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Mechanisms underlying neglect recovery after prism adaptation☆

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Abstract

Prism adaptation (PA) has been demonstrated to be effective in improving hemispatial neglect. However not all patients seem to benefit from this procedure. Thus, the objective of the present work is to provide behavioural and neuroanatomical predictors of recovery by exploring the reorganization of low-order visuo-motor behaviour and high-order visuo-spatial representation induced by PA. To this end, 16 neglect patients (experimental group) were submitted to a PA treatment for 10 daily sessions. Neglect and oculo-motor responses were assessed before the treatment, 1 week, 1 and 3 months after the treatment. Eight control patients, who received general cognitive stimulation, were submitted to the same tests at the same time interval. The results showed that experimental patients obtained, as a consequence of PA, a long lasting neglect recovery, a reorganization of low-order visuo-motor behaviour during and after prism exposure (error reduction and after-effect, respectively) and a leftward deviation of oculo-motor responses. Importantly, the level of error reduction obtained in the first week of treatment was predictive of neglect recovery and the amelioration of oculo-motor responses, and the degree of eye movement deviation was positively related to neglect amelioration. Finally, the study of patients' neuroanatomical data showed that severe occipital lesions were associated with a lack of error reduction, poor neglect recovery and reduced oculo-motor system amelioration. In conclusion, the present results suggest that low-order visuo-motor reorganization induced by PA promotes a resetting of the oculo-motor system leading to an improvement in high-order visuo-spatial representation able to ameliorate neglect.

Keywords: Hemispatial neglect; Prism adaptation; Eye movements; Spatial attention; Rehabilitation

1. Introduction

In the last few years it has been shown that hemispatial neglect – i.e. right brain damaged patients' failure to respond, report or orient toward stimuli presented in the left contralesional space (Heilman, Valenstein, & Watson, 2000) – could be ameliorated by a treatment based on prism adaptation (PA) (Farnè, Rossetti, Toniolo, & Ladavas, 2002; Frassinetti, Angeli, Meneghello, Avanzi, & Ladavas, 2002; Rossetti et al., 1998). Prismatic lenses induce an optical deviation toward the ipsilesional side as demonstrated by *a rightward* error in limb pointing to a visual target. If the visual feedback is available, patients make a motor correction toward the controlesional side to compensate for the prism effect; thus the initial disorganization of the visuo-motor behaviour is corrected through visuo-motor adaptation, i.e. error reduction. When the prismatic goggles are removed and the limb pointing to the visual target is not visible to the subject, patients show a systematic leftward deviation of visuo-motor response with the adapted limb, the so-called after-effect. In neglect patients this after-effect is accompanied by improvements in visuo-spatial neglect tasks lasting several hours (Rossetti et al., 1998), days (Farnè et al., 2002) or weeks (Frassinetti et al., 2002). This amelioration is present both in visuo-spatial attention tasks requiring a motor response with the adapted limb, such as line cancellation, line bisection, drawing by copying or by memory (Rossetti et al., 1998) and also in visuo-spatial tasks requiring verbal responses, such as object description, object naming, word and non-word reading (Farnè et al., 2002; Frassinetti et al., 2002), or naming towns from a mental map (Rode, Rossetti, Li, & Boisson, 1998). These findings suggest that the leftward correction of the visual motor bias induced by PA could be responsible for the amelioration of

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neglect and this effect could influence not only low-order visuo-motor factors, but also higher-level spatial representations.

However, some patients described by different studies (Dijkerman et al., 2003; Ferber, Danckert, Joanisse, Goltz, & Goodale, 2003; Frassinetti et al., 2002; Morris et al., 2004; Pisella, Rode, Farnè, Boisson, & Rossetti, 2002) seem not to benefit from PA treatment or the improvement was limited only to some aspects of the syndrome. This finding suggests that PA is not effective in improving the deficits of all neglect patients, but some behavioural and anatomical characteristics may play an important role in determining visuo-motor responses and related neglect amelioration. This may be of crucial relevance in the clinical practice since it might allow us to distinguish patients who can or cannot benefit from the treatment. Thus, the analysis of the behavioural and neuroanatomical predictors of neglect recovery after PA is the main objective of the present study.

First of all, to individuate a possible behavioural predictor of recovery, the interaction between low-order visuo-motor and high-order visuo-spatial effects of PA was investigated, since a direct relationship between these two aspects has not been yet demonstrated. Typically, as a consequence of PA, two main modifications in visuo-motor behaviour can be observed, i.e. error reduction and after-effect.

The after-effect has been traditionally considered the core of adaptation (Harris, 1974; Welch, 1978) and in many studies the effects of PA on neglect amelioration took into account only this measure as the index of visuo-motor modification (Farnè et al., 2002; Rossetti et al., 1998). However, the relationship between after-effect and neglect amelioration is controversial. On the one hand, Farnè et al. (2002) found that the decay of after-effect has the same temporal evolution as the improvement of visuo-spatial deficits: indeed these authors found that both the after-effect and neglect improvement persisted 24 h after a single PA session and they both disappeared after 1 week. On the basis of this finding the authors speculated that this temporal relationship could have a potential causative role. On the other hand, the results from another two studies seem to contradict this conclusion. Pisella et al. (2002) described a double dissociation in two patients between the presence of after-effect in a straight-ahead pointing task and performance in a line bisection task: patient S.A. presented no deviation of pointing after prism exposure and an amelioration in line bisection after PA, whereas patient P.E. presented a significant leftward deviation of pointing, but a resistant rightward error in line bisection. Moreover, a strong dissociation between the duration of the after-effect and neglect recovery was found studying the long term effects of PA: Frassinetti et al. (2002) found that the improvement on visuo-spatial tasks, obtained after an intensive PA program, lasted at least 5 weeks from the end of treatment, whereas the after-effect decayed with time and vanished in 84 h. In addition, in this study a single patient (RD) did not show a neglect amelioration although he manifested a significant after-effect. Finally, Girardi, McIntosh, Michel, Vallar, and Rossetti (2004) recently found that straight-ahead measures of after-effect do not correlate with visuo-spatial effects of PA in normal subjects. Thus, the lack of a clear relationship between after-effect and neglect improvement represents an important question to be solved.

On the other hand, after-effect is not the only change in visuo-motor behaviour induced by prismatic visual field shift: for example, error reduction might be a good predictor of the neglect recovery. Patient RD (Frassinetti et al., 2002), who presented a substantial after-effect without an amelioration of neglect, did not show an error reduction during prismatic exposure, thus suggesting that error reduction could be an important factor to be considered in determining neglect amelioration. The relationship between the indices of visuo-motor modification and neglect amelioration can be considered at the same time both an important clinical and theoretical question to address. On the one hand, once this relation is clear, it would be possible to predict the success of the treatment for each patient starting from the first few trials of PA. On the other hand, the explanation of this relation could shed light onto the mechanism underlying neglect recovery after PA.

Thus, the first aim of the present study is to identify the relationships between visuo-motor effects of PA and neglect improvement and, in particular, to investigate whether error reduction or after-effect could predict the amelioration in visuo-spatial attention tasks. To this end, a group of 16 neglect patients were submitted to 10 daily sessions of PA treatment and visuo-spatial abilities were assessed before the treatment, 1 week, 1 and 3 months after the end of the treatment. In order to exclude the possibility that neglect amelioration was due to practice with the tests, to spontaneous recovery, or to general stimulation, eight neglect patients (control group), who received non-specific rehabilitation treatment, performed the same tests in four sessions with the same time interval as the experimental group.

A second intriguing question concerns the mechanism by which low order visuo-motor effects may produce a recovery in high-level visuo-spatial representations. It has been recently proposed that PA, by inducing a leftward eye deviation, produces a resetting of ocular scanning behaviour which facilitates the exploration of the left neglected side of the space (Angeli, Benassi, & Ladavas, 2004). Indeed it is well known that severe neglect patients present with a rightward deviation of the eyes (Hornak, 1992) and that mild neglect patients show a failure to make eye movements towards the left side of the space (Chedru, Leblanc, & Lhermitte, 1973; Girotti, Casazza, Musicco, & Avanzini, 1983; Walker & Findlay, 1996). Angeli et al. (2004) showed that a single session of PA reduced the rightward oculo-motor bias in neglect patients and induced an amelioration of reading abilities. Therefore, due to hand-eye coordination, the leftward deviation obtained in pointing during PA might also have an effect on eye movement responses. To test this hypothesis, patients' eye movements during a reading task were measured before and after the treatment and the relationship between indices of oculo-motor and visuo-motor response was studied.

The third aim of the present study was to investigate the relationship between the locations of brain lesions and the degree of neglect recovery affected by PA, in order to find out possible neuroanatomical predictors. Neglect can result from damage to different regions of the right hemisphere, mostly centred on the parietal lobe, but commonly involving also the frontal, temporal, occipital lobe, the basal ganglia and the thalamus (see Karnath,