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Research report

# Contributions of pitch and bandwidth to sound-induced enhancement of visual cortex excitability in humans

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ABSTRACT

Multisensory interactions have been documented within low-level, even primary, cortices and at early post-stimulus latencies. These effects are in turn linked to behavioral and perceptual modulations. In humans, visual cortex excitability, as measured by transcranial magnetic stimulation (TMS) induced phosphenes, can be reliably enhanced by the co-presentation of sounds. This enhancement occurs at pre-perceptual stages and is selective for different types of complex sounds. However, the source(s) of auditory inputs effectuating these excitability changes in primary visual cortex remain disputed. The present study sought to determine if direct connections between low-level auditory cortices and primary visual cortex are mediating these kinds of effects by varying the pitch and bandwidth of the sounds co-presented with single-pulse TMS over the occipital pole. Our results from 10 healthy young adults indicate that both the central frequency and bandwidth of a sound independently affect the excitability of visual cortex during processing stages as early as 30 msec post-sound onset. Such findings are consistent with direct connections mediating early-latency, low-level multisensory interactions within visual cortices.

## 1. Introduction

Responses to auditory and visual stimuli have been shown to interact in humans at early stages post-stimulus onset (i.e., within the initial 100 msec; Giard and Peronnet, 1999; Molholm et al., 2002; Cappe et al., 2010; Raij et al., 2010) and within a network of regions including primary auditory as well as primary visual cortices (Martuzzi et al., 2007; Cappe et al., 2010; Raij et al., 2010). Moreover, there have been some demonstrations of the behavioral relevance of such early-latency and low-level multisensory interactions in terms of being linked to reaction time speed, perceptual outcome, or discrimination abilities (e.g., Romei et al., 2007, 2009; Van der Burg et al., 2011; Cappe et al., 2012; Murray et al., 2012).

Whereas support for the latency and locus of these effects is reasonably convincing, establishing the extent to which early-latency effects within primary visual cortex are the consequence of either direct projections from primary or near-primary auditory cortex and/or inputs from higher-level association cortices (e.g., the superior temporal sulcus and/or parietal structures) has been less forthcoming and was our focus here. To address this question, the tactic in the present

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study was to vary low-level acoustic features using a within-subject factorial design so as to draw inference regarding the putative source(s) of auditory inputs that are effectuating modulations in visual cortex excitability as indexed by TMS-induced phosphene perception. Specifically, we manipulated the bandwidth and center frequency (pitch) of sounds. This design was predicated on observations in non-human primates that the sharpness of tuning of neurons to frequency and bandwidth progressively decreases from core to belt and to parabelt auditory cortices (e.g., Kosaki et al., 1997; Rauschecker and Tian, 2004; Lakatos et al., 2005; Petkov et al., 2006; Hackett, 2011). Any differential efficacy of either or both of these features in modulating visual cortex excitability (viz. phosphene induction) would therefore be taken as an indication of the extent to which low-level auditory cortices contribute to (and perhaps mediate) such effects.

Anatomical studies in non-human primates have identified monosynaptic projections to primary visual cortex from both primary auditory cortex as well as the superior temporal polysensory region (Falchier et al., 2002; Rockland and Ojima, 2003; Clavagnier et al., 2004; Cappe and Barone, 2005; reviewed in Falchier et al., 2012), making it feasible for direct information transfer between primary cortices (in addition to established indirect, poly-synaptic pathways). Corresponding anatomical data in humans are currently unavailable, though diffusion-based imaging has recently provided evidence for fiber tracts between the superior temporal gyrus and the calcarine sulcus (i.e., low-level auditory regions and primary visual cortex, respectively) (Beer et al., 2011). Additional efforts have been made to apply dynamic causal modeling and effective connectivity to functional magnetic resonance imaging data so as to infer relevant pathways (Lewis and Noppeney, 2010; Noesselt et al., 2010; Powers et al., 2012; Werner and Noppeney, 2010). Despite such evidence, to our knowledge no data have been published associating specific anatomic pathways and early-latency multisensory effects within primary visual cortex.

TMS has contributed to these efforts by allowing for more causal inference on the role of specific brain regions at specific latencies in multisensory interactions (Bolognini and Maravita, 2011). For example, several laboratories have shown that the excitability of primary visual cortex, as indexed by phosphene induction[2], is enhanced by the co-presentation of a sound (Romei et al., 2007, 2009; Bolognini et al., 2010; Leo et al., 2011) or a touch (Ramos-Estebanez et al., 2007). In an effort to reveal likely sources of auditory inputs into human primary visual cortex, the authors of these studies identified variations in the efficacy of different sound features (in combination with the latency of observed effects) to modulate visual cortex excitability. Romei et al. (2007) furthermore showed that TMS over the occipital pole over the 60–90 msec post-sound onset period had opposing effects on the simple detection of auditory and visual stimuli (facilitation and slowing, respectively). In fact, the facilitation of simple detection obtained by combining occipital TMS with external auditory stimuli was as great as and correlated with the facilitation of reaction times observed when presenting participants with external auditory–visual stimuli. It has additionally been demonstrated that not all sounds are equally effective in modulating visual cortex excitability. Romei et al. (2009) showed that structured looming sounds selectively and pre-perceptually enhanced visual cortex excitability, and Bolognini et al. (2010) provide evidence for maximal enhancement of visual cortex excitability when the sounds were co-localized at the position of the induced phosphenes.

## 2. Methods

### 2.1. *Participants*

Ten healthy volunteers participated in the study (five women, one left-handed, mean age = 23.1 years, range 20–28 years). All participants reported normal hearing and had normal or corrected-to-normal vision. The study was approved by the Ethics Committee of the Faculty of Biology and Medicine at the University Hospital Center and University of Lausanne. All participants provided written informed consent.

### 2.2. *Stimuli*

The stimuli were 300 msec tones and bandpass-filtered noise bursts (22 kHz digitization, 16 bits, 10 msec linear rise/fall time). These sounds were generated according to a 2 × 2 design with factors of center frequency [250 Hz (low) and 6000 Hz (high)] and bandwidth [1 Hz (narrow) and 460 Hz range (broad)]. This resulted in four conditions: 250 Hz (Low/Narrow, LN condition); 6000 Hz (High/Narrow, HN); 20–480 Hz (Low/Broad, LB); and 5770–6230 Hz (High/Broad, HB). These auditory stimuli were presented through two loudspeakers located on each side of the computer monitor at a level judged comfortable by the participant. Because all data were analyzed according to a within-subject design, differences in the intensity of sound presentation across participants cannot influence the statistical outcome. The two center frequencies were chosen to be perceived with comparable loudness according to the revised ISO 226:2003 equal-loudness-level contours standard between 50 and 90 dB SPL.

### 2.3. *TMS apparatus and determination of phosphene threshold (PT)*

A 70 mm figure of eight coil (maximum field strength, 2.2 T) and a Magstim Rapid2 Transcranial Magnetic Stimulator were

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[2] Phosphenes are the perceived sensation of flashes of light in the absence of visual stimulation following occipital TMS. Phosphenes elicited in low-level visual areas (V1/V2) are generally perceived as brief, static sensations along the horizontal meridian or in the lower quadrant of the hemifield contralateral to the stimulated hemisphere. They are thought to be generated by activation current that is induced by the magnetic field of the TMS pulse (e.g., Allen et al., 2007; Moliadze et al., 2003). When phosphenes are identified and defined, they remain stable within the same participant, thereby providing a reliable measure of visual cortical excitability. The minimum intensity of occipital TMS required to elicit phosphenes (i.e., phosphene threshold or PT) has been routinely used to provide a measure of this excitability (e.g., Pascual-Leone and Walsh, 2001). In studies of cross-modal effects on visual cortex excitability, the PT was first determined for each participant and then stimulator intensity was set at levels below PT. The frequency of phosphenes reported at stimulator intensities below PT was taken as a baseline, with any increases thereupon by non-visual stimuli taken as evidence for cross-modal influences on visual excitability.

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