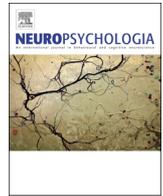




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# Multisensory integration in hemianopia and unilateral spatial neglect: Evidence from the sound induced flash illusion



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## ABSTRACT

Recent neuropsychological evidence suggests that acquired brain lesions can, in some instances, abolish the ability to integrate inputs from different sensory modalities, disrupting multisensory perception. We explored the ability to perceive multisensory events, in particular the integrity of audio-visual processing in the temporal domain, in brain-damaged patients with visual field defects (VFD), or with unilateral spatial neglect (USN), by assessing their sensitivity to the 'Sound-Induced Flash Illusion' (SIFI). The study yielded two key findings. Firstly, the 'fission' illusion (namely, seeing multiple flashes when a single flash is paired with multiple sounds) is reduced in both left- and right-brain-damaged patients with VFD, but not in right-brain-damaged patients with left USN. The disruption of the fission illusion is proportional to the extent of the occipital damage. Secondly, a reliable 'fusion' illusion (namely, seeing less flashes when a single sound is paired with multiple flashes) is evoked in USN patients, but neither in VFD patients nor in healthy participants. A control experiment showed that the fusion, but not the fission, illusion is lost in older participants (> 50 year-old), as compared with younger healthy participants (< 30 year-old). This evidence indicates that the fission and fusion illusions are dissociable multisensory phenomena, altered differently by impairments of visual perception (i.e. VFD) and spatial attention (i.e. USN). The occipital cortex represents a key cortical site for binding auditory and visual stimuli in the SIFI, while damage to right-hemisphere areas mediating spatial attention and awareness does not prevent the integration of audio-visual inputs in the temporal domain.

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## 1. Introduction

Crossmodal illusions can result from the integration of discordant information from different sensory modalities. These illusions represent perceptual strategies for dealing with intersensory conflicts, yielding coherent to incoherent perceptual experiences across sensory systems (Bolognini et al., 2015a). Recent studies indicate that the perception of crossmodal illusions can be selectively altered in brain-damaged patients, depending on their neuropsychological disorder (reviews in Bolognini et al., 2013a, 2015a). This is, for instance, the case of the ventriloquist illusion (Howard and Templeton, 1966), whereby the perceived location of a sound is captured by the location of a synchronous, but spatially

disparate, visual stimulus (Thurlow and Jack, 1973; Welch and Warren, 1980; Warren et al., 1981). The ventriloquist illusion is disrupted in patients with homonymous Visual Field Defects (VFD), contralateral to the side of the hemispheric lesion, but is preserved in right-brain-damaged patients with left Unilateral Spatial Neglect (USN) (Bertelson et al., 2000; Leo et al., 2008; Passamonti et al., 2009). These findings suggest that the ability to integrate conflicting visual and auditory information in the spatial domain can be selectively compromised by a primary sensory visual deficit, but not by a higher-order disorder of spatial attention.

The present study went one step further, by investigating whether and how cerebral lesions impairing vision (i.e., homonymous VFD), or spatial attention (i.e., USN), impact the ability to bind audio-visual signals in the temporal domain. To explore multisensory perception in brain-damaged patients with VFD or left USN, we took advantage of a powerful crossmodal audio-visual illusion, namely the Sound-Induced Flash Illusion (SIFI) (Shams et al., 2000, 2002),

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In the SIFI, two rapid tones (beeps) accompanying a single brief visual flash induce the illusory perception of seeing a double flash, an effect known as the ‘fission’ illusion; by increasing the number of beeps, the number of seen flashes tends to increase. A complementary ‘fusion’ illusion may also occur, whereby two, or more, flashes fuse into one, when presented along with a single beep (Andersen et al., 2004, 2005; Mishra et al., 2008; Shams et al., 2005; Watkins et al., 2006). Electrophysiological and brain imaging studies show that the neural underpinnings of the SIFI involve a rapid interplay between the primary auditory and the primary visual areas (V1 and V2), along with a crossmodal modulatory feedback from the Superior Temporal Sulcus and the Posterior Parietal Cortex (PPC) to the visual cortex (Shams et al., 2001; Watkins et al., 2006; Mishra et al., 2007; 2010). Accordingly, the SIFI can be altered by transcranial Direct Current Stimulation (tDCS) of the occipital cortex and of the Superior Temporal Gyrus (STG) of the right hemisphere (Bolognini et al., 2011): the fission illusion is increased by anodal (excitatory) tDCS over the STG, but decreased by anodal tDCS over the occipital cortex; conversely, cathodal tDCS over the STG decreases the fission illusion, and increases it when delivered over the occipital cortex. By contrast, the fusion illusion is not modulated by either occipital or temporal (anodal and cathodal) tDCS (Bolognini et al., 2011). The link between the level of excitability of the occipital cortex and the SIFI is further supported by evidence from studies on patients with migraine. The pathophysiology of migraine involves a hyper-excitability of the occipital cortex. Accordingly, migraineurs (in particular those with aura) show a reduced fission illusion, and normal fusion illusion (Brighina et al., 2015): this is consistent with the above-discussed findings that anodal occipital tDCS decreases the fission illusion (Bolognini et al., 2011).

The role of the posterior parietal areas in the SIFI remains controversial. Neither anodal nor cathodal tDCS of the right PPC modulates the SIFI (Bolognini et al., 2011). Conversely, low frequency (1 Hz) repetitive Transcranial Magnetic Stimulation (rTMS) delivered to the angular gyrus, but not to the supramarginal gyrus, of the right inferior parietal lobule, reduces the fission illusion in neurologically healthy participants (Kamke et al., 2012; Hamilton et al., 2013).

Homonymous VFDs are brought about by damage to the retinohiasmatic visual pathways, causing blindness in the sectors of the visual field (i.e., VFD), which retinotopically correspond to the damaged tissue (Zihl and Kennard, 1996). In homonymous hemianopia, vision is lost in the entire half-field contralateral to the side of the hemispheric lesion (contralesional), whereas in homonymous quadrantanopia the VFD is restricted to the upper or lower quadrant of the contralesional half-field. Patients with VFD may show additional non-visual deficits, such as spatial impairments in the auditory modality (Kerkhoff et al., 1999; Lewald et al., 2009a,b), suggesting that the primary visual deficit may affect aspects of processing in other sensory modalities.

In contrast, left USN is most frequently associated with lesions affecting the higher-order, association, fronto-temporo-parietal areas of the right hemisphere. Right-brain-damaged patients with left USN are unable to report sensory events occurring in the contralesional (left) side of space, and to explore it through motor acts; USN is currently conceived as a higher-order disorder of spatial attention and representation (Vallar and Bolognini, 2014). Whereas the core clinical symptoms and signs of VFD involve visual deficits, USN has multisensory features (see, e.g., Jacobs et al., 2012), and may involve the somatosensory and auditory modalities (De Renzi et al., 1970; De Renzi, 1982; Bisiach et al., 1984; Beschin et al., 1996; Clarke and Thiran, 2004; Pavani et al., 2003; Gainotti, 2010). USN-related deficits in the visual, somatosensory, and auditory modalities can occur in various combinations, suggesting that spatial cognition and awareness are based on the

interaction between multiple, modality-specific, neural systems (Umiltà, 1995; Brozzoli et al., 2006; Vallar and Bolognini, 2014).

Despite the presence of modality-specific deficits, a number of multisensory abilities are preserved in brain-damaged patients with USN or with VFD (see for a review, Bolognini et al., 2013a; Vallar and Bolognini, 2014). These spared abilities for multisensory integration may even help compensating for modality-specific disorders. For example, brain-damaged patients with USN or with VFD show a higher detection rate of visual stimuli in the contralesional visual half-field, when tactile or auditory stimuli are presented at the same spatial location, and at the same time, of the visual target (e.g., Frassinetti et al., 2005; Schendel and Robertson, 2004; Leo et al., 2008). This evidence has guided the development of treatments for VFD with multisensory features, which have been shown to be more effective than the standard purely visual therapies (Bolognini et al., 2005; Passamonti et al., 2009; Keller and Lefin-Rank, 2010; Tinelli et al., 2015).

In the light of this evidence, we investigated whether brain-damaged patients with left USN and brain-damaged patients with VFD (without USN) experience the SIFI, as compared to healthy participants. We aimed at exploring whether a cerebral lesion bringing about a primary sensory deficit in the visual modality (VFD), or an impairment of visuo-spatial attention (USN), can alter multisensory capabilities, as indexed by the fission and fusion illusions. This, in turn, allows investigating whether lesions affecting the primary visual cortex (in patients with VFD) and higher-level association areas (in patients with USN) may disrupt the fission and fusion illusions.

## 2. Materials and methods

### 2.1. Participants

Thirty-one right-handed participants took part in the experiment, which was conducted at the Neuropsychological Laboratory of the IRCCS Istituto Auxologico Italiano (Milan, Italy). All participants had normal hearing, no history of hearing disorders, and normal or corrected-to-normal vision. Participants were naïve as to the purpose of the experiment and provided written informed consent to the protocol. The study was approved by the Ethical Committee of the Hospital, and carried out in accordance with the ethical standards of the Declaration of Helsinki (World Medical Association, 1991). Three groups of participants entered the study.

- 1) Twelve neurologically unimpaired individuals (5 males; mean age = 65.41, Standard Deviation  $\pm$  9.17 years, range = 50–82; mean years of schooling =  $9.83 \pm 3.83$ , range = 5–18), without history or evidence of neurological or psychiatric diseases, served as control participants.
- 2) Eleven brain-damaged patients had homonymous VFD (9 males; mean age =  $50.5 \pm 14.49$  years, range = 25–69; mean years of schooling =  $11.7 \pm 5.16$ , range = 5–18). Patients had suffered a cerebral ischemic or hemorrhagic stroke. Seven patients had a left-hemispheric lesion (6 with a right-sided homonymous hemianopia, 1 with a right-sided quadrantanopia), 4 patients had a right-hemispheric lesion (2 with a left-sided homonymous hemianopia, 2 with a left-sided quadrantanopia). The visual field loss was assessed by a standard Humphrey visual field perimetry. Patients were tested in a chronic stage after stroke (duration of disease =  $14.68 \pm 10.6$  months, range = 3–37 months), when visual sensitivity is stable (Zhang et al., 2006).
- 3) Eight right-brain-damaged patients showed left USN (6 males; mean age =  $71.25 \pm 9.28$  years, range = 51–83; mean years of schooling =  $11.37 \pm 4.13$ , range = 5–18). Seven patients had suffered a cerebrovascular disease and were tested in a chronic

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