Transient increase of intact visual field size by high-frequency narrow-band stimulation

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ARTICLE INFO

ABSTRACT

Three patients with visual field defects were stimulated with a square matrix pattern, either static, or flickering at frequencies that had been found to either promote or not promote blindsight performance. Comparison between pre- and post-stimulation perimetric maps revealed an increase in the size of the intact visual field but only for flicker frequencies previously found to promote blindsight. These changes were temporary but dramatic – in two instances the intact field was increased by an area of $\sim$30 deg^2 of visual angle. These results indicate that not only does specific high-frequency stimulus flicker promote blindsight, but that intact visual field size may be increased by stimulation at the same frequencies. Our findings inform speculation on both the brain mechanisms and the potency of temporal modulation for altering the functional visual field.

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1. Introduction

Lesions to primary visual cortex (V1) lead to blindness in the contralesional part of the visual hemifield which has been believed to be irreversible for decades. However, detection, discrimination, or the localization of visual stimuli presented in the affected part of the visual field often remain possible (Humphrey, 1974; Pöppel, Held, & Frost, 1973; Sahraie et al., 2006; Stoerig & Cowey, 1997; Weiskrantz, 1980; Weiskrantz, Barbur, & Sahraie, 1995; Weiskrantz, Warrington, Sanders, & Marshall, 1974; Zihl, 1980) and are sometimes accompanied by visual awareness. Based upon dissociation between visual performance and awareness, the term "blindsight" refers to visual capacity in a field defect in the absence of acknowledged awareness (Sanders, Warrington, Marshall, & Weiskrantz, 1974). The dynamic characteristics of visual stimulation of patients with vision loss play an important role for blindsight to occur (Hess & Pointer, 1989). For example, Teuber, Battersby, and Bender (1960) found cortically blind soldiers were able to discriminate light/dark onsets; Weiskrantz (1986) reported better discrimination given rapidly flickering stimuli presented in the blind field of patient DB; and targets have been reported to be better localized in space by blindsight patients when flickered (Perenin, Ruel, & Hécaen, 1980). Interestingly, the specific frequency of dynamic stimulation seems to be crucial for blindsight performance. For example, Barbur, Harlow, and Weiskrantz (1994) studied temporal processing in patient GY and discovered that forced-choice detection scores were significantly better than chance when gratings were presented at frequencies between $\sim$6 and 40 Hz;

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Trevethan and Sahraie (2003) also found detection of temporally modulated gratings to be enhanced compared to rapid onset/offset but otherwise static presentation (see Sahraie, Weiskrantz, Trevethan, Cruce, & Murray, 2002, also Sahraie, Trevethan, & MacLeod, 2008). Their results indicate the existence of a narrowly tuned temporal channel mediating blindsight performance given presentation within a narrow frequency band between 10 and 33 Hz and with maximum sensitivity at 20 Hz. Similarly, Seifert, Falter, Strasburger, and Elliott (2010) presented data from patient RP, who, in spite of a unilateral right homonymous quadrantanopia, demonstrated better-than-chance discrimination for stimuli flickered on and off in the blind field at temporal frequencies between 33 and 47 Hz.

Findings such as these have led to the conclusion that blindsight performance can be promoted using stimuli either flickered or otherwise temporally modulated indicating that cortical dynamics play an important role in the mediation of blindsight. This conclusion refers to the idea that visual organization (in lesioned as well as in the healthy visual system) is based on patterns of oscillatory neural synchronization (Singer, 1999). Hence, dynamic stimulation at specific frequencies which enhance those oscillation patterns may influence visual capability, possibly enhancing blindsight performance.

This leads to the proposal that, in blindsight, repeating stimulation at rapid frequencies encourages oscillation and consequent synchronization of neurons in surviving areas of cortex with this bringing about the limited visual capability reported in these studies. Some imaging studies have presented results consistent with the idea that stimulus-related neural dynamics can promote blindsight. For example, Vanni, Raninen, Nasanen, Tanskanen, and Hyvarinen (2001) used magneto-encephalography (MEG) to examine cortical activity in response to dynamic visual stimulation in the intact vs. the lesioned hemisphere of a patient with vision loss. The authors found that flickering checkerboard and letter stimuli presented in the affected hemifield failed to generate an early, fast transient response at posterior cortical regions but showed a relatively strong response in the contralateral, superior temporal regions. This later response was interpreted as enhanced processing in higher-order visual areas, with the effect of compensating for lost function in visual areas earlier in the functional hierarchy of the visual system. In another study, Schurger, Cowey, and Tallon-Baudry (2006) presented an orientation-discrimination task including stationary stimuli at a near-threshold level of contrast, to which patient GY responded 'aware' or 'unaware'. Gamma-band oscillations in the range 44–66 Hz, recorded over the left occipito-parietal region, correlated significantly with awareness (but not accuracy), whereas activity at alpha-band frequencies (i.e. 8–12 Hz) did not. Both studies (i.e. Vanni et al., 2001, as well as Schurger et al., 2006) support the idea that the brain is capable of organizing itself in response to stimulation at particular frequencies, and that this response may, for stimulation at certain frequencies, bring about blindsight. With this in mind, it seems reasonable to extend this argument and propose that the stimulus frequencies which promote blindsight may also serve to restore visual function in the field defect. This general expectation has been expressed previously and in the context of studies linking blindsight performance to stimulus presentation at frequencies between 10 and 20 Hz (Sahraie et al., 2008). Several behavioral and neuroimaging studies have confirmed the idea that the visual system is plastic beyond an early, critical period of development, indicating that visual field loss resulting from brain lesions should no longer be considered permanent and irreversible. One line of evidence comes from rehabilitation studies (Bergsma & van der Wildt, 2010; Huxlin, 2008; Julkunen, Tenovuo, Jääskeläinen, & Hämäläinen, 2003; Kasten, Wüst, Behrens-Baumann, & Sabel, 1998; Kasten, Wüst, & Sabel, 1998; Kerkhoff, 1999; Poggel, 2002; Poggel, Kasten, & Sabel, 2004; Raemaekers, Bergsma, van Wezel, van der Wildt, & van den Berg, 2011; Sabel, 1999, 2008; Sahraie, 2007; van der Wildt & Bergsma, 1997; reviewed in Sabel, Henrich-Noack, Fedorov, & Gall, 2011) that have demonstrated training-induced improvement of function, particularly of light-detection performance. There is evidence for the partial restoration of visual function (with about one-third of patients showing either large, small, or no improvement, respectively), and that the training effect, when present, cannot be explained as side effects from behavioral changes like eye movements (Kasten, Bunzenthal, & Sabel, 2006) or observer-criterion shift (Poggel, 2002; Poggel et al., 2004).

Most training methods are specifically designed to improve detection of visual stimuli and are oriented toward measures amenable to perimetric testing, which is still the gold standard for determining the extent of visual field loss. There are some studies suggesting the generalization of training effects to other visual functions, e.g. to the recovery of form or color discrimination (Kasten, Poggel, & Sabel, 2000). More recently, Poggel, Treutwein, and Strasburger (2011) showed that patients with visual field loss after brain lesions also suffer from deficits in temporal resolution as well as in visual reaction times, with topographies for these functions that are partially dissociated from the perimetric maps for light detection. Temporal performance depends in part on the degree of intactness of the respective visual field position – in particular at the border zone of the visual field defect (i.e., areas of residual vision or *transition zones)* – but is not fully determined by these. In an unpublished training study, Poggel, Treutwein, Sabel, and Strasburger (submitted for publication) have shown that a training regime designed for improvement of light detection in brain-lesioned patients also led to improvement in dynamic variables, such as general temporal resolution (i.e., double-pulse resolution, Poggel et al., 2011) and visual reaction times, in areas of residual vision along the visual field border (see Strasburger, Rentschler, & Jüttner, 2011, for review).

The present study aimed to evaluate the potential for modifying the functional visual field using stimuli presented at temporal frequencies found to elicit optimal blindsight performance. The optimal frequencies for blindsight performance were determined empirically, and visual field maps were determined with static perimetry prior to and following a number of treatment sessions. In these sessions, a matrix of illuminated pixels was repeatedly presented in the individually defined area of residual vision (as determined before treatment). Presentation was at frequencies to which patients had previously shown some evidence of blindsight when stimulated in the completely blind field, or, for comparison, at frequencies not associated with blindsight. Treatment outcomes were variable between patients, but in some cases – for frequencies that had previously promoted blindsight but not for those not associated with blindsight – there were large transient shifts of the visual field border.