Progetto di ricerca – Neural plasticity in visual processing

Background and aim of the project
Patients with cortical lesions may develop neurological deficits in which, though perceptual awareness is impaired, they still exhibit unconscious implicit processing of the same stimuli. Exemplary patients are hemianopic patients, who lack vision in one hemifield due to posterior visual pathway lesions. Although these patients are not able to consciously perceive visual stimuli presented in their blind hemifield, they might retain some implicit visual processing even in the absence of visual awareness, a phenomenon known as “blindsight”. For instance, previous evidence has shown that fearful faces presented in the blind field facilitate behavioural responses to stimuli in the intact field (Bertini et al., 2013; Cecere et al., 2013). Similarly, an implicitly processed visual stimulus presented in the blind field is able to enhance localization of auditory stimuli concurrently presented in the same spatial position (Leo et al., 2008a). It has been suggested that these implicit visual abilities are mediated by an alternative visual pathway bypassing the primary visual cortex (V1) and projecting visual inputs from the retina to subcortical structures, such as the Superior Colliculus (SC), and finally reaching the extrastriate cortical areas. If the retino-colliculo-extrastriate pathway (RCE) drives implicit visual behavior, training aimed at enhancing its activity might improve visual abilities in hemianopics. Evidence from both animals (Stein & Meredith, 1993) and humans (Leo et al., 2008b; Bertini et al., 2008; Bertini et al., 2010) has shown that RCE is involved in multisensory integrative processing. In line with these findings, recent studies on hemianopics have revealed that audio-visual training, based on systematic audio-visual stimulation and presumably relying on the activity of the RCE, can promote visual orienting responses, resulting in an effective compensation for the visual field defect (Bolognini et al., 2005; Passamonti et al, 2009).

The present project aims to: 1) investigate whether an enhancement of the activity in the RCE underlies the beneficial effects of the audio-visual training in a group of healthy participants in whom hemianopia is simulated using near-threshold visual stimuli in one hemifield and inhibitory transcranial direct current stimulation (tDCS) over contralateral V1 (Experiment 1); 2) test whether excitatory tDCS over the extrastriate areas is able to enhance the activity of the RCE in hemianopic patients, boosting the effects of the audio-visual training (Experiment 2).

Experiment 1
The first study aims to disambiguate the neural correlates subserving the improvements observed after systematic audio-visual training in hemianopic patients (Bolognini et al., 2005; Passamonti et al., 2009) by testing healthy participants with near-threshold visual stimuli and inhibitory tDCS over V1 to simulate hemianopia.

Materials and methods. 20 healthy participants will take part in the study. In order to simulate hemianopia, participants will receive inhibitory tDCS over left or right V1 and will undergo ten sessions of systematic audio-visual training, in which they will detect near-threshold visual stimuli (low intensity red LEDs) presented alone (unisensory visual condition) or coupled with concurrent auditory stimuli in the same spatial position (multisensory audio-visual condition). There will also be catch trials, in which only the auditory stimulus will be presented (unisensory auditory condition). Stimuli will be disproportionately allocated to the side of the simulated hemianopia. The training session will last 2 hours. Before and after training, visual abilities will be tested with different visual tasks relying on different neural circuits to test the possible neural pathways enhanced by the audio-visual training. A motion-discrimination task, in which participants will be presented with patches composed of moving high-luminance dots in both visual fields, will test the involvement of the RCE in the audio-visual training, since there is evidence that the RCE circuit is selectively tuned to moving stimuli (Billington et al., 2011). In addition, participants will undergo an orientation-discrimination task, in which they will be presented with simple bars of different orientations in both visual fields, a task which is known to rely on the properties of V1 (Ferster & Miller, 2000).

Expected results. After the multisensory audio-visual training, participants are expected to show significant improvements in the motion-discrimination task for the stimuli presented in the visual field where hemianopia was simulated (contralateral to the inhibited V1), while no improvement in performance is expected for stimuli presented in the other visual field. Indeed, this task requires the
activation of the RCE, which was supposedly activated during the audio-visual multisensory training. In contrast, no change is expected in the orientation-discrimination task because it relies on the abilities of V1, which is not believed to be involved in the multisensory training.

**Experiment 2**

This experiment investigates the possibility of boosting the effects of the audio-visual training in hemianopic patients by directly enhancing the activity of the RCE via excitatory tDCS over the extrastriate areas.

**Materials and methods.** 20 patients with chronic hemianopia and without concurrent neurological deficits will be selected to participate in the study. A sub-group of 10 patients will undergo a course of audio-visual training and excitatory tDCS over the perilesional extrastriate cortex to enhance the activity of this cortical site. Another sub-group of 10 patients will undergo the same multisensory training coupled with sham tDCS over the perilesional extrastriate cortex to exclude any nonspecific effects of tDCS. During the audio-visual training (Bolognini et al., 2005; Passamonti et al., 2009), different kinds of sensory stimulation will be presented: (i) a unisensory visual condition, in which only the visual target will be present; (ii) a multisensory visual-auditory condition, i.e. a sound presented together with the visual target in the same spatial position; (iii) a unisensory auditory condition, in which only the auditory stimulus will be presented, i.e. catch trial. Training will require participants to explore for stimuli and respond with a button press when a visual stimulus (either unisensory or multisensory) is observed. Stimuli will be disproportionately allocated to the hemianopic side to encourage exploration of this field. The training will consist of 10 daily sessions of 2 hours each. Before and after training, patients will be assessed with a complete clinical evaluation, comprising visual detection tasks, visual search tasks and questionnaires to assess subjective perceived impairment in daily life. In addition, patients will be tested before and after training with a motion-discrimination task, in which they will be presented with patches composed of moving high-luminance dots in the blind and the intact field, and an orientation-discrimination task, in which they will be presented with simple bars of different orientations in the blind and the intact field, to specifically test for any improvements in abilities relying on the RCE (Billington et al., 2011) or V1 (Ferster & Miller, 2000), respectively.

**Expected results.** In line with previous literature (Bolognini et al., 2005; Passamonti et al., 2009), all the patients are expected to show improvements at the clinical evaluation after audio-visual training. However, a greater clinical improvement is expected for the sub-group of patients in whom the audio-visual training was coupled with excitatory tDCS over the perilesional extrastriate areas compared to the one that underwent sham tDCS. Indeed, if the multisensory training recruits the RCE to ameliorate clinical signs of hemianopia, a direct enhancement of the activity of this neural circuit, via excitatory tDCS over the extrastriate areas, should boost the effects of the training. Furthermore, patients should demonstrate a significant improvement after training only in the motion-discrimination task, which relies on the properties of the RCE, for stimuli presented in the blind field, while no improvement should be evident in the intact field. On the other hand, no improvements are expected in the orientation-discrimination task, which instead relies on the properties of V1.

**Implications**

The results of these studies will shed light on the neural basis of the beneficial effects of audio-visual training in hemianopic patients. Evidence from research on implicit visual processing in hemianopics and multisensory integration suggests that the RCE pathway could be responsible for the improvements observed after training. The results of the first experiment on simulated hemianopia in healthy participants will provide evidence for this hypothesis. On the other hand, the results of the second experiment will reveal whether direct stimulation of the RCE could enhance the effectiveness of the audio-visual training. Overall, the results of the present project will provide a significant theoretical contribution to the understanding of the mechanisms underlying the recovery of visual abilities and, from a clinical perspective, this knowledge will also greatly contribute to devising new effective neurorehabilitation treatments.
References


Attività formativa dell’assegnista

L’attività formativa sarà incentrata su:

1 - approfondimento delle conoscenze dei modelli teorici fondamentali e delle principali aree tematiche riguardanti le neuroscienze cognitive, in generale, e della percezione visiva, in particolare.
2 - acquisizione della metodologia di ricerca scientifica (qualitativa e quantitativa) per la progettazione e la realizzazione di progetti di ricerca nelle neuroscienze cognitive;
3 - acquisizione delle conoscenze sulle tecniche di analisi statistiche appropriate con l’utilizzo dei più significativi pacchetti statistici;
4 - acquisizione delle competenze tecniche e teoriche per l’utilizzo della stimolazione transcranica con Correnti Dirette (tDCS) e della stimolazione magnetica transcranica (TMS);
5 - acquisizione di competenze di ideazione, progettazione, realizzazione di un progetto di ricerca scientifica;
6 - acquisizione delle competenze per la diffusione dei risultati della ricerca scientifica (congressi nazionali ed internazionali e pubblicazioni scientifiche nazionali e internazionali);
7 - acquisizione delle competenze per l’applicazione dei risultati della ricerca scientifica per l’ideazione e lo sviluppo di nuovi trattamenti riabilitativi.