditions. In order to minimize motor artifacts, stimulus sequences were programmed so as to minimize the co-occurrence of imperative central task stimuli (targets) and peripheral distractors. Instructions stressed that randomly occurring distractors in the periphery were task-irrelevant and to be ignored. Each block lasted approximately six minutes, including a short break after half of the trials had been completed.

Data Recording and Analysis

Scalp-EEG was recorded from 62 Ag/AgCl electrodes (Neuroscan, Synamps, El Paso, TX) positioned according to the extended international 10-20 EEG system and referenced to the tip of the nose. Signals were amplified at 30K and bandpass-filtered between 0.01–100Hz; a 50 Hz notch-filter was applied to filter line noise. Horizontal and vertical electro-oculograms (EOG) were monitored using 4 bipolar electrodes. Both EEG and EOG were acquired continuously at 500Hz.

Using Brain Vision Analyzer 1.05 (Brain Products, Munich, Germany), eye-blink artifacts were semi-automatically corrected using the procedure described by (Gratton, Coles, & Donchin, 1983) and a 0.5 Hz high-pass filter was applied. Epochs from –100 ms to +600 ms around stimulus-onset were extracted for task-only as well as task-plus-distractor trials and baseline-corrected for the 100 ms preceding stimulus-onset. Epochs with EEG or residual EOG exceeding ±80μV were rejected. Single trials were then averaged and low-pass filtered at 30 Hz and the C1 (only on task-plus-distractor trials), P1, and N1 components were semi-automatically identified based on their distinctive polarities, latencies, and topographic properties. Their peak amplitudes and latencies were measured in each participant for electrode sites and time-windows determined from the grand averages. Repeated-measures analyses of variance (ANOVAs) were conducted on peak amplitude and latency values, with load-condition, hemisphere (if applicable), and electrode locations as within-subjects factors. Greenhouse-Geisser correction of degrees of freedom was applied where appropriate.

We subsequently tested for topographical differences between load conditions using a microstate segmentation analysis (Pasqual-Marqui, Michel, & Lehmann, 1995), as implemented in the software Cartool (http://brainmapping.unige.ch/Cartool.htm). This analysis is based on the assumption that while a given distribution of voltage values across the scalp may reflect any combination of neural generators, different distributions necessarily imply different neural generators (Lehmann & Skrandies, 1980). As scalp voltage distributions typically remain stable for tens of milliseconds, it has been proposed that they reflect EEG microstates associated with distinct stages of processing (Michel, Seeck, & Landis, 1999; Pourtois, Delplanque, Michel, & Vuilleumier, 2008). In order to detect such periods of topographic stability, voltage maps corresponding to each time-frame of grand-average ERPs were subjected to a K-means cluster analysis (Pasqual-Marqui et al., 1995). Analyses were calculated for the first 300 ms post-stimulus of grand averages from both load conditions, and individual microstates were considered as reliable if they persisted for at least 3 time-frames (i.e. 6 ms). Separate analyses were run for 5 up to 25 initial clusters and the optimal number of clusters was determined objectively using both cross-validation (Pasqual-Marqui et al., 1995) and Krzanowski-Lai (Tibshirani, Walther, & Hastie, 2001) criteria.

Finally, a Local Auto-Regressive Average (LAURA) procedure (Grave de Peralta Menendez, Murray, Michel, Martuzzi, & Gonzalez Andino, 2004) was used to estimate electrical sources in the brain volume during selected periods of interest. This distributed source localization analysis does not require any a-priori assumptions about the number and position of neural generators, but determines the most likely configuration of activity simultaneously in a large number of solution points (4024 in the present study) evenly distributed throughout the grey matter. Effects of attentional load were assessed via paired t-tests conducted on the activity of each solution point in each subject across conditions.

Results

In addition to the results of the present study, we also provide brief descriptions of the results previously obtained with asynchronous task-distractor presentations (Rauss et al., 2009) where appropriate.

Behavioral Performance

Non-parametric Friedman tests were used to assess the influence of Attentional Load and Block on the number of misses and false alarms. For both variables, significant differences were observed between load-conditions (misses: $p < 0.05$, one-tailed; false alarms, $p < 0.001$), although overall error rates were low, with no subject committing more than 3 misses per block and only one subject committing more than 10 false alarms in one block.

Analysis of variance (ANOVA) was conducted on the mean reaction-time (RT) data, with Attentional Load (low vs. high) and Block (first vs. second) as within-subjects factors. As expected, the effect of Attentional Load was highly significant ($F[1, 13] = 229.75$, $p < 0.001$, partial $\eta^2 = 0.946$), indicated by reliably slower detection of imperative central task stimuli in the high load (mean ± SE, 613 ± 9 ms) relative to the low load condition (481 ± 7 ms). The main effect of Block and the Load × Block interaction were not significant (both $p > 0.19$).

These behavioral results are comparable with our previous study using a similar paradigm with asynchronous task-distractor presentations (Rauss et al., 2009). They confirm clear effects of the load manipulation, and indicate that task difficulty was successfully equated between the different stimulation protocols (see Methods). Indeed, ANOVAs across both datasets including a factor for the two different experiments indicated significant main effects of Attentional Load on RT and performance variables, but no main or interaction effects involving the Experiment factor. Note that a direct comparison of performance on trials with and without distractors was not possible due to the fact that stimulation parameters were chosen so as to minimize the co-occurrence of imperative targets and peripheral distractors (see Methods).

Task-only VEPs

We first analyzed VEPs elicited by the central-stream stimuli, excluding those that required a motor response and any false alarms. These analyses were conducted to verify that the classic pattern of ERP components corresponded to earlier studies using similar paradigms, and thus to ensure that the task was comparable to our previous experiment (Rauss et al., 2009). As shown in Figure 2, non-imperative central task stimuli elicited a conspicuous occipital P1 component (Hillyard & Anllo-Vento, 1998), followed by an occipital N1 component (Vogel & Luck, 2000). As expected, no earlier C1 component could be detected for these foveally presented stimuli (Clark et al., 1995).

The P1 component to these non-imperative central task stimuli was measured at posterior occipital electrodes P7, P5, P3, P4, P6, P8, PO7, PO5, PO6, and PO8. Peak amplitudes were entered into a repeated-measures ANOVA with factors Attentional Load (low/high), Hemisphere (left/right), and Electrode. Results indicated a highly significant effect of Load (F[1, 13] = 19.93, p = 0.001, partial $\eta^2 = 0.605$), with high load eliciting substantially higher P1 amplitudes than low load (mean ± SE = 6.21±0.82 vs. 4.83 ± 0.75 μV), consistent with an early gain control mechanism acting on attended visual stimuli (Hillyard et al., 1998; S. J Luck, 1995). No significant main or interaction effects of Hemisphere were observed. Analyses of peak latencies showed no significant main effects of any of the factors, nor their interactions.

Raw amplitude values for the N1 component, measured at the same electrodes as the P1, did not show any significant effects of interest. However, considering the effect of Attentional Load on P1, we repeated our N1 analyses using peak-to-peak measurements (Picton et al., 2000). These did show a significant effect of Attentional Load (F[1, 13] = 9.32, p = 0.009, partial $\eta^2 = 0.417$), as well as a marginally significant effect of Hemisphere (F[1, 13] = 4.24, p = 0.06, partial $\eta^2 = 0.246$): N1 amplitudes were larger for high load (8.81 ± 0.81 vs. 6.83 ± 0.60 μV) and tended to be larger over the right hemisphere (8.73 ± 0.89 vs. 6.91 ± 0.64 μV). Peak latency data suggested no significant influence of any of the factors, nor their interactions. Figure 2A displays P1 and N1 effects as evident in the grand averages.

Insert Figure 2 around here

Note that although the main effect of the Electrode factor on peak amplitudes was significant for both the P1 and N1 analyses, it did not interact with Attentional Load, thus suggesting that the topographies of both components were not systematically affected by differing attentional demands (McCarthy & Wood, 1985), in agreement with a gain control mechanism of endogenous attention affecting the strength, but not the topography or latency of early visual responses (Hillyard et al., 1998).

Figure 2B shows the corresponding grand-average ERPs from our previous study (Rauss et al., 2009) with asynchronous presentation of central task stimuli and peripheral distractors. It can be seen that significant differences in N1 amplitudes were observed in both experiments, whereas earlier effects on the P1 component were observed only in the present study, where subjects were expecting concurrent interference by peripheral distractors. In order to statistically test this difference, we entered P1 and N1 amplitudes from both studies into separate repeated-measures ANOVAs with the same factors as above plus Experiment as between-subjects factor. Results for the P1 component indicated a highly significant effect of Load across the two datasets (F[1, 26] = 16.32, $p < 0.001$, partial $\eta^2 = 0.386$) as well as a marginally significant effect of the Experiment factor (F[1, 26] = 4.08, $p = 0.054$, partial $\eta^2 = 0.135$): P1 amplitudes were higher under high load (4.89 ± 0.54 vs. 4.14 ± 0.47 μV) and tended to be higher in the present experimental group (5.52 vs. 3.51 ± 0.71 μV). However, both effects were mainly due to the significant Load × Experiment interaction (F[1, 26] = 11.08, $p = 0.003$, partial $\eta^2 = 0.299$), as expected from the significant P1 differences observed in the present but not our previous study. Thus, overall group differences cannot fully explain the distinct behavior of P1 in the two experiments. The same analysis for the N1 component revealed a significant effect of Load only (F[1, 26] = 7.50, $p = 0.011$, partial $\eta^2 = 0.224$), in accordance with the more negative N1 amplitudes under high load observed in both experiments. The Experiment factor was non-significant ($F < 1$).

Task-plus-distractor VEPs

We then analyzed critical trials in which the central stimulus did not require a motor response (non-imperative central task stimuli), but was accompanied by an irrelevant and non-predictive peripheral distractor, as described in the Methods section. Based on the grand-averages, central-parietal and parietal electrodes CP1, CPz, CP2, P1, Pz, and P2 were selected for analyses of the C1 component, in keeping with previous ERP studies which showed that this primary visual cortex ERP component reaches its maximum amplitude over occipito-parietal leads along the midline (Clark et al., 1995; Di Russo & Spinelli, 1999; Jeffreys & Axford, 1972). Peak voltages were analyzed with Attentional Load (low/high) and Electrode as within-subjects factors.

Results demonstrated a significant effect of Load (F[1, 13] = 5.85, $p = 0.031$, partial $\eta^2 = 0.310$), with higher C1 amplitudes observed under high load (-6.58 ± 0.76 μV) compared to low load (-5.06 ± 0.75 μV). While the Electrode factor was significant, it did not interact with Attentional Load ($F < 1$), thus suggesting that there were no systematic changes in local C1 topography associated with the experimental manipulation (McCarthy & Wood, 1985). The lack of reliable change in the electric field configuration for the C1 as a function of the attentional load condition was further verified by additional topographic analyses (see below). Latency effects were found only for the Electrode factor ($p = 0.001$; Load and Load × Electrode, both $F < 1$) and were therefore not followed up.

We also investigated subsequent ERP components elicited by the combination of central task and peripheral distractor stimuli. Analysis of P1 amplitudes on task-plus-distractor trials followed the same procedure as for task-only trials, i.e. electrodes P7, P5, P3, P4, P6, P8, PO7, PO5, PO6, and PO8 were analyzed with Attentional Load, Hemisphere, and Electrode as within-subjects factors. No significant effect of Attentional Load was observed ($F < 1$), and no other main or interaction effects of interest were present. The same results were obtained in additional peak-to-peak analyses (P1 relative to C1). Similarly, analysis of P1 peak latencies did not uncover any significant main or interaction effects (all $p > 0.10$). In order to examine whether activity elicited by the peripheral distractors might have masked effects of endogenous attention on task-plus-distractor P1 amplitudes, we calculated additional analyses across both task-only and task-plus-distractor trials, with Distractor Presence as an additional within-subjects factor. Using peak-to-peak P1 amplitudes as above, results indicated a significant effect of Load ($F[1, 13] = 9.15$, $p = 0.01$, partial $\eta^2 = 0.413$) and Distractor Presence ($F[1,13] = 51.60$, $p < 0.001$, partial $\eta^2 = 0.229$), but no interaction between those two factors: P1 amplitudes were higher in the high load condition (8.2 ± 0.76 vs. 7.0 ± 0.81 μV) and in the presence of a distractor (9.68 ± 0.85 vs. 5.52 ± 0.77 μV). Thus, higher attentional load seems to augment P1 amplitudes in the presence of distractors, even though this effect does not reach statistical significance if task-plus-distractor trials alone are considered.

Analyses of N1 peak amplitudes, conducted on the same set of electrodes and using the same factors as for the P1 component, did not reveal any significant main or interaction effects either (all $p > 0.10$), but the component peaked slightly earlier under high (154 ± 2.3) than under low load (161 ± 3.0 ms), $F(1, 13) = 6.66$, $p = 0.023$, partial $\eta^2 = 0.339$. As for P1 amplitudes, we examined whether the lack of change in N1 amplitudes when compared to task-only trials was due to the presence of peripheral distractors by computing additional ANOVAs across task-only and task-plus-distractor trials, based on peak-to-peak measurements. As opposed to what was observed for the P1, these analyses indicated no significant effect of Load ($p > 0.1$), but significant effects of Distractor Presence ($F[1, 13] = 6.26$, $p = 0.026$, partial $\eta^2 = 0.325$) and a significant Load × Distractor Presence interaction ($F[1, 13] = 9.93$, $p = 0.08$, partial $\eta^2 = 0.433$):

N1 amplitudes were higher when a distractor was present (9.81 ± 0.98 vs. 7.82 ± 0.64 μV), but were affected by the load manipulation only in the absence of distractors. While these results could reflect ceiling on task-plus-distractor N1 amplitudes, they might also be due to an interaction between exogenous and endogenous attention during the N1 interval, as previously described by (Hopfinger & West, 2006). We will return to this issue in the Discussion.

Insert Figure 3 around here

While simultaneous presentation of central task stimuli and peripheral distractors would be expected to disrupt attentional filtering (Kritikos, McNeill, & Pavlis, 2008), these results are striking in that they demonstrate a reversal of the effect of attentional load on early visual processing, as indexed by the C1, as a function of task-distractor synchrony (Figure 3). In order to corroborate these findings, we performed additional analyses. First, we examined the possible role of stimulus differences between the present and our previous study (Rauss et al., 2009). Here, full-screen distractors were employed while in our previous experiment, we manipulated the eccentricity of task-irrelevant stimulation, such that distractors covered half of the vertical extent of the screen, either close to or far from the central task stimuli. Using the latter setup, we observed a reduction of distractor-elicited C1 amplitudes when distractors were presented close to fixation, while there was no modulation of the C1 for more eccentric distractor presentation, probably because unambiguous identification of C1 was possible only in a minority of participants following the more eccentric distractors. Considering the functional anatomy of human visual cortex and particularly the cortical magnification of locations closer to the fovea (Slotnick, Klein, Carney, & Sutter, 2001), eccentric stimulation should lead to visual activations that are weaker and less comparable across subjects than those following parafoveal stimulation (Amunts et al., 2000; Dougherty et al., 2003; Hasnain et al., 1998). Thus, the larger vertical extent of distractors used in the present study should not have led to a systematic increase of C1 amplitudes. To formally examine this possibility, we compared C1 amplitudes across all subjects from both experiments, with Attentional Load and Electrodes as within-subjects factors and Experiment as between-subjects factor. While the Load × Experiment interaction was highly significant ($p = 0.002$), in accordance with the reversed effects of attention on C1 amplitudes, no overall differences between C1 amplitudes in the two groups were observed ($F < 1$). Accordingly, the inverted effect of attentional load observed in the present experiment cannot be explained in terms of low-level stimulus differences between the two studies.

Secondly, the grand-averages displayed in Figure 3 suggested differences in peristimulus activity between load conditions in the present but not our previous experiment. We therefore explored the strength of this early activity and tested whether it could have affected the VEP effects described above. Running t-tests comparing load conditions across all subjects and electrodes for each time-frame, with a liberal significance criterion of $p < 0.01$ (uncorrected for multiple comparisons), indicated that the peristimulus differences evident from Figure 3A were indeed significant across the parieto-occipital region. However, correlations between mean peristimulus differences from -40 to 40 ms and attentional modulations of early VEP components were non-significant (C1: $r = 0.30$, $p = 0.29$; task-only P1: $r = -.37$, $p = 0.19$; task-only N1: $r = 0.25$, $p = 0.39$). This was also the case for correlation coefficients based on C1, P1, and N1 differences raised to the power of 2 or 3 (all $p > 0.10$), excluding exponential relationships. We conclude that peristimulus differences constitute an unlikely explanation for the effect of attentional load on C1, P1, or N1 amplitudes.

Finally, we tested whether the load-related modulation of C1 amplitudes correlated with P1 and N1 effects observed in task-only trials. No significant correlation was observed between C1 amplitude differences and modulations of task-only P1 ($r = -.266$, $p > 0.35$); however, C1 modulation correlated positively with the effect of Attentional Load on task-only N1 amplitudes (Pearson's $r = 0.607$, $p = 0.021$; Fig. 4A). This result suggests a linear relationship between the extent of attentional focusing on the central task as indexed by stronger N1 modulations and *lack of* attentional filtering in early visual cortex, as indexed by increased C1 amplitudes. Going back to the data of our previous study (Rauss et al., 2009), we found a similar absence of correlation between C1 and P1 amplitudes ($r = 0.385$, $p = 0.17$), but a significantly negative relationship between C1 and N1 modulations ($r = -.546$, $p = 0.043$, results not reported in the original study; Fig. 4B). Thus, attentional filtering in early visual cortex as indexed by reduced C1 amplitudes was linearly related to attentional focusing as indexed by increased N1 amplitudes. These analyses provide further quantitative evidence for the opposite effects of attentional load on distractor processing as a function of task-distractor synchrony.

Insert Figure 4 around here

Topographic and Source Localization Analyses

In our previous study (Rauss et al., 2009), we described very early topographic differences between attentional load conditions, associated with significant differences of activity for sources within anterior cingulate and dorsomedial prefrontal cortex. In order to compare the present dataset with these results, we conducted the same analyses, using the same settings and parameters.

Results of the microstate topographic analyses (Michel et al., 1999; Pasqual-Marqui et al., 1995) did not show any conspicuous differences in voltage topographies between the two load conditions, either for task-only or for task-plus-distractor grand averages. By contrast, distributed source localization analyses on the task-plus-distractor ERPs using LAURA (Fig. 5; Grave de Peralta Menendez et al., 2004) uncovered significant differences in activity of the reconstructed neural generators during the C1 interval. As shown in Figure 5B, average activity across the time-window during which the C1 topography persisted (50 – 90 ms) differed significantly ($p < 0.01$) between load conditions in midcingulate cortex (MCC), as well as in the right temporo-parietal junction (TPJ), with low load eliciting higher activity in both areas. Differences in early visual cortex activity corresponding to the ERP effects reported above may have been masked by the limited spatial resolution of the inverse solution technique, particularly because the template brain used to define solution points does not capture individual variations in visual cortex anatomy (Amunts et al., 2000).

Insert Figure 5 around here

The right panel in Figure 5B shows similar analyses from our earlier experiment which suggested differences in neural activity in dorsomedial prefrontal and anterior cingulate regions. In order to verify that these differences between experiments were not attributable to the presence of central task stimuli during the synchronous condition of stimulus and distractors presentation, we subtracted task-only from task-plus-distractor ERPs in inverse space, separately for each subject and condition. We then conducted a running t-test between load conditions across all solution points and time-frames on these difference scores. Due to the large divergence between task-only and task-plus-distractor VEPs (most notably, the absence of a C1 in the former, compare Figs. 2 and 3), we could not use topographic analyses to determine time-windows of interest and opted for a relatively liberal significance criterion of $p < 0.05$ across at least 10 time-frames (i.e. 20 ms). Significant differences were observed during the early phase of the C1 in MCC (50-70 ms, data not shown). During the interval immediately preceding the C1 peak (70-90 ms), activity in right dorsolateral prefrontal cortex, right TPJ, and right orbitofrontal cortex differed significantly between load conditions (data not shown). Again, activity in these areas was higher under low attentional load.

These results suggest that the inverse solutions obtained for task-plus-distractor trials (Fig. 5B, left panel) largely reflect distractor processing, in that activity differences persist in MCC and right TPJ even when the contribution of task-related activity is removed from the inverse solution space. On the other hand, distractor-related activity in frontal areas seems to be masked by task-related processing, because it was not visible in the task-plus-distractor solutions. Altogether, these results suggest that partly distinct neural networks are implicated in attentional filtering during synchronous vs. asynchronous distractor interference.

Discussion

Our study adds to the increasing evidence for attentional (Kelly et al., 2008; Poghosyan & Ioannides, 2008; Rauss et al., 2009) and other high-level influences (Pourtois et al., 2004; Pourtois, Rauss et al., 2008; Stolarova et al., 2006) on the earliest sweep of visual evoked activity in human occipital cortex. By comparing the present data to a previously published experiment (Rauss et al., 2009), we show that the attentional load of a task at fixation may either decrease or increase C1 responses to peripheral, irrelevant stimuli, depending on the relative timing of task- and distractor-streams. Specifically, the present study demonstrates that C1 amplitude increases with increasing attentional load when central task stimuli and peripheral distractors are presented simultaneously, while C1 was decreased with increasing load in our previous ERP study, where a variable SOA was introduced between the presentation of central task stimuli and peripheral distractors.

Extrastriate ERP components also showed distinct effects as a function of task-distractor synchrony. Task-only P1 amplitudes, elicited by the same physical stimuli at the center of gaze, were increased for high compared to low load conditions in the present study. P1 effects were less evident in task-plus-distractor trials, but additional analyses across task-only and task-plus-distractor trials did suggest an effect of attentional load over and beyond the mere stimulus-driven increases of P1 in the presence of peripheral distractors. These findings contrast with the absence of P1 effects reported in our previous study (Rauss et al., 2009) for asynchronous task-distractor presentation. It seems likely that the simultaneous presence of peripheral distractors in the current experiment raised attentional requirements for achieving a similar level of behavioral performance on the central task stimuli as during the asynchronous protocol. Thus, in the present task, higher demands on initial attentional filtering due to expected simultaneous interference could explain the increase in task-only P1 amplitudes (Handy et al., 2001; Hillyard & Anllo-Vento, 1998; Hopfinger & Handy, 1998; S. J Luck, 1995).

On the other hand, N1 amplitudes in the present experiment were only modulated by attentional load in the absence of peripheral distractors and this mirrors the findings of our previous study. As the component was overall more pronounced when distractors were simultaneously presented, one might suspect a ceiling effect, where attentional modulations could not be observed due to strong stimulus-driven activity. However, the fact that amplitudes of the preceding P1 component did not show saturation effects speaks against such an explanation. Rather, we believe that the significant interaction of attentional load and distractor presence/absence observed in the present dataset reflects an interaction of exogenous and endogenous attention at the level of the N1, as has been reported previously (Hopfinger & West, 2006).

Importantly, significant correlations between changes in distractor-elicited C1 and task-only N1 amplitudes in both experiments point to a link between attentional modulations at the level of early visual cortex and subsequent extrastriate processing stages. The striking finding that increased attentional focusing on a central task may relate to opposite effects on distractor processing at the level of V1 clearly requires further examination. In particular, it will be interesting to test whether these opposite effects are specific to simultaneous visual onsets, which may act as reliable indicators of importance under natural viewing conditions and may thus be difficult to split up into relevant and irrelevant parts at early processing levels. Alternatively, our findings may reflect a fundamental limitation of early attentional filtering in the face of highly salient events; in that case, other manipulations of exogenous attentional demands should yield similar results.

Taken together, the ERP effects observed in the present study and their comparison with a previously published experiment (Rauss et al., 2009) suggest, for the first time to our knowledge, that exogenous attentional capture may interact with endogenous attentional demands at the level of V1. Specifically, increased distractor saliency, as operationalized here by simultaneous presentation of task and distractor stimuli, appears to revert the effects of endogenous attentional filtering mechanisms operating at the earliest stages of cortical visual processing. Furthermore, this effect relates to attentional modulations observed at the level of extrastriate cortex, as evidenced by significant correlations between C1 and task-only N1.

If early attentional filtering is affected by distractor saliency, later processing stages should be modulated as well. We tested this hypothesis by correlating task-only N1 modulations with behavioral performance (mean RT differences, high minus low load). In the present study, this correlation was significant ($r = -0.598$, $p = 0.024$), but not in our previous experiment ($r = 0.206$, $p = 0.48$). Since we did not observe correlations between C1 effects and behavioral variables in any of the two studies, the interpretation of these results requires some caution. Nevertheless, they may indicate that due to the augmentation of neural activity at early processing stages, attentional mechanisms associated with the N1 component are engaged to a higher degree when distractors are highly salient and therefore selectively correlate with behavioral performance if competition between exogenous and endogenous attentional demands is exacerbated.

Results of microstate segmentation and distributed source localization analyses support these interpretations. The absence of topographical differences in combination with the observed modulations of source activity in right temporo-parietal and mid-cingulate structures suggest the involvement of a network dedicated to exogenous orienting of attention (Corbetta & Shulman, 2002; Ruff & Driver, 2006) and a relative reduction of activity in this same network under higher attentional demands. While we expected to see differences in neural activity within early visual cortex, the limited spatial resolution of distributed inverse solutions may have masked any such differences – which are presumably more variable across subjects in early visual cortex than in the fronto-parietal network involved in the endogenous control of spatial attention (see Corbetta & Shulman, 2002; S. Kastner & Ungerleider, 2000) – particularly because large individual differences in functional anatomy of the visual cortex (Amunts et al., 2000; Dougherty et al., 2003; Hasnain et al., 1998) cannot be appropriately captured using a canonical template brain.

Nevertheless, we believe that the observed differences in higher-level brain regions are of interest in that they may indicate sustained or ‘tonic’ attentional influences linked to different task-sets in the low and high load conditions, respectively. Such tonic attentional influences have been proposed to interact with the local circuitry in sensory cortices, gating stimulus-evoked activity early in the cortical hierarchy (Chawla, Rees, & Friston, 1999; C. D. Gilbert & Sigman, 2007). In our previous experiment, distributed source localization results also suggested load-related differences for neural activity in higher-level cortical regions, but these were distinct from those observed in the present study and included dorsomedial prefrontal and anterior cingulate cortex. Distinct topographies for early load effects between the two studies may indicate the use of different processing strategies as a function of task-distractor synchrony, in accordance with an interpretation of different filtering requirements during high vs. low demands on exogenous attention.

Our interpretations rest on the assumption that synchrony between task and distractor stimuli captured exogenous attention to a higher degree than their asynchronous appearance in our previous experiment (Rauss et al., 2009). Although this assumption is well-supported by the literature on exogenous attentional capture (Egeth & Yantis, 1997; Fournier, 1994; Kahneman et al., 1983; Santangelo & Spence, 2007; Van der Burg et al., 2008a, 2008b; Wilson & Singer, 1981; Yantis & Jonides, 1984), alternative interpretations need to be considered.

First, it could be argued that the effects observed in the present study are a consequence of attentional spillover onto the peripheral distractors. Thus, if part of the distractor fell into the attentional spotlight, distractor-elicited C1 might be enhanced as a result of increased attentional gain within the spotlight during the high-load condition. Our previous results (Rauss et al., 2009) could in turn be interpreted as attentional suppression of the whole visual field because distractors were fully decoupled from central targets, and were isolated both in space and in time. However, we believe that this alternative interpretation is unlikely because our stimulation parameters including distractor eccentricity were based on an earlier fMRI study using the same experimental task (Schwartz et al., 2005), which demonstrated effects of surround suppression starting from visual angles ≥ 2°. As detailed in the Methods section, in the present experiment the minimal distance between task and distractor stimuli was 3.8° and thus distractors were in all likelihood falling within this surround suppression zone. In addition, this interpretation would require the assumption of an attentional spotlight whose size increases or at least remains constant with increasing levels of attentional load, contradicting findings of load-related surround suppression (Schwartz et al., 2005), which suggest a narrowing of the attentional focus under increasing attentional demands, in agreement with the predictions of the load theory of selective attention (Lavie, 1995).

Secondly, the effects reported for asynchronous task-distractor presentation (Rauss et al., 2009) could be interpreted as an attentional blink-like phenomenon. We do not entertain this possibility because the timing of our stimuli was clearly different from the values reported in the attentional blink literature. In particular, SOAs in attentional blink paradigms are usually smaller than 500 ms (Hommel et al., 2006) and stimuli are presented during very short periods (e.g. 15 ms in the original study of Raymond, Shapiro, & Arnell, 1992), whereas our SOAs were > 500 ms and both task and distractor stimuli were presented for 250 ms.

Finally, one might posit a role for temporal grouping in producing the effects observed in the present experiment. As reviewed by Blake and Lee (2005), perceptual grouping can occur on the basis of temporal stimulus characteristics, a notion extending the Gestalt law of common fate to temporal modulations simpler than movement. However, all studies reviewed by these authors used stimulus elements of similar shape such as dots (Fahle, 1993) or Gabor patches (Lee & Blake, 1999) to produce grouping by temporal structure. Thus, an extension to the present study, where central task stimuli were colored T-shapes presented foveally, and peripheral distractors consisted of large rectangular arrays of white line elements, is not straightforward and would require further investigation. Nevertheless, an interpretation in terms of task-distractor grouping may be relevant, as grouping-related increases in primary visual cortex activity have been reported for stimuli obeying classical Gestalt laws of perception (Han, Jiang, Mao, Humphreys, & Qin, 2005; Nikolaev, Gepshtein, Kubovy, & van Leeuwen, 2008). We note that if such an account were to prove valid, it would not necessarily contradict our interpretations: Temporal grouping could conceivably engage exogenous attentional mechanisms, which in turn could interact with endogenous attentional processes. In this case, exogenous attention would be relegated to the role of a mediator of more basic grouping effects. However, even if temporal grouping does not entail exogenous attentional capture, it is most readily conceptualized as a bottom-up phenomenon whose presence or absence would have to interact with endogenous attentional mechanisms in order to explain the differences between the effects reported here and in our previous study.

In summary, we believe that interactive effects between exogenous and endogenous attentional processes are the most parsimonious way of explaining the opposite effects of attentional load on early visual cortex activity observed for synchronous vs. asynchronous task-distractor presentation. Our results demonstrate that relatively small changes in stimulation parameters can have profound effects on the assessment of top-down effects on the earliest cortical stages of sensory processing in humans. As the number of studies demonstrating early attentional effects on visual processing increases, an important aim is to better characterize the conditions under which these effects may be observed. Recent work from our (Pourtois et al., 2004; Pourtois, Rauss et al., 2008; Rauss et al., 2009) and other groups (Kelly et al., 2008; Khoe et al., 2005; Poghosyan & Ioannides, 2008; Stolarova et al., 2006) shows that attentional suppression or enhancement may be observed at the level of V1, as a function of stimulus relevance and task demands. The current study adds important information to these previous reports by demonstrating that exogenous attentional capture due to task-distractor synchrony may override the effects of endogenous attention on early visual cortex. Thus, our findings help delineate the boundary conditions for observing effects of selective attention at the level of V1.

In conclusion, we have demonstrated that effects of attentional load on the processing of irrelevant distractors are reversed at the earliest stages of cortical visual processing when peripheral distractors are presented in synchrony vs. asynchronously with central task stimuli. Based on ERP and distributed source localization results, we propose that early attentional filtering mechanisms are not effective if synchrony serves to attract exogenous attention or to group peripheral with central events. Our results have important implications for the interpretation of previous studies that did not observe attentional modulations of the C1 component (Martinez et al., 1999; Noesselt et al., 2002), and help delimit the stimulus and task conditions under which such modulations may and may not be observed.

Acknowledgements

This work was supported by grants from the Swiss National Science Foundation (grants #310000-114008 to S.S., #105314-118267 to P.V., and NCCR 51NF40-104897) and a Geneva Neuroscience Center PhD fellowship (K.S.R.). G.P. is supported by grants from the European Research Council (Starting Grant #200758) and Ghent University (BOF Grant #05Z01708).

We would like to thank Mélanie Genetti, Christoph Michel, Tonia Rihs, and Gregor Thut for helpful discussions, and Rolando Grave de Peralta and Sara Gonzalez for the realistic head model and inverse solutions used in this work.

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Figure Legends

Figure 1

Experimental paradigm. (A) During EEG recording, subjects performed either an easy, pop-out detection task or a more demanding, conjunction detection task on the same stream of centrally presented stimuli. (B) Irrelevant distractors were presented simultaneously with the central stimulus on 22% of trials. (C) Trial time-course in the previous experiment (Rauss et al., 2009), where central task stimuli and peripheral distractors were presented asynchronously. For display purposes, the width of the lines on all the stimuli are thicker than the original ones.

Figure 2

Task-only VEPs. (A) Responses elicited by non-imperative task stimuli when unaccompanied by peripheral distractors. Significant effects of attentional load were seen on P1 (raw values, $p = 0.001$) and N1 amplitudes (peak-to-peak values, N1 relative to P1, $p = 0.01$). Maps represent grand-average difference topographies (high minus low attentional load). (B) Task-only VEPs from our previous published experiment (Rauss et al., 2009). Only N1 differences were significant. The map represents difference topography for the N1 as in (A). In both studies, statistics for N1 and P1 were calculated across the 12 highlighted electrodes.

Figure 3

Task-plus-distractor VEPs. (A) A large negative C1 is evident in the grand averages, with high load leading to significant amplitude increases ($p=0.031$). No effects of attention were observed at the level of the P1 or N1 components. Difference topography (high minus low load) is shown on the right. Grand-averages are for 6 electrodes highlighted. (B) Distractor-only VEPs from our previous experiment (Rauss et al., 2009); all conventions as in (A). Note that C1 is significantly reduced under high load.

Figure 4

Correlation between the attentional modulation on task-plus-distractor C1 and task-only N1. (A) Differences between experimental conditions (high minus low load) were significantly correlated ($p=0.021$), with a positive relationship indicating that both components were more negative under high load. (B) The same correlation performed on data from our previous experiment (p=0.043; Rauss et al., 2009). The sign of the correlation coefficient was reversed when comparing both experiments, due to opposite effects of attentional load on C1 amplitudes (see Fig. 3).

Figure 5

Results of distributed inverse solutions using a local autoregressive average (LAURA) approach. (A) Raw inverse solutions for task-plus-distractor trials in the present study (*left*, 50-90 ms) and distractor trials from our previous experiment (*right*, 60-100 ms; Rauss et al., 2009), scaled to the same arbitrary units. Maximal activity was observed near the occipital pole in both studies, in accordance with neural generators located in early visual cortex. (B) Images show inverted p-values from electrode-wise t-tests, scaled to unity. *Left:* differences (high minus low load) between inverse solutions of target-plus-distractor trials for the C1 time-window. *Right:* differences between high and low attentional load in our previous study. Time-windows shown are the same as in (A). Differences were considered significant if p<0.05 for a duration of at least 20 ms.

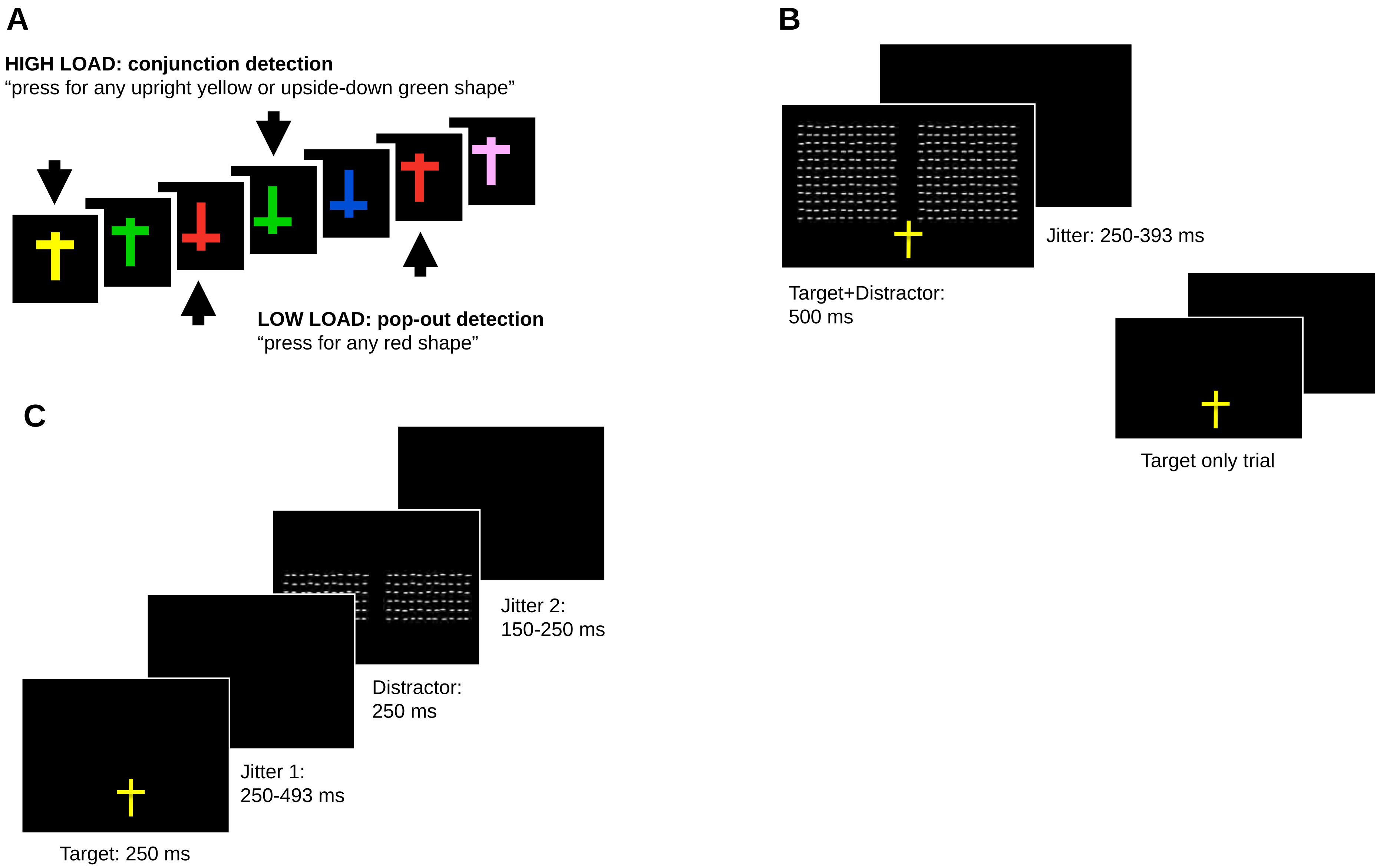
A
HIGH LOAD: conjunction detection
"press for any upright yellow or upside-down green shape"
LOW LOAD: pop-out detection
"press for any red shape"
B
Jitter: 250-393 ms
Target+Distractor:
500 ms
Target only trial
C
Jitter 2:
150-250 ms
Distractor:
250 ms
Jitter 1:
250-493 ms
Target: 250 ms

Figure 1

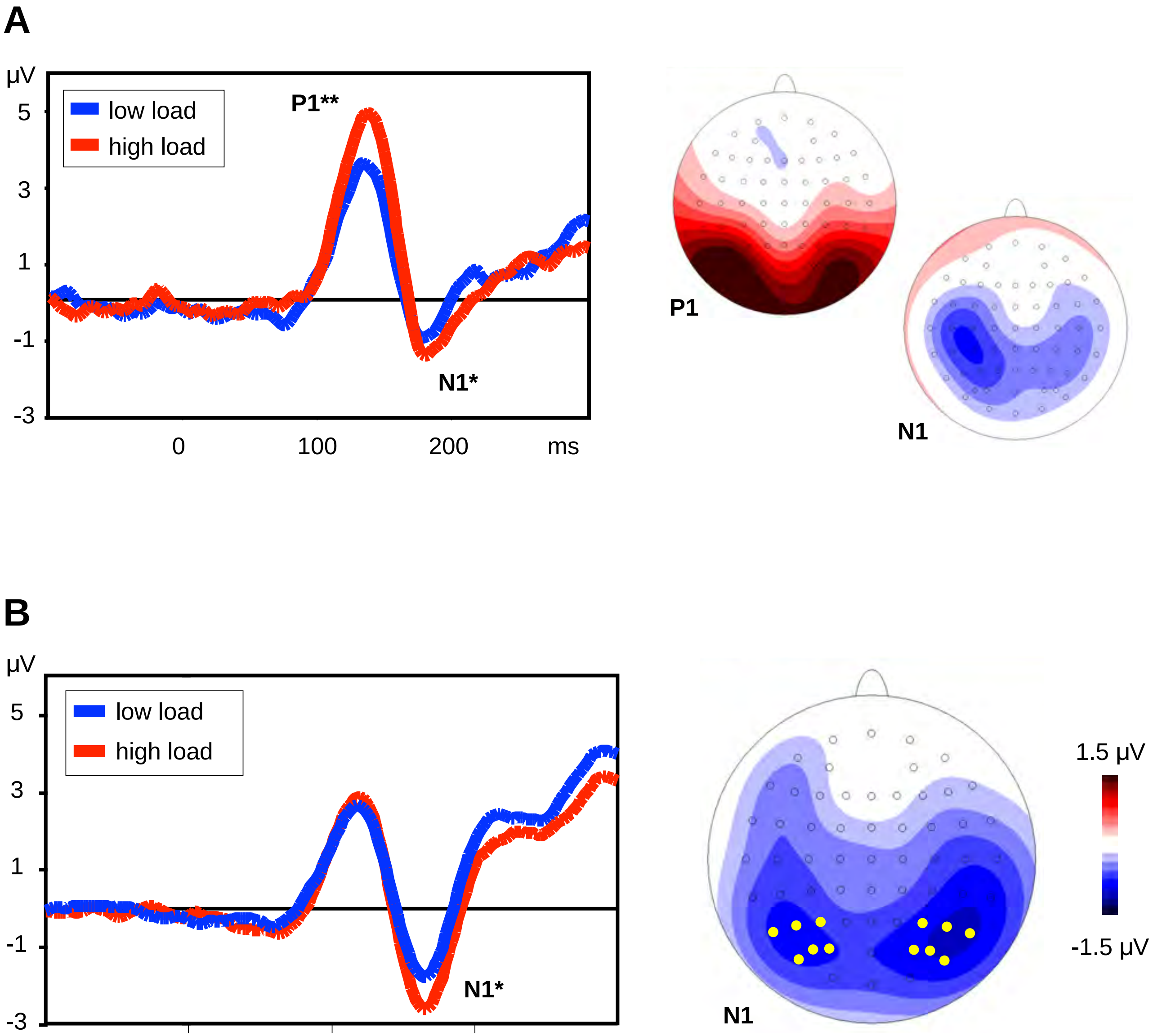
A
µV
5
3
1
-1
-3
low load
high load
P1**
N1*
0
100
200
ms
P1
N1
B
µV
5
3
1
-1
-3
low load
high load
N1*
0
100
200
ms
N1
1.5 µV
-1.5 µV

Figure 2

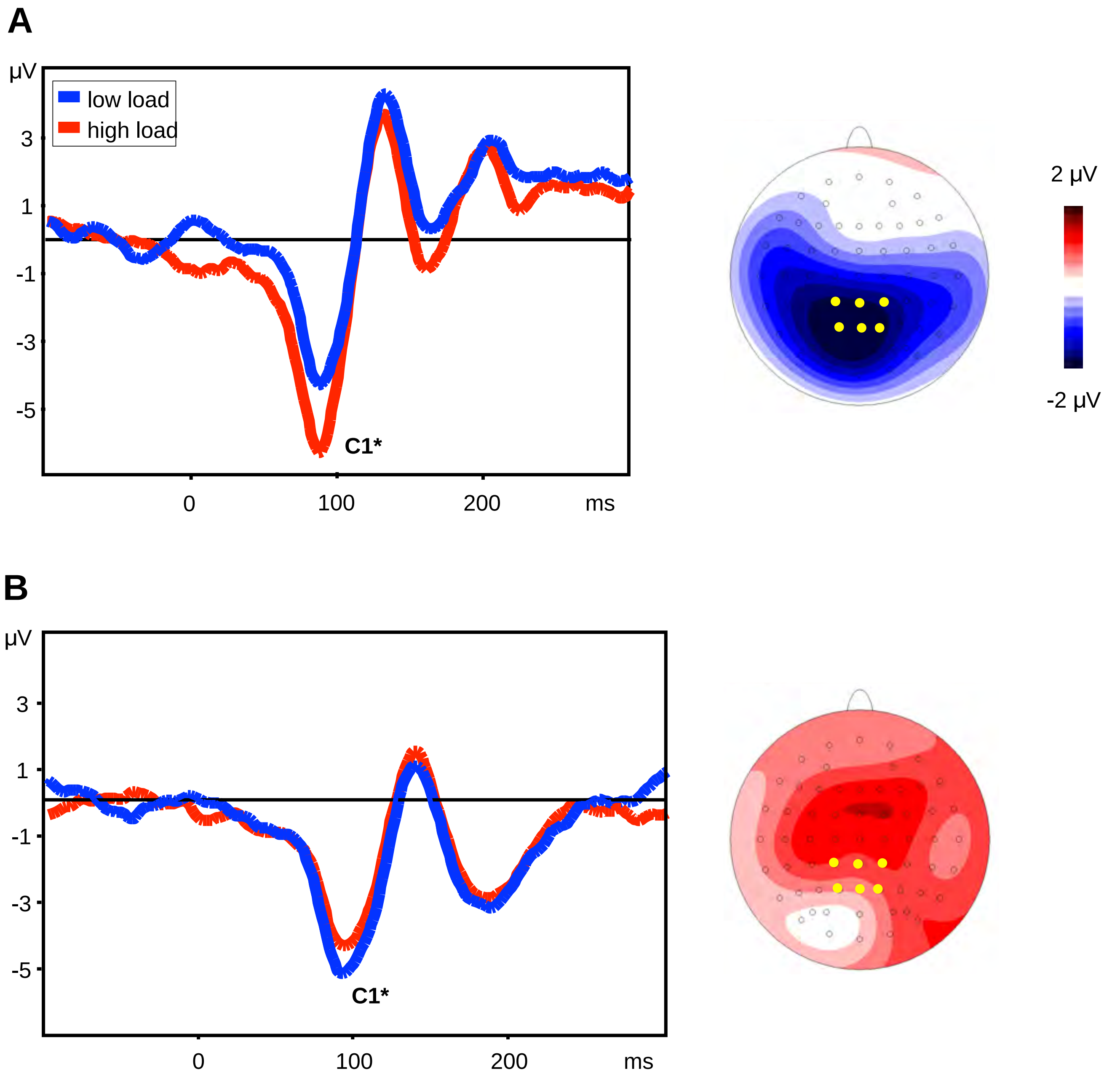
A
μV
low load
high load
3
1
-1
-3
-5
C1*
0
100
200
ms
2 μV
-2 μV
B
μV
3
1
-1
-3
-5
C1*
0
100
200
ms

Figure 3

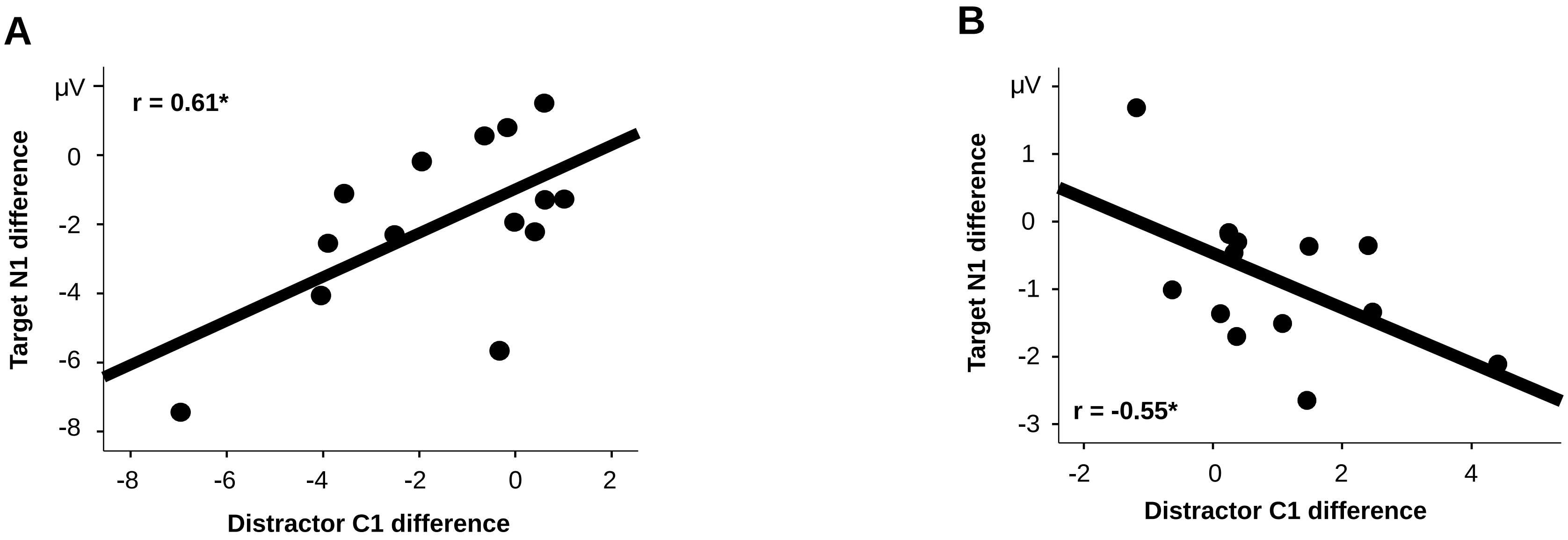
A
μV
r = 0.61*
0
-2
-4
-6
-8
Target N1 difference
-8
-6
-4
-2
0
2
Distractor C1 difference
B
μV
1
0
-1
-2
-3
Target N1 difference
r = -0.55*
-2
0
2
4
Distractor C1 difference

Figure 4

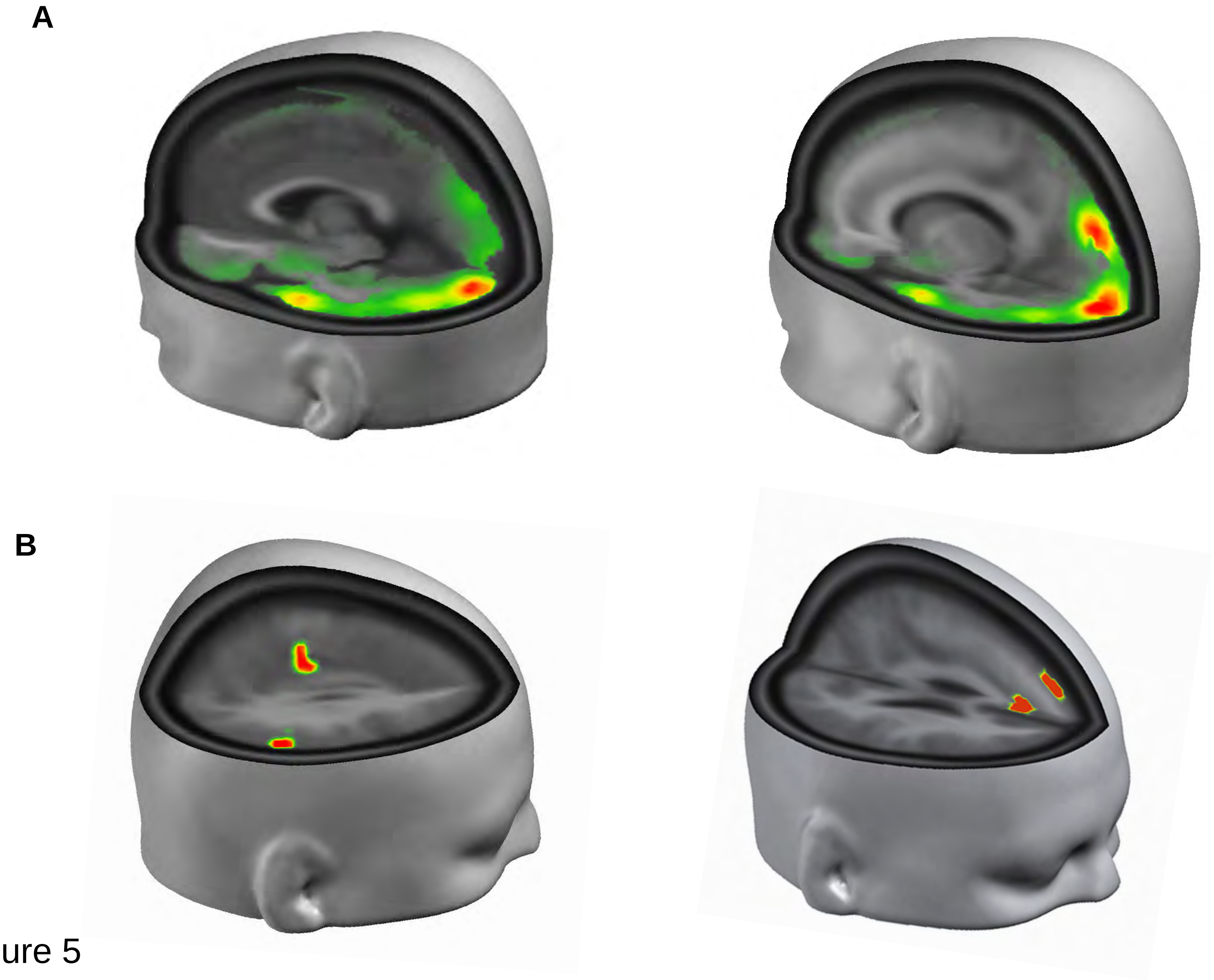

Figure 5