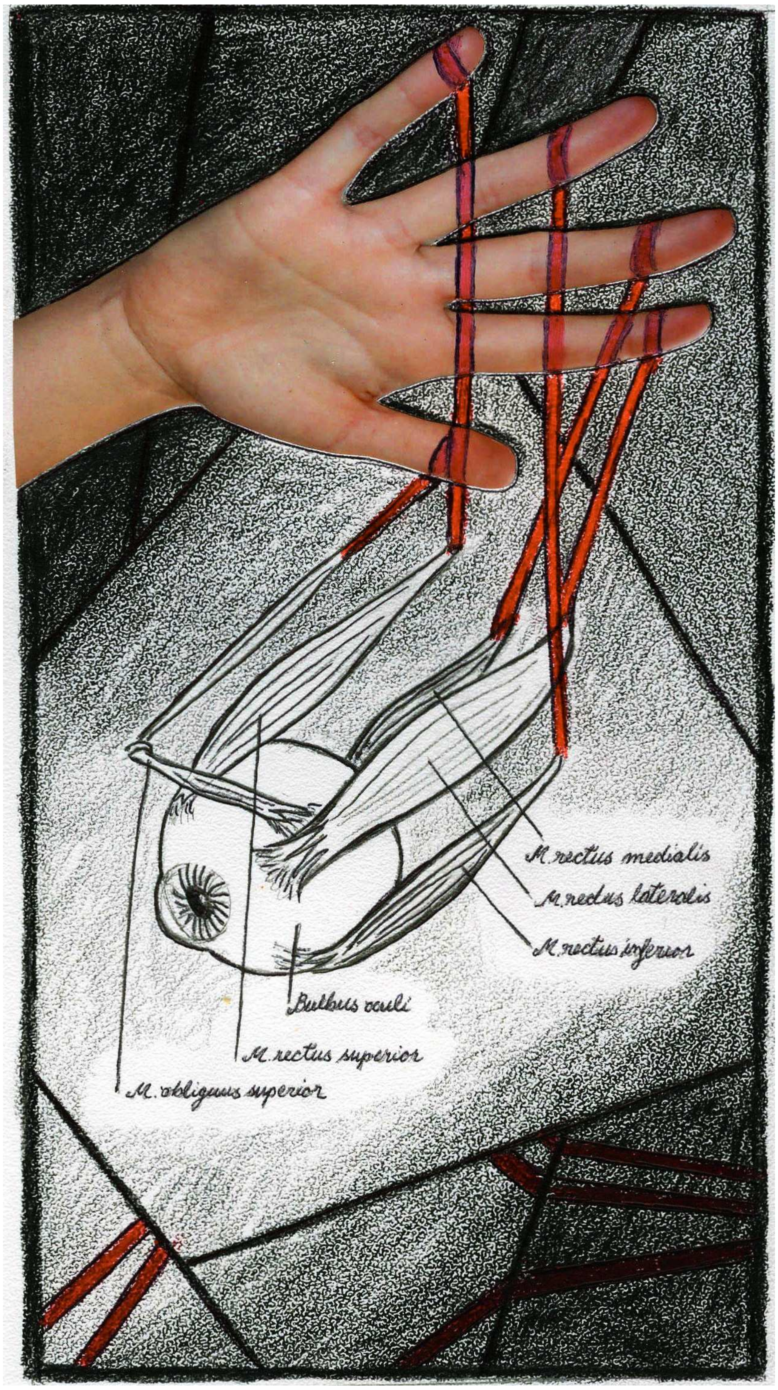

Proprioception - an obstacle for motor control in conditions with a visuoproprioceptive conflict

Daniela Balslev
PhD thesis
2005

Cover art by Dr. Pauliina Aarnio, illustrates one of this dissertation’s conclusions that proprioception influences visuospatial orienting.

Proprioception - an obstacle for motor control in conditions with a visuoproprioceptive conflict

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CONTENTS

ABSTRACT

This PhD dissertation is an overview of the findings presented in three papers. The topic of these papers is the contribution of proprioception to motor control in conditions when vision and proprioception transmit incompatible information about the direction in which the hand has moved. Spatial misalignment of visual and proprioceptive spaces occurs for instance whenever a surgeon who performs a laparoscopic intervention adjusts the direction of view of the video camera.

The methods used in the experiments are: 1Hz-repetive transcranial magnetic stimulation, functional magnetic resonance imaging and analysis of error rate/reaction time.

The results suggest that:

- Proprioception is an obstacle for trajectory control in conditions with a spatial conflict between vision and proprioception.
- Spatially incompatible proprioception slows down visual processing.
- Anterior parietal 1Hz-repetitive transcranial magnetic stimulation (rTMS) is an easy and safe method for acute proprioceptive deafferentation that can be applied to investigate the contribution of proprioception to motor control.

LIST OF PAPERS

1. Daniela Balslev, Lars O.D. Christensen, Ji-Hang Lee, Ian Law, Olaf B. Paulson, R. Christopher Miall. (2004). Enhanced accuracy of mirror-drawing after rTMS induced proprioceptive deafferentation. **J Neurosci** 24: 9698-702.

2. Daniela Balslev, Finn Å. Nielsen, Olaf B. Paulson, Ian Law. (2005) Right temporoparietal cortex activation during visuo-proprioceptive conflict. **Cereb Cortex** 15: 166-9

3. Daniela Balslev, Søren Kyllingsbæk, Olaf B. Paulson, Ian Law (2004). Proprioceptive modulation of visuospatial orienting. **Exp Brain Res** *(submitted 30. august 2004, revised 27. january 2005)*

AIM

The aim of this PhD project was:

- to test whether proprioception is an obstacle for trajectory control in conditions with visuo-proprioceptive misalignment
- to explore which brain processes are affected by the spatial discrepancy between visual and proprioceptive information
- to test for an interaction between vision and proprioception in spatial attention

SPATIAL ALIGNMENT OF VISUAL AND PROPRIOCEPTIVE FEEDBACK

Real-life conditions with a novel visuoproprioceptive alignment

During visually-guided movements, both vision and proprioception feed back into the brain the direction in which the hand has moved. Devices such as mirrors, video cameras or virtual environments on a computer display perturb the usual congruence between the visual and proprioceptive spaces. For instance, a surgeon who performs a laparoscopic intervention watches a video monitor instead of looking directly into the operation field. The direction of hand movement on the monitor depends not only on the direction in which the hand has moved but also on the direction of view of the camera. The surgeon often adjusts the direction of view of the camera to get at all times the best possible view of the operating field. Each time the endoscope is rotated, its angle of view changes, causing a novel visuoproprioceptive spatial alignment. A similar situation would arise for a dentist that monitors his hand in a mirror oriented under various angles or for someone who uses a joystick, a mouse or a data glove to move objects in computer-created virtual environments– e.g during computer games or during computer-assisted design.

Novel conditions with visuo-proprioceptive discrepancy are usually associated with a sense of conflict (Fink et al., 1999) and a decrease in motor performance (Ghez et al., 2000). Because most of these applications require a high level of motor accuracy, it is important to understand the nature of visuo-proprioceptive conflict in order to suggest solutions for improving performance.

The neurophysiological substrate for aligning the visual and proprioceptive spaces

During natural movements the spatial relation between the direction of hand movement conveyed by the visual and proprioceptive channels depends on the direction of gaze. The angle of rotation of the eye in the orbitae and the rotation of the head on the shoulders dictates the correspondence between the direction of hand movement and the direction in which its projection moves on the retinae. The transformation between the visual and other sensory spaces is implemented in the brain using the gain-field mechanism (Andersen, 1997). In the monkey posterior parietal cortex, the firing rate of the neurons with retinal receptive fields is modulated by the orbital eye position, in other words, the position of the eyes determines the amplitude of the visual response. For each head position, the activity across a population of cells with different eye-position and retinal-position sensitivities has a unique pattern of firing. In neurons with both eye- and head-position gain, the gain is specific for the direction of gaze, independent of whether the eyes or the head were used to direct the gaze (Andersen, 1997). This gaze direction-specific population of neurons is an ideal candidate for implementing the spatial transformation between visual and proprioceptive locations.

It seems likely that the synaptic connections and weights of the gain-field neurons reflects the natural arrangement of the eye-head-shoulder-hand system in the human body. Viewing the hand in a mirror would correspond to having the head removed from the shoulders and placed at some distance in front of the body with the eyes facing the body. So, exposure to novel visuo-proprioceptive transformations created by mirrors, video cameras or computers are unnatural and evolutionary very recent.

Is proprioception an obstacle for motor performance in conditions with a new visuoproprioceptive alignment?

Research in neurological patients with a chronic proprioception loss suggests that proprioception is an obstacle for motor performance in novel conditions with discrepant visual feedback. Thus, while normal controls needed more than four trials to draw a star-shaped contour while monitoring their hand in a mirror, a deafferented patient completed the task already in the first trial (Lajoie et al., 1992). Several other studies report on the advantages of the lack of proprioception for the adaptation to novel visuomotor transformations. Indeed, in comparison with a group of healthy controls, deafferented subjects maintain trajectory accuracy despite the new visuomotor transformation (Guedon et al., 1998), move more accurately during early trials (Fourneret et al., 2002; Vercher et al., 1996) and show stronger after effects (Taub and Goldberg, 1974). Together, these studies suggest that in conditions with a visuoproprioceptive conflict, the absence of proprioception is an advantage for motor control and learning.

There are, however, several alternative explanations for the observed performance advantages in these chronically deafferented patients. First, the patients were included in the studies more than ten years after their deafferentation. During this time they underwent rehabilitation programs involving motor skill learning. They were also repeatedly included in experiments that required them to solve a wide range of motor tasks (Cole and Paillard, 1995). Second, it is quite unclear what effect this chronic deafferentation has had centrally – either in the sensory cortices or in the motor areas that have had to undergo reorganization to allow continued motor performance. Hence, it is difficult to tell whether these advantages in performance are directly related to the loss of proprioception, reflect the patients' familiarity with motor learning (a so called ”learning to learn” effect (Seidler, 2004), or reflect more profound changes in their motor system.

To avoid these confounds and test specifically whether proprioception is an obstacle for trajectory control during conditions with discrepant visual and proprioceptive feedback it is necessary to decrease proprioception acutely and record the effect of deafferentation on motor performance.

One method for transitory sensory deafferentation is the ischemic peripheral nerve block. However, ischemia appears to block both afferent and efferent inputs equally – when the loss of sensation in the finger is complete, most subjects are unable to move their finger (Glencross and Oldfield, 1975). Therefore this method is less suitable for studying motor performance.

A relatively new method, low frequency (1Hz) repetitive transcranial magnetic stimulation (rTMS), produces a long-term suppression of cortical excitability that lasts several minutes after the cessation of the stimulation pulses. This effect has been demonstrated neurophysiologically in the motor cortex (Chen et al., 1997) and confirmed behaviourally for various cortical areas including the sensory cortices (Kosslyn et al., 1999; Boroojerdi et al., 2000;Knecht et al., 2003). For instance, 10-20 minutes of rTMS at 1Hz and 110% motor threshold applied over the somatosensory cortex increases the threshold for discriminating tactile stimuli for a period of 4-8 minutes post-rTMS (Knecht et al., 2003). In neurological patients, a lesion of the anterior parietal cortex impairs the sense of position of the contralateral arm (Corkin et al., 1970), while sparing the ability to perform voluntary movements (Pause et al., 1989). This opened the possibility that rTMS in the sensorimotor hand area can reversibly reduce the processing of proprioceptive feedback in healthy people, (Experiment 1) , and thus be a useful paradigm for studying the effect of central proprioceptive deafferentation on motor control, in particular for testing whether reducing proprioception acutely would improve performance in a mirror drawing task (Experiment 2).

Contribution of visual and proprioceptive feedback to trajectory control

The long delay in sensorimotor loops relative to the duration of movement has fueled a long-standing debate about the contribution of sensory feedback to movement control (Jeannerod, 1988;Desmurget and Grafton, 2000). Although the details about how sensory feedback influences the motor command are incompletely understood, most authors agree on the importance of sensation for trajectory control (Wolpert et al., 1995; Sabes, 2000; Desmurget and Grafton, 2000). The main argument for this view is the observation that accuracy decreases in the absence of both visual and proprioceptive information from the moving hand (Rothwell et al., 1982; Ghez et al., 1995).

Because movement is coded vectorially (Georgopoulos et al., 1982;Georgopoulos et al., 1986), hand location has to be known in order to plan or to ammend movement trajectory (Bock and Eckmiller, 1986; Ghez et al., 1991; Gordon et al., 1994; Sainburg et al., 2003). During visually guided reaching both vision and proprioception provide this information. However, the importance of these two sensory channels for trajectory control is unequal. Observations in chronically deafferented patients (Sanes et al., 1984; Ghez et al., 1995; Bard et al., 1995) supported by results in acutely deafferented subjects (Balslev et al., 2004) suggest that proprioception is not critical for trajectory control as long as visual feedback is available. Indeed, with visual feedback, deafferented patients are able to reach accurately to visual targets, although their velocity profiles deviate subtly from normal by showing for instance a longer movement duration or secondary velocity peaks (Jeannerod, 1988). On the contrary, in healthy people who reach to visual targets without receiving any visual feedback, the accuracy of movements decreases within seconds (Miall et al., 1995; Sheth and Shimojo, 2002; Brown et al., 2003).

Thus, visual feedback is essential for trajectory control when reaching to visual targets, whereas proprioceptive feedback is not. Proprioception in turn may make more subtle contributions to movement control.

Why is proprioception an obstacle for trajectory control in conditions with a visuoproprioceptive conflict ?

A. Inaccurate bimodal estimate of hand position

When both modalities provide information about hand location, the brain merge these sensory signals into a single, bimodal estimate (Rossetti et al., 1995; van Beers et al., 1999; Sober and Sabes, 2003). This point was clearly demonstrated by an experiment in which the visual and proprioceptive hand locations were artificially dissociated (Rossetti et al., 1995). The subjects viewed their fingertip through a prism lens before reaching to an undisplaced visual target. The measured error in reaching was best explained by assuming that the initial hand location used for trajectory planning lay in between the real and the optically displaced locations. This result indicates that the brain takes both vision and proprioception into account when estimating hand location.

Using both sources of information and weighting each source according to its reliability reduces the uncertainty or ”noise” in the sensory systems and thus increases the reliability of the estimate of hand location (van Beers et al., 2002a). In conditions with visuoproprioceptive misalignment, the bimodal estimate would be inaccurate.

This error in estimating hand location may outweigh the benefits of using two sensory modalities instead of one for trajectory control, explaining why a reduction in proprioceptive accuracy is advantageous in such conditions. There is however an objection to this interpretation that motivates the search for additional models for the interaction between visual and proprioceptive information. The weigthing of visual and proprioceptive information in the estimate of hand position is flexible (Welch and Warren, 1986; van Beers et al., 2002b;Sober and Sabes, 2003). The weights change for instance with the subject's experience with the visuomotor transformation, so that with training the weight of proprioception in the estimate of hand location relative to a visual target increases (Sober and Sabes, 2004). This finding shows that the brain can flexibly adjust the contribution of proprioception to the estimate of hand position to avoid trajectory errors. Because the brain already has the necessary mechanisms to decrease the weight of proprioception in the position estimate, a decrease in proprioceptive accuracy is expected to improve the hand position estimate very little or not at all.

B. Less efficient processing of visual feedback

Visual feedback is essential during early stages of adaptation to visual perturbations because it is the only source of error information needed for trajectory correction and motor learning.

Under the assumption that the brain's stimulus processing ressources are limited, attention is the ability to selectively enhance the processing of a salient stimulus relative to less important aspects in a complex scene (Digirolamo and Posner, 2000). Although people may choose to attend to sources of information they find relevant in the context of their present activities (goal-driven attention), their attention can also be captured involuntarily by salient stimuli (stimulus-driven attention). Presenting a sound or a touch on the hand short time before a visual stimulus speeds up the processing of the visual stimulus when the two stimuli appear at a similar as compared with a different location (Spence and Driver, 1997; Spence et al., 1998). This facilitation of visual processing occurs even if the first stimulus does not predict the spatial location of the second stimulus. This suggests that the mechanisms that capture attention towards the spatial location of the first stimulus operate involuntarily. Such exogenous multisensory interactions in which a non-predictive cue in one modality influences the judgment of targets appearing in another modality have been found for all modality pairings that have been tested within vision, touch and audition

(Spence et al., 2004). It seems thus likely that a similar link exist between vision and proprioception and that its role is to facilitate the processing of visual feedback among other visual stimuli.

Visual feedback is essential for trajectory control during visually guided movements. During natural movements, the visual scene is complex, so mechanisms that allow the brain to favour sampling and processing of the visual feedback over other visual objects may be called upon. The facilitation of visual processing for stimuli sampled from a proprioceptively congruent location may serve this purpose. In artificial movement environments that introduce a novel spatial alignment between visual and proprioceptive information, this mechanism would malfunction and interfere with motor control.

OVERVIEW OF OWN EXPERIMENTS

Experiment 1. Does 1Hz-rTMS reduce proprioception ? (Paper 1)

Design:

- Two experimental sessions, real and sham rTMS, in random order, scheduled on separate days
- Proprioceptive accuracy for right hand was tested using a finger to finger matching task (Figure 1) before and after 15 minutes of 1Hz-rTMS at 110% motor threshold applied 3 cm posterior to the motor hotspot of the left hemisphere.
- Post-TMS proprioceptive error was calculated as the distance between target and indicator finger, normalized to pre-TMS value and compared across sessions using a paired-samples t-test.

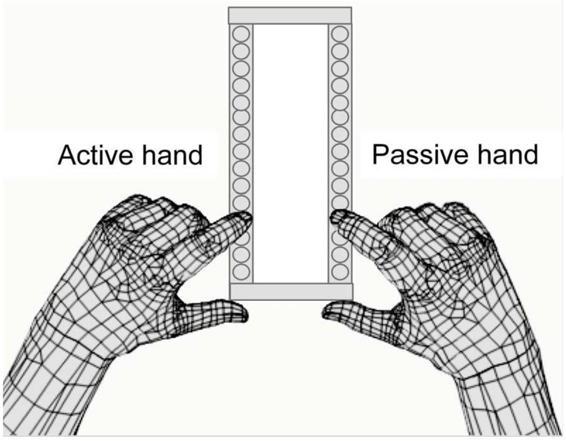

Figure 1. The apparatus used to test proprioceptive accuracy. The apparatus consisted of two LEGO bricks fixated on a horizontal table so as to be parallel with the subject's midsagittal plane. Before each trial, the examiner positioned both fingers on the studs situated at the proximal end of the apparatus. Then, the subject's right index finger was passively moved to one of the studs on the right brick, at variable distance from the start position. Finally, the subject moved the left index finger to place it on a stud of the left brick so as to match the position of the

right index finger. The subjects had their eyes closed throughout the experiment and received no feedback on performance.

Experiment 2. Does 1Hz-rTMS improve trajectory accuracy during novel mirror drawing ? (Paper 1)

Design:

- Two groups matched for age and gender who received either real or sham rTMS with the same parameters as for experiment 1.
- The subjects used a mouse to move a cursor along a circular path on a computer screen. Tracing accuracy was tested before and after rTMS, mirror tracing accuracy was tested after rTMS (Figure 2). Tracing: $x_{screen} = x_{mouse}$, $y_{screen} = y_{mouse}$; Mirror tracing: $x_{screen} = x_{mouse}$, $y_{screen} = -y_{mouse}$
- Error was calculated as the average of the modulus radial error and normalized to the subject's pre-TMS tracing performance. Mirror tracing error was compared across groups using a Mann-Whitney U-test

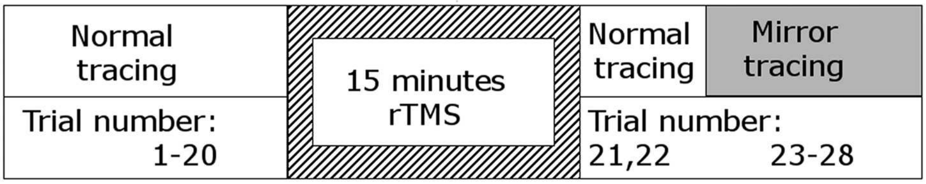

Figure 2 . The design of the mirror tracing experiment. Normal tracing skill was tested before and immediately following 15 minutes of 1 Hz rTMS. Mirror tracing was tested during 6 trials given post rTMS. Each trial lasted 10 seconds with an intertrial interval of 10 seconds.

Experiment 3. Which brain area is responsible for the decrease in proprioception after 1Hz-rTMS at 3-cm posterior to the hand representation in the primary motor cortex? (Paper 1)

Design:

- 3 groups that received real rTMS at 3 different scalp locations: i) primary motor cortex (M1), at the motor hotspot, ii) anterior parietal cortex (APC), 3 cm posterior to the motor hotspot, the same site as that used for experiments 1 and 2. iii) posterior parietal cortex (PPC), 6 cm posterior to the motor hotspot.
- Proprioceptive accuracy for right hand was tested using a finger to finger matching task before and after 15 minutes of 1Hz-rTMS at 110% motor threshold. The protocol of the experiment was identical with the protocol of experiment 1.
- The effect of stimulation site on proprioceptive error was assessed using a Kruskal-Wallis test.

Experiment 4. Which brain areas are sensitive to the spatial alignment between vision and proprioception ? (Paper 2)

Design:

- Two conditions – exposure to congruent or incongruent visual and proprioceptive trajectories of movement (Figure 3). The conditions were matched for speed of movement and task demands.
- Regional neural activity was measured with fMRI and compared across conditions with a one-tailed t-test for the difference incongruent > congruent.

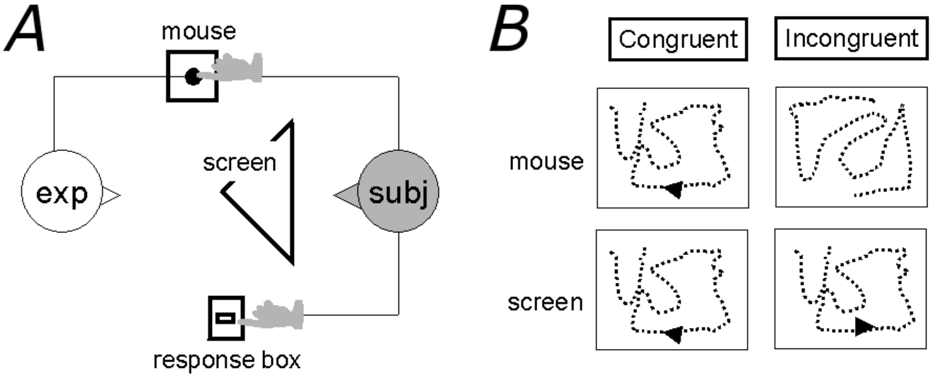

Figure 3. Diagram of the experimental set-up and behavioral conditions. A. The experimenter (Exp) stood beside the scanner moving the subject's right index finger on a mouse field. The subject (Subj) lay in the scanner facing an LCD screen and responded with the left hand by pressing the response box key. B. In the congruent condition finger and cursor movement followed the same trajectory. In the incongruent condition, the movement of the cursor was played from a memory buffer recorded during a previous trial of the congruent condition. The arrowhead indicates the direction of movement.

Experiment 5. Does spatially congruent proprioception speed up processing of visual information ? (Paper 3)

Design:

- Two conditions: exposure to compatible or incompatible visual and proprioceptive trajectories (Figure 4).
- Subjects discriminated the vertical component (upwards or downwards) of visually presented movement. The visual stimulus - a screen cursor with an oblique trajectory - was moving synchronously with a proprioceptive stimulus – passive finger movement along a horizontal line in the left or right direction. The horizontal component of the cursor movement was either in the same direction (compatible condition) or in the opposite direction as the direction of proprioceptive distractor (incompatible condition). The orthogonal paradigm (Spence and

Driver, 1994;Spence and Driver, 1997) ensured that the required response (upwards/downwards discrimination) was completely independent from the direction of finger movement (to the right or to the left, on a horizontal line). This manipulation rules out the confounding effect of the proprioceptive distractor on the motor response, independently of the visual stimulus.

- Reaction time for judging the vertical component of visual movement was compared across conditions using a one-sided paired-samples t-test.

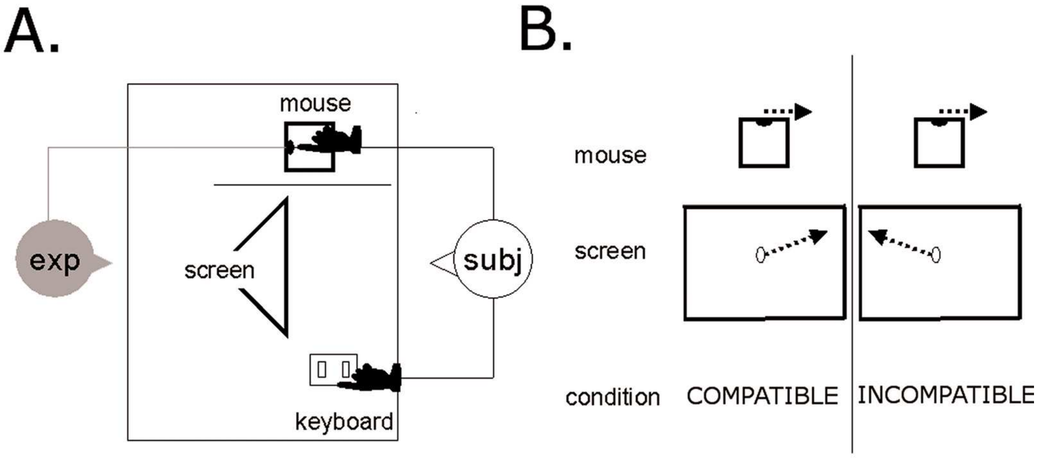

Figure 4 . Diagram of the experimental set-up and behavioural conditions. A. The experimenter (Exp) moved the subject's right index finger on the mouse field. The subject (Subj) watched visual cursor movement presented on a computer screen and responded with the left hand by pressing a key on a keyboard. B. For each trial, the finger was moved on a horizontal line, to the left or to the right. The horizontal component of the movement of the cursor was either in the same direction (compatible) or in the opposite direction (incompatible) relative to the trajectory of the mouse.

METHODOLOGICAL CONSIDERATIONS

For a detailed description of the methods please refer to the individual papers. In this section I discuss the limitations of the techniques used and the implications for the design of the experiments and the interpretation of the results.

Measuring proprioceptive accuracy

Proprioceptive acuity is usually assessed using position matching tasks in which the blindfolded subject reproduces with an indicator finger the position of a target finger that is passively displaced (Paillard and Brouchon, 1968; Velay et al., 1989). It has been observed that the error in a position matching task depends on various factors such as i) where the tested position is located in relation to the range of joint rotation allowed by the subject's hand anatomy (Rossetti et al., 1994;Janwantanakul et al., 2001), ii.) whether the subject exerts force against passive movement (Rymer and D'Almeida, 1980) or iii) whether tactile information is available during the externally imposed movement (Paillard and Stelmach, 1999). Other factors such as iv) attention or motivation may also affect the accuracy of the matching task. To address these concerns, when testing position sense:

i) We have used a paired design with the same group of subjects undergoing both sham and real TMS sessions and identical target and start position for all sessions. In this way there was no difference between sessions concerning where the target positions were located in relation to the range of joint rotation allowed by the subject's hand anatomy.

ii) The paired design and the normalization of postTMS accuracy to the subject's preTMS level allowed the cancellation of subject or session specific differences in the ability to relax the finger.

iii) No tactile information about the extent of movement was given. The finger was lifted from the start position and landed directly on the target.

iv) The paired design and the normalization of postTMS accuracy to the subject's preTMS level

cancelled out subject or session specific differences in attention and motivation. A general effect of rTMS on attention is ruled out by the results of experiment 2 in which mirror tracing performance was found to be more accurate after real compared with sham TMS.

Targetting the proprioceptive projection to the cerebral cortex with TMS

The afferent input from the muscle spindles, the main proprioceptive receptors, travel in fast, myelinated nerve fibers into the spinal cord. From there, the signal is transmitted either to the cerebellum or to the primary somatosensory cortex via the dorsal column nuclei and the thalamus. Within the primary somatosensory area, the input from the muscle spindles is channeled towards Brodmann Area 3a and 2 (Phillips et al., 1971, Burchfiel and Duffy, 1972). Area 3a is located in the depth of the central sulcus, at the border with the primary motor cortex, whereas area 2 is located at the surface, on the convexity of the postcentral gyrus (Bodegard et al., 2003; McGonigle, 2004). The posterior parietal area 5 is believed to process higher-order proprioceptive information because its neurons have larger receptive fields that encompass several joints located on both the ipsi- and contralateral limb (Sakata et al., 1973). Neurons that directly receive thalamic input related to passive joint movement have also been discovered in the primary motor cortex (Lemon and van der Burg, 1979).

The effect of TMS decays with the distance from the center of the coil and is estimated to decay to zero at 25 mm under the coil (Barker, 1999). By positioning the coil at 3 cm posterior to the location of the hand representation in the primary motor cortex we have thus most probably interfered with the function of the somatosensory areas 2 and 5 or the motor cortex and not area 3a, which is located in the depth of the central sulcus. Thus the effects of TMS on motor performace highlighted by the present experiments are the result of interfering with a subset and not the entire cortical projection of proprioceptive afferents.

Spatial specificity of anterior parietal rTMS for decreasing proprioceptive accuracy

There are at least three brain regions involved in proprioceptive processing whose direct or transsynaptical inactivation may cause the decrease in proprioceptive accuracy after rTMS stimulation 3 cm posterior to the motor cortex. First, the primary somatosensory cortex is the first cortical station for proprioceptive afferents (Maendly et al., 1981) and its lesion impairs all somatosensory modalities (Corkin et al., 1970). Second, the primary motor area has neurons that respond to passive movement (Strick and Preston, 1982) and evidence has recently been put forth for its importance in somatosensation (Nudo et al., 2000;Naito et al., 2002). A third candidate area is the left posterior parietal cortex in which a lesion in neurological patients can cause deficits in locating body parts (Wolpert et al., 1998;Semenza, 2001). To find out which brain region was most likely to be responsible for the decrease in proprioception in Experiment 1, we compared position-matching error following rTMS at the motor hotspot, anterior and posterior parietal cortex (Experiment 3). The effect of rTMS on proprioceptive accuracy was maximal 3 cm posterior to the motor cortex. It decreased significantly when the coil was placed directly over the motor cortex, at the motor hotspot. The size of the effect also decreased when the coil was moved 3 cm further posterior, although this difference was not statistically significant. Thus, the brain area responsible for the rTMS-induced decrease in proprioception to the anterior parietal lobe, probably corresponding to the location of the hand in the somatosensory cortex. Further experiments combining rTMS and neuroimaging techniques may map in more detail the brain area that is responsible for this effect.

Inferring brain function from an activated brain region

To explore how visuoproprioceptive mismatch affects normal brain function we started off by mapping the brain areas that are sensitive to the spatial congruence between the visual and proprioceptive information.

Functional neuroimaging experiments manipulate behavior and measure the effect of this manipulation on the regional synaptic activity (Logothetis et al., 2001). More than three decades of functional brain mapping has produced a large number of statistical maps that associate brain areas with sensory, motor, cognitive and emotional processes. An increasing number of reviews and meta-analyses investigate the consensus in these findings, strengthening the validity of the functional maps of the brain. This opens the possibility to understand the processes engaged by some complex task by looking at the patterns of functional activation in the brain when subjects engage in the task.

It is not possible to demonstrate a cross-modal link between vision and proprioception in spatial orienting based on this exploratory fMRI experiment. Although both lesion and imaging studies establish a connection between the right temporo-parietal cortex and spatial attention, this area has also been activated in non-spatial tasks, such as for instance during exposure to oddball stimuli (Downar et al., 2000). Thus, the activation of this area suggests, but it does not prove, the connection between the visuo-proprioceptive spatial conflict and the allocation of processing ressources in the visual space.

To strengthen this association, one possibility would be to vary parametrically the angle between the visual and proprioceptive locations and investigate whether the level of activity in the right temporoparietal cortex reflects this manipulation. This has not been done. Another possibility would be to test directly, using reaction time measures, whether visual processing is indeed faster when vision and proprioception show convergent rather than discordant information. Experiment 5 tested this prediction.

Inferring the speed of visual processing from the reaction time of a motor response

We measured the effect of visuo-proprioceptive compatibility on visual discrimination indirectly using the reaction time of a motor response. This opens the possibility that the increase in reaction time in the incompatible condition reflects a disruption of the response rather than of visual perception. This could arise if, for instance, the proprioceptive distractor preactivates a response or if the subject's surprise at the visuo-proprioceptive incompatibility delays their response. None of these confounds are likely to be responsible for the difference in reaction times observed in experiment 5. First, the orthogonal paradigm (Spence and Driver, 1994;Spence and Driver, 1997) ensured that the required response (upwards/downwards discrimination) was completely independent from the direction of finger movement (to the right or to the left, on a horizontal line). This manipulation rules out the confounding effect of the proprioceptive distractor on the motor response, independently of the visual stimulus. Second, if the increase in reaction times in the incompatible condition reflected a response disruption caused by the subjects' surprise, then one would have expected a decay over time in this difference in reaction time between conditions, as the subjects were becoming accustomed with the large incompatibility angle. To test for a time-by-condition interaction, reaction time data were re-analysed by a within-subjects repeated-measures two-way ANOVA with factor 1- condition and factor 2 - block number. Neither this interaction

($F(2,16) < 1$) nor the main effect of test time ($F(2,16) = 1.041$, $p = 0.376$) were statistically significant.

Inferring the effect of proprioception on processing visual feedback from the effect of proprioception on visual perception

The neural and behavioral differences between vision-for-perception and vision-for-action systems are well-known (Goodale and Westwood, 2004). Hence, the effect of proprioception on visuospatial orienting demonstrated by Experiment 5 may be restricted to perceptual processes and do not influence the processing of visual feedback during movement. The connection between proprioception and vision for action needs to be specifically investigated using an experimental paradigm in which the dependent variable relates to hand trajectory adjustment rather than to perceptual decision making.

RESULTS AND DISCUSSION

Experiment 1

rTMS over the somatosensory cortex contralateral to the hand reduced proprioception in comparison to sham stimulation (Figure 5). Following real rTMS proprioceptive error increased to 192.14 ± 31.67 % (mean ± standard error) of pre-TMS performance, whereas following sham, proprioceptive error was 95.68 ± 15.37 % . The difference between groups was significant (paired t-test, $p<0.05$). The absolute value for proprioceptive error following rTMS was median= 4.22 mm, range 1.78 –7.56 mm for real-rTMS and median = 3.33, range = 1.33 –6.67 mm for sham.

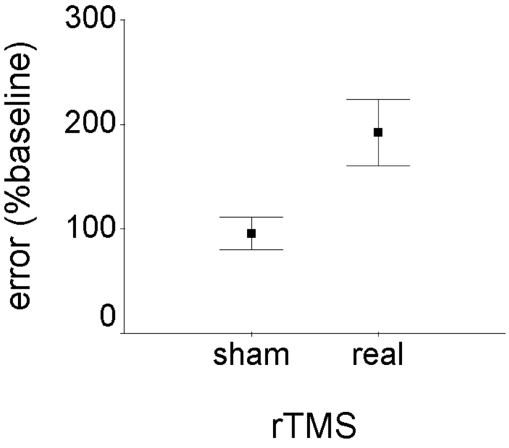

Figure 5. Proprioceptive error in the finger-position matching task following real and sham rTMS (mean ± standard error). Post- rTMS error is expressed as percentage of the baseline error, sampled before rTMS . Paired t-test, $p<0.05$; N=10 subjects in each group.

Experiment 2

After repetitive transcranial magnetic stimulation over the brain's somatosensory cortex trajectory accuracy in a condition with a novel visuoproprioceptive alignment was improved (Figure 6). This result suggests that proprioception is an obstacle for motor performance in conditions with a spatial discrepancy between vision and proprioception. It also shows that in such conditions it is possible to improve motor performance by reducing proprioception with anterior parietal rTMS.

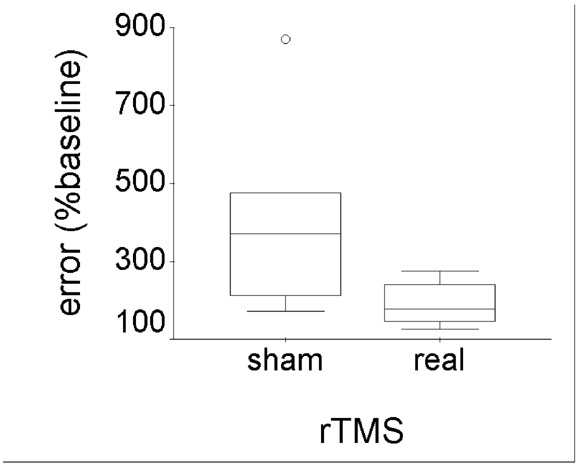

Figure 6. **Trajectory error.** Box-plot of trajectory error during novel mirror tracing in the groups that received either real- or sham-rTMS. Post-rTMS error is expressed as percentage of the baseline error, sampled before rTMS. Mann-Whitney U-test, $p<0.05$; N= 6 subjects in each group.

Experiment 3

There was a significant difference between the three groups in their proprioceptive matching accuracy after rTMS (Kruskal-Wallis test, chi-square = 7.51, $p < 0.05$, Figure 7), with the greatest reduction in proprioception for the group stimulated over the anterior parietal cortex (APC). This result suggests that the brain site responsible for the decrease in proprioceptive accuracy after anterior parietal rTMS is the anterior parietal cortex.

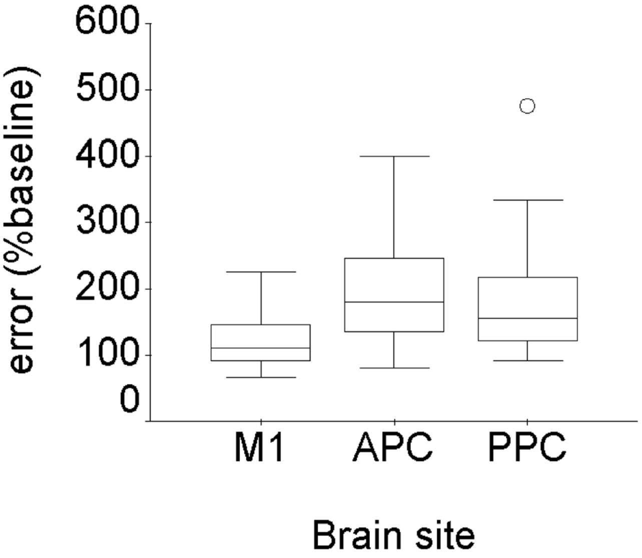

Figure 7. Box-plot of proprioceptive error following rTMS applied at various scalp sites. The coil was placed over three different brain sites: motor cortex (M1 - at the motor hotspot), anterior parietal cortex (APC - at 3 cm posterior to the motor hotspot) and posterior parietal cortex (PPC – at 6 cm posterior to the motor hotspot). The effect of rTMS site on proprioceptive error was significant (Kruskal-Wallis test, $p<0.05$). Post- rTMS error is expressed as percentage of the baseline error, sampled before rTMS. N = 15 subjects in each group.

Experiment 4

In this fMRI experiment we compared brain activity across two conditions with similar sensory stimulation and task demands that differed by the spatial congruence of the visual and proprioceptive input. The main finding of this study was the relative increase of activity in the right temporoparietal cortex (marked with an arrow on Figure 8). The right temporoparietal cortex is the brain site that is most often lesioned in patients suffering from visuospatial neglect (Karnath et al., 2001;Vallar, 2001;Karnath et al., 2004;Ringman et al., 2004), a disorder in which deficits in orienting attention in space are common (Bartolomeo and Chokron, 2002). Functional imaging studies in humans have implicated this brain area in stimulus-driven spatial attention (Corbetta and Shulman, 2002).

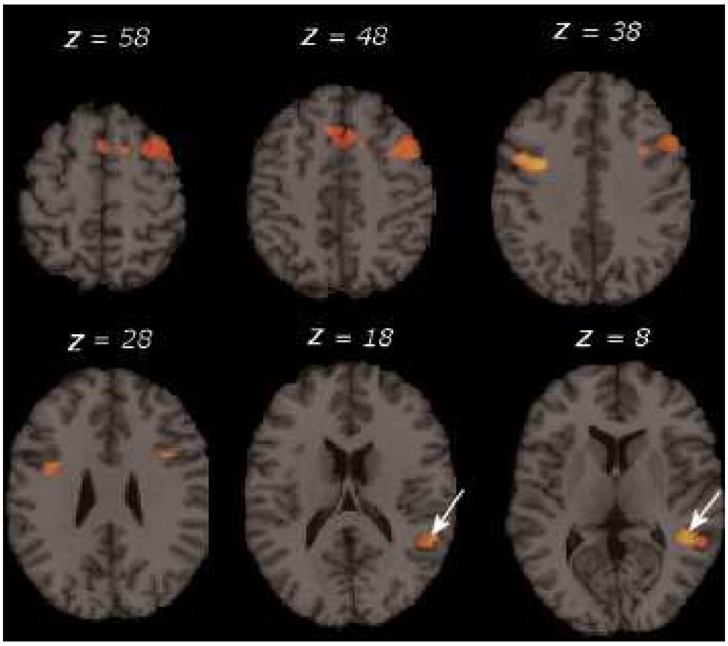

Figure 8. Brain areas with higher activity in the incongruent compared with the congruent condition. The congruent condition was subtracted from the incongruent condition and the result is showed as a parametric map of the t-statistic. The map is thresholded at a corrected p-value < 0.001 at the cluster level (random-effects analysis). For the purpose of anatomical localization, the map is superposed on a single-subject T1-weighted image in corregistration with the stereotactic space of the MNI template. The *z*-

value for each transversal slice is the stereotactic coordinate in vertical direction in the MNI space. The arrowhead indicate the right temporoparietal cortex

Experiment 5

To test specifically whether proprioception modulates visuospatial orienting we conducted a psychophysical experiment in which we measured how fast the subjects were able to judge a visual stimulus when simultaneously exposed to spatially congruent or incongruent proprioception. Discriminating the direction of visual motion was 41.09 ± 15.48 milliseconds (mean ± standard deviation) faster in the compatible as compared with the incompatible conditions (one-sided paired samples t-test, p <0.05, Figure 9).

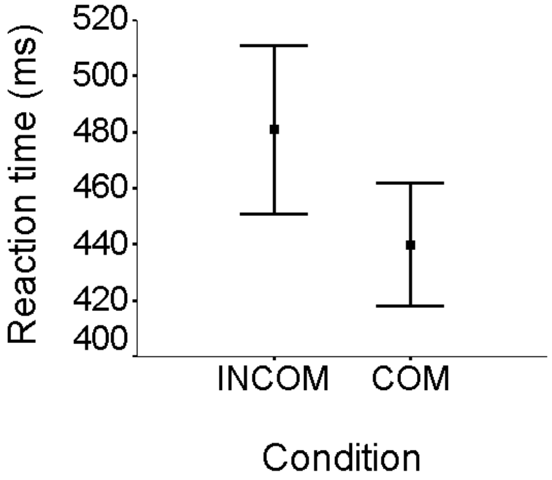

Figure 9. Reaction time (mean ± SE) for visual discrimination in the two experimental conditions. The difference in reaction time between conditions was significant (p < 0.05). COM – spatially compatible visual and proprioceptive trajectories; INCOM – spatially incompatible visual and proprioceptive trajectories.

CONCLUSIONS

- An intervention that decreases proprioceptive accuracy improved trajectory control in a visuomotor task with incompatible visual and proprioceptive feedback. Proprioception appears thus to be an obstacle for trajectory control in such conditions. This result confirms previous observations in deafferented patients and establishes a stronger, causal link between the decrease in proprioceptive accuracy and performance improvement.
- Spatially incompatible proprioception slows down visual processing. This suggesting an interaction between vision and proprioception in spatial attention. Cross-modal interactions in spatial attention have previously been found within vision, touch, audition. The present result extends these findings to include also the visual and proprioceptive modality pair.
- Anterior parietal 1Hz-rTMS is a useful method for central proprioceptive deafferentation in order to investigating the role of proprioception in human motor control. The advantages of this method are: a) it is easy to apply and safe and b) it allows to study motor effects of acute deafferentation in healthy people. Its main disadvantage is that it targets only a subset of the cortical projections of proprioceptive receptors.

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SUMMARY IN DANISH

Denne PhD afhandling udgør en oversigt over fund som er rapporteret i tre artikler. Artiklerne handler om hvordan proprioception bidrager til motorisk kontrol ved tilstande hvor syn og proprioception sender modstridende information om retningen af håndbevægelse til hjernen. Et spatialt misforhold mellem det visuelle og det proprioceptive rum finder sted for eksempel hver gang en kirurg justerer kameravinklen under en laparoskopisk operation.

Til belysning af denne problemstilling har jeg brugt følgende metoder: 1-Hz repetitiv transkranial magnetstimulation, funktional magnetisk resonans billeddannelse og analyse af feljprocent/reaktionstider.

Resultaterne antyder at:

- Proprioception er en forhindring for retningskontrol ved tilstande med spatiel misforhold mellem syn og proprioception
- Spatialt inkompatibel proprioception forsinker hjernens processering af visuel information
- Anterior parietal 1 Hz- repetitiv transkraniel magnetstimulation (rTMS) er en nem og sikker metode for akut proprioceptiv deafferentering hos raske som kan anvendes til at undersøge hvordan proprioception bidrager til motorisk kontrol.

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Brief Communication

Enhanced Accuracy in Novel Mirror Drawing after Repetitive Transcranial Magnetic Stimulation-Induced Proprioceptive Deafferentation

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When performing visually guided actions under conditions of perturbed visual feedback, e.g., in a mirror or a video camera, there is a spatial conflict between visual and proprioceptive information. Recent studies have shown that subjects without proprioception avoid this conflict and show a performance benefit. In this study, we tested whether deafferentation induced by repetitive transcranial magnetic stimulation (rTMS) can improve mirror tracing skills in normal subjects. Hand trajectory error during novel mirror drawing was compared across two groups of subjects that received either 1 Hz rTMS over the somatosensory cortex contralateral to the hand or sham stimulation. Mirror tracing was more accurate after rTMS than after sham stimulation. Using a position-matching task, we confirmed that rTMS reduced proprioceptive acuity and that this reduction was largest when the coil was placed at an anterior parietal site. It is thus possible, with rTMS, to enhance motor performance in tasks involving a visuoproprioceptive conflict, presumably by reducing the excitability of somatosensory cortical areas that contribute to the sense of hand position.

Key words: proprioceptive; visual; somatosensory; hand; parietal; motor activity

Introduction

Exposure to a novel visuomotor spatial transformation results in an immediate decrease in movement accuracy (Ghez et al., 2000). This problem arises when movements are visually monitored in a mirror or a video display and the performer has insufficient experience with the transformation from the hand to the visual space. In real life, for instance, it can happen to a surgeon who adjusts the view direction of the laparoscope to get a better view of the operation field or to a dentist who needs a mirror to work on the backside of the tooth.

Intriguingly, performance deteriorates less in proprioceptively deafferented patients than in healthy controls when they change from normal to mirror drawing. In the absence of proprioception, it is easier to maintain movement speed and accuracy when the new mapping from the hand to the visual space is introduced (Lajoie et al., 1992; Guedon et al., 1998). Furthermore, in healthy persons who are adapting to a visuomotor transformation, movement accuracy correlates negatively with the firing activity of the muscle spindles (Jones et al., 2001). These findings lead to the hypothesis that reducing proprioceptive inflow to the brain improves performance in situations with a visuoproprioceptive conflict.

To test this hypothesis, it is necessary to reduce proprioceptive accuracy in healthy people. To this end, we applied 15 min of 1 Hz repetitive transcranial magnetic stimulation (rTMS) over the anterior parietal cortex, at the putative location of the hand area in the primary somatosensory cortex. rTMS at 1 Hz reduces cortical excitability, producing a so-called "virtual lesion" (Pascual-Leone et al., 1999; Siebner and Rothwell, 2003). In neurological patients, a lesion of the anterior parietal cortex impairs the sense of position of the contralateral arm (Corkin et al., 1970) but spares the ability to perform voluntary movements (Pause et al., 1989). Here, we show that rTMS applied at an anterior parietal site improved trajectory accuracy during a novel mirror drawing task performed with the contralateral hand. In two separate control experiments, we confirmed that rTMS decreased proprioceptive accuracy and that this effect could be located in the anterior parietal lobe.

Materials and Methods

Experiment 1: mirror tracing

Subjects. Twelve healthy, right-handed volunteers (six females, 18–42 years of age, median 28) gave written informed consent and participated in the experiment. All of the subjects had normal or corrected-to-normal vision and used a computer mouse daily. The study was approved by the Central Oxfordshire Research Ethics Committee.

Study design. Each subject was randomly assigned to an intervention group, either real-rTMS or sham-rTMS stimulation. There was no significant difference between groups in median age or female/male ratio.

Task. The task was a computer implementation of the classic mirror

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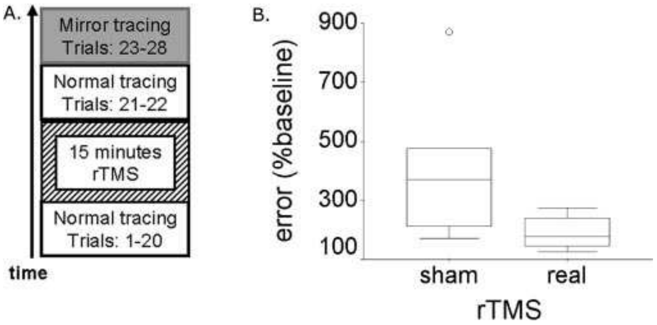

Figure 1. The mirror tracing experiment. *A*, Study design. Normal tracing skill was tested before and immediately after 15 min of 1 Hz rTMS. Mirror tracing was tested during six trials given after rTMS. Each trial lasted 10 sec with an intertrial interval of 10 sec. *B*, Results. Box plot of trajectory error during novel mirror tracing in the groups that received either real or sham rTMS. Post-rTMS error is expressed as percentage of the baseline error sampled before rTMS. Mann–Whitney *U* test, $p < 0.05$; $n = 6$ subjects in each group.

drawing task (Milner et al., 1968) on which patients without proprioception outperform healthy controls (Lajoie et al., 1992). Trials of normal tracing were performed before (20 trials) and after (two trials) rTMS, followed immediately by six trials of mirror tracing (Fig. 1*A*).

The subjects sat comfortably at a table, with the chin on a support that aligned the head to the body midline. A computer screen (330 × 240 mm, 640 × 480 pixels) was placed at 56 cm in front of them. With the right index finger, the subjects operated a sliding computer "mouse" (FELIX Pointing Device; Altra, Rawlins, WY), which moved in an active area of 30 × 24 mm. The mouse controlled a screen cursor (radius, 2 mm; visual angle, 0.42°). The subjects were instructed to move the cursor in a clockwise direction along a circular path (radius, 90 mm; visual angle, 18.82°; path width, 10 mm) and to choose the highest possible speed of tracing that allowed them to stay within the path. Each trial lasted 10 sec. Between trials, the subjects had 10 sec to place the cursor in the start position marked at the leftmost point of the circular path and to prepare for a new trial. During normal tracing trials and all of the intertrial intervals, the trajectory of the cursor was similar to the trajectory of the mouse ($x_{\text{cursor}} = x_{\text{mouse}}$; $y_{\text{cursor}} = y_{\text{mouse}}$). During the mirror tracing trials, the position of the cursor was up–down reversed relative to the position of the mouse ($x_{\text{cursor}} = x_{\text{mouse}}$; $y_{\text{cursor}} = -y_{\text{mouse}}$). A laptop running E-prime (Psychology Software Tools, Pittsburgh, PA) on Windows 2000 presented the stimuli and recorded the position of the mouse and cursor every 50 msec.

rTMS. Each rTMS session consisted of 900 biphasic stimuli produced by a Magstim Rapid magnetic stimulator (The Magstim Company, Whitland, UK) and delivered with a frequency of 1 Hz over 15 min.

One of two identical, standard 70-mm-diameter figure-of-eight coils was centered over the stimulation site and maintained in this position by a coil holder. This site was mapped in each subject in relation to the "motor hotspot" of the left hemisphere, which is the scalp projection of the primary motor cortex (Wassermann et al., 1996). The site of stimulation was located at 3 cm posterior to the motor hotspot, measured on a line oriented at 45° from the sagittal plane and perpendicular on the central sulcus. Previous TMS studies that successfully targeted the somatosensory hand area report a coil position at 1–4 cm posterior to the motor hotspot (Sugishita and Takayama, 1993; Harris et al., 2002; McKay et al., 2003; Ragert et al., 2004). Thus, we assumed that positioning the coil at 3 cm from the motor hotspot would reduce the activity of the primary somatosensory cortex with minimum effect on the primary motor cortex. The motor hotspot was defined as the point of maximum evoked motor response in the relaxed first dorsal interosseus (FDI) muscle of the right hand. Stimulation intensity was set at 110% of resting motor threshold of the right FDI muscle. To identify the resting motor threshold, the subjects were asked to rest the right hand on the table with the fingers slightly spread. The resting motor threshold was defined as the lowest intensity that reliably elicited a visible twitch in the FDI muscle when the stimulation was given over the motor hotspot. During real rTMS, the coil was positioned tangential to the scalp with the long axis of the figure-of-eight coil oriented at 45° to the parasagittal plane. The current flow of the initial rising phase of the biphasic pulse in the TMS coil induced a current flowing from posterior to anterior in the brain. During sham rTMS, the coil was tilted at 90° to the scalp, with one wing of the coil in contact with the scalp over the site of stimulation. This coil arrangement reproduces the acoustic sensation of real rTMS, with minimal effects on the cortex (Lisanby et al., 2001). During each session, the active coil was exchanged for the spare coil after exactly 4 and 11 min of rTMS to avoid overheating. All of the subjects were tested on the mirror tracing task (experiment 1) within 3 min after the cessation of the rTMS train and on the finger-to-finger matching task (experiments 2 and 3) within 5 min after the last rTMS pulse.

Data analysis. Motor performance during each trial was quantified by the speed of movement (calculated as the ratio between total distance covered by the cursor and movement time) and by the modulus of the radial trajectory error (Poulton, 1974). Radial trajectory error was calculated as the difference between the distance from the center of the circular path to the cursor and radius of the circular path. For each 10 sec trial, the absolute radial trajectory error was averaged over measurements taken at 20 Hz. For each subject, the measures of performance were averaged over baseline, tracing, and mirror tracing trials, respectively. Post-rTMS performance was expressed as a percentage of the subject's pre-TMS baseline performance. Data were inspected for normality and outliers using box plots. The effect of rTMS on performance was tested across groups, using the Mann–Whitney *U* test as implemented in SPSS version 11.5 (SPSS, Chicago, IL). Furthermore, the effect of rTMS on rate of learning during mirror tracing was investigated by comparing between groups the slope of the regression line through error values over the six mirror tracing trials.

Experiment 2: finger matching

Subjects. Ten subjects (three females, 18–48 years of age, median 29) participated in this experiment.

Study design. Each subject participated in two experimental sessions, real rTMS and sham rTMS, scheduled on 2 separate days, 2 d apart. The order of session presentation was randomized and counterbalanced across subjects. During each session, proprioception was tested twice, before and after rTMS.

Task. Proprioception was tested using a "matching" paradigm (Paillard and Brouchon, 1968; Velay et al., 1989). Without seeing their hands, the subjects matched with their left index finger the position of their right index finger that was passively moved by the examiner.

The apparatus consisted of two LEGO bricks (LEGO Company, Billund, Denmark) (Fig. 2) (length, 125 mm; 16 cylindrical protrusions or "studs"; distance between studs, 8 mm) fixated at 56 mm from each other and placed on the table parallel with and symmetrical about the subjects' midsagittal plane. The subjects sat comfortably in front of the table with the chin on a support that aligned the head to the body midline, the elbows were flexed, and the forearms were placed on the table symmetrically about the midsagittal plane. They were instructed to keep their eyes closed during the test. At the beginning of each trial, the subjects placed their index fingers on the studs located at the proximal end of both bricks. The examiner then lifted the subject's right index finger from this start position and placed it on a target stud located along the right brick, at variable distance from start. Then, the subject lifted their left index finger and put it down on the left brick on a stud that best matched the felt position of the right finger. Subjects were allowed to correct the position of their indicator finger until they were satisfied with the position match. The proprioceptive error was recorded as the number of studs by which the indicator finger missed the position of the target finger. This error was transformed in metric units using the following transformation: one interstud interval = 8 mm. Finally, the examiner moved the subject's index fingers back to the start position to prepare for a new trial. No feedback on performance accuracy was provided. Each test consisted of 18 trials and took <5 min to complete. The target positions were located at 8, 16, 24, 32, 40, and 48 mm from start. Each target position was presented three times in a predetermined random order. The order of

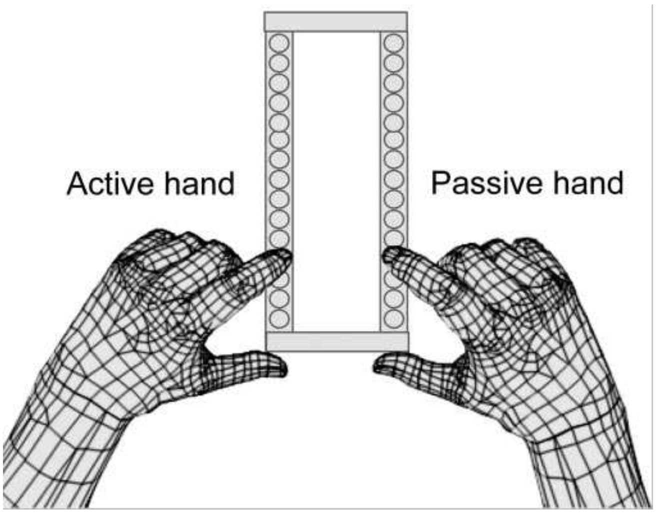

Figure 2. The apparatus used to test proprioceptive accuracy. The apparatus consisted of two LEGO bricks fixated on a horizontal table so as to be parallel with the subject's midsagittal plane. Before each trial, the examiner positioned both fingers on the studs situated at the proximal end of the apparatus. Then, the subject's right index finger was passively moved to one of the studs on the right brick, at variable distance from the start position. Finally, the subject moved the left index finger to place it on a stud of the left brick so as to match the position of the right index finger. The subjects had their eyes closed throughout the experiment and received no feedback on performance.

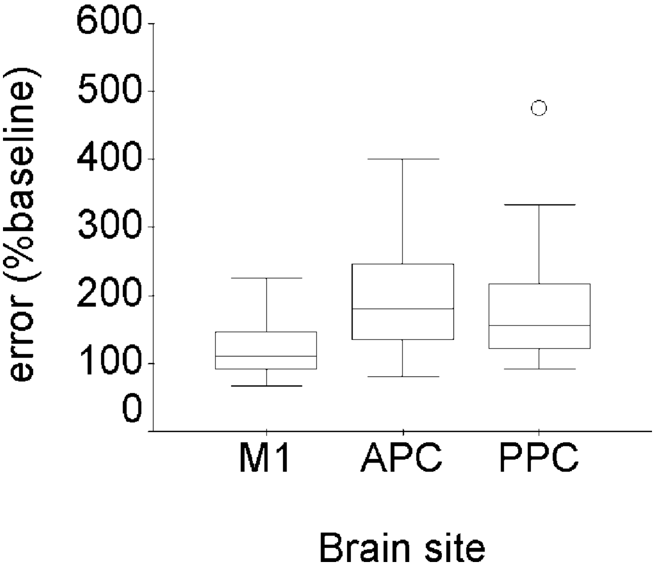

Figure 3. Box plot of proprioceptive error after rTMS applied at various scalp sites. The coil was placed over three different brain sites: M1, at the motor hotspot; APC, at 3 cm posterior to the motor hotspot; and PPC, at 6 cm posterior to the motor hotspot. The effect of rTMS site on proprioceptive error was significant (Kruskal–Wallis test, $p = 0.023$). Post-rTMS error is expressed as percentage of the baseline error, sampled before rTMS. $n = 15$ subjects in each group.

target presentation was constant between subjects but differed within subject between tests.

Before the experiment, the subjects received three practice trials to become familiar with the task. The practice trials followed the same procedure, except that the subjects were allowed to keep their eyes open.

rTMS. rTMS sessions followed the same protocol as for experiment 1.

Data analysis. For each subject, proprioceptive error was averaged across trials and expressed as a percentage from the subject's baseline (pre-TMS) error. Data was inspected for normality and outliers using box plots. The difference in accuracy after rTMS between the two intervention groups was tested using a paired-sample *t* test, implemented in SPSS version 11.5.

Experiment 3: finger matching (variable location of rTMS coil)

Subjects and task. Forty-five healthy, right-handed volunteers participated in the experiment. Each subject was assigned to one of three intervention groups that differed by the scalp location at which rTMS was applied: (1) primary motor cortex (M1) at the motor hotspot, (2) anterior parietal cortex (APC), 3 cm posterior to the motor hotspot, the same site as that used for experiments 1 and 2, and (3) posterior parietal cortex (PPC), 6 cm posterior to the motor hotspot. These distances were measured on a line oriented at 45° from the sagittal plane, perpendicular to the central sulcus. Each group consisted of 15 subjects, aged between 19 and 42 years (median 24; M1 group), 18 and 48 years (median 29; APC group), and 19 and 33 years (median 26; PPC group). The subjects completed the finger-to-finger matching task from experiment 2 before and after rTMS. The rTMS protocol was the same as that used for experiments 1 and 2.

In all of the experiments in this study, the statistical analysis was done on performance data that were normalized to the subject's pre-TMS performance and not on absolute post-rTMS performance measures. The reason for performing the statistical analysis on normalized data was to eliminate sources of nuisance variation between subjects. Subject-specific factors, such as attention or motivation, are likely to influence motor performance and are difficult to control experimentally. Individual differences are especially important when proprioception is assessed using a position-matching test. For instance, the ability of the subject to reproduce the position of a finger that is moved passively to some target position depends on the location of this target within the range of finger motion allowed by the subject's hand anatomy (Janwantanakul et al., 2001) or on the ability of the subject to relax the finger during passive movement (Rymer and D'Almeida, 1980). We reasoned that subject-specific effects were likely to affect both pre-TMS and post-TMS performance, so normalizing post-rTMS error relative to baseline would reduce noise and increase statistical power in this relatively small data sample.

Results

Experiment 1

Trajectory error during mirror tracing trials was significantly higher after sham than after real rTMS (Fig. 1*B*) (Mann–Whitney *U* test, $U = 5$; $p = 0.037$). The absolute mirror tracing error in the real-rTMS group was median 5.69 mm, range 3.86–8.09 mm and in the sham group was median 8.81 mm, range 4.18–22.24 mm.

No difference was found across intervention groups in the speed of mirror tracing ($p = 0.180$), the speed of post-rTMS tracing in the normal task ($p = 0.937$), the error of post-rTMS normal tracing ($p = 0.485$), or learning speed (the slope of the regression of error score against trial number for the six mirror tracing trials; $p = 0.485$). Thus, rTMS over the somatosensory cortex contralateral to the hand improved performance in the mirror tracing task compared with the sham stimulation.

Experiment 2

rTMS over the somatosensory cortex contralateral to the hand reduced proprioception compared with sham stimulation. After real-rTMS, proprioceptive error increased to 192.14 ± 31.67% (mean ± SE) of pre-TMS performance, whereas after sham, proprioceptive error was 95.68 ± 15.37%. The difference among the groups was significant (paired *t* test, $p = 0.043$). The absolute value for proprioceptive error after rTMS was median 4.22 mm, range 1.78–7.56 mm for real-rTMS and median 3.33, range 1.33–6.67 mm for sham.

Experiment 3

There was a significant difference among the three groups in their proprioceptive matching accuracy after rTMS (Fig. 3), with the greatest reduction in proprioception for the group stimulated over the APC. The effect of rTMS site on proprioceptive accuracy was significant (Kruskal–Wallis test, $\chi^2 = 7.51$; $p = 0.023$). In pairwise comparison among the three groups, the difference between APC and M1 (Mann–Whitney *U* test, $U = 52$; $p = 0.012$) and the difference between PPC and M1 (Mann–Whitney *U* test, $U = 61$; $p = 0.033$) were significant, whereas the difference between stimulation over APC and PPC was not significant ($U = 99.5$; $p = 0.58$). The absolute post-rTMS proprioceptive error was as follows: M1 group, median 4.89 mm, range 1.78–12 mm; APC group, median 4.89 mm, range 1.78–9.33 mm; and PPC group, median 5.77 mm, range 3.11–8.44 mm.

Discussion

rTMS applied to the anterior parietal cortex improved trajectory accuracy during the novel task of mirror tracing (experiment 1). A control experiment confirmed that the rTMS intervention reduced hand proprioception (experiment 2). These results support the hypothesis that motor control in situations with a visuoproprioceptive conflict benefits from a reduction in proprioception. We have put forth this hypothesis in the light of previous studies that report advantages in motor performance when the proprioceptive input is low (Jones et al., 2001) or absent (Lajoie et al., 1992; Guedon et al., 1998).

The rTMS protocol used in this experiment is known to produce a decrease in neural activity that lasts several minutes after the cessation of the stimulation pulses. This effect has been demonstrated neurophysiologically in the motor cortex (Chen et al., 1997) and confirmed behaviorally for various cortical areas, including the sensory cortices (Kosslyn et al., 1999; Boroojerdi et al., 2000; Knecht et al., 2003). For instance, 10–20 min of rTMS at 1 Hz and 110% motor threshold applied over the somatosensory cortex increases the threshold for discriminating tactile stimuli for a period of 4–8 min post-rTMS (Knecht et al., 2003). To the best of our knowledge, no study has investigated previously whether low-frequency rTMS decreases proprioceptive ability.

There are at least three possible brain regions involved in proprioceptive processing whose inactivation may have caused the decrease in the sense of finger position that followed rTMS stimulation 3 cm posterior to the motor hotspot. First, the primary somatosensory cortex is the first cortical station for proprioceptive afferents and its lesion impairs all of the somatosensory modalities (Corkin et al., 1970). Second, the motor area has neurons that respond to passive movement (Strick and Preston, 1982), and evidence has been put forth recently for its importance in somatosensation (Nudo et al., 2000; Naito et al., 2002). A third candidate area is the left posterior parietal cortex, whose lesion in neurological patients can cause deficits in locating body parts (Wolpert et al., 1998; Semenza, 2001). To find out which brain region was most likely to be responsible for the decrease in proprioception in this study, we compared position-matching error after rTMS at the motor hotspot and the anterior and posterior parietal cortex (experiment 3). The effect of rTMS on proprioceptive accuracy was maximal 3 cm posterior to the motor cortex. It decreased significantly when the coil was placed directly over the motor cortex at the motor hotspot. The size of the effect also decreased when the coil was moved 3 cm further posterior, although this difference was not statistically significant. Thus, the brain area responsible for the rTMS-induced decrease in proprioception is located anterior in the parietal lobe, probably corresponding to the representation of the hand in the somatosensory cortex. Additional experiments combining rTMS and neuroimaging techniques may identify more directly the brain area that is responsible for this effect.

Patients with a decrease in proprioception have great difficulties with controlling their hand (Rothwell et al., 1982; Jeannerod et al., 1984; Sanes et al., 1985; Pause et al., 1989). Visual feedback, however, improves the accuracy of their movements (Ghez et al., 1995), reducing (Sanes et al., 1984) or even eliminating (Bard et al., 1995) the difference in performance between patients and healthy controls. Furthermore, in novel situations with optical displacement, proprioceptively deafferented patients are less impaired compared with healthy controls (Lajoie et al., 1992; Guedon et al., 1998). These observations in patients demonstrate that, when visual feedback is available, proprioception is less important and may even be an obstacle for adapting to visual perturbations. Because patients who have lost proprioception are usually included in experiments many years after the onset of deafferentation, it is difficult to tell whether their improved performance follows directly from the lack of proprioception or is merely a side effect reflecting, for instance, their familiarity with motor learning situations or their use of compensatory strategies. The present study demonstrates a performance benefit in healthy persons after proprioceptive deafferentation by rTMS over the anterior parietal cortex. This finding confirms that the cortical processing of proprioceptive inflow has a limited contribution to trajectory control during adaptation to visual perturbations. It also suggests that it is possible to improve trajectory accuracy in healthy persons in conditions with a visuoproprioceptive conflict by reducing the activity of the somatosensory areas. This finding may be applied in the future to improving trajectory control when movements are monitored from an unfamiliar angle in a mirror or a video camera.

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Right Temporoparietal Cortex Activation during Visuo-proprioceptive Conflict

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The conflict between vision and proprioception has been proposed to explain why healthy subjects perform worse than proprioceptively deafferented patients in conditions with optical displacement, e.g. novel mirror drawing. It is not known which brain processes depend upon the successful integration of visual and proprioceptive information and are therefore impaired when these modalities disagree. With fMRI in healthy subjects we compared brain activity across two conditions with similar visual and proprioceptive stimulation and similar task demands that differed by the congruence of movement showed by the two modalities. Subjects felt the passive movement of the right index finger on a rectangular field and watched a cursor moving on a computer screen. Cursor and finger locations either mapped onto each other (congruent condition) or did not (incongruent condition). Monitoring incongruent compared with congruent movement activated the premotor area bilaterally and the right temporoparietal junction. These brain areas have previously been associated with shifts in the attended location in the visual space. These findings suggest an interaction between vision and proprioception in orienting to spatial locations.

Keywords: fMRI, multisensory, proprioception, spatial attention, vision

Introduction

When movements are monitored in a mirror or a video display, the usual congruence between the visual and the proprioceptive hand spaces is disrupted. In such situations movement accuracy initially decreases, improving as a result of practice. It has been repeatedly observed that patients who lack proprioception outperform healthy controls when performance is tested during early stages of adaptation to a new visuomotor transformation (Lajoie *et al.*, 1992; Vercher *et al.*, 1996; Guedon *et al.*, 1998; Fourneret *et al.*, 2002). This intriguing finding has been explained by assuming that the visuo-proprioceptive conflict experienced by healthy people impairs performance and delays adaptation (Lajoie *et al.*, 1992).

Although there are many studies that have investigated the brain's response during exposure to visual and proprioceptive stimulation separately, little is known about the brain areas that integrate spatial information across modalities. Knowing which brain areas react to the spatial disagreement between visual and proprioceptive feedback may shed light on the brain processes that are affected by the visuo-proprioceptive conflict. The aim of this fMRI study was to identify brain areas that respond to conflicting as opposed to coordinated visual and proprioceptive movement. To this end we compared brain activity across two conditions that differed by the congruence of movement trajectory conveyed by the visual and proprioceptive sensory channels. To dissociate hand movement and its visual image we used a computer with a finger-operated mouse and a visual display. Proprioceptive stimuli were delivered by passive movement. Passive movement stimulates receptors in the muscle, skin and joints and provides directional cues in the absence of a motor command (Jones *et al.*, 2001).

Materials and Methods

Subjects

Eleven right-handed healthy volunteers (eight female, median age 27 years, range 22–31 years) gave written consent to participate in this study. The study was performed according to the Helsinki II Declaration and was approved by the local Ethics Committee (KF01-028/02).

Task

Throughout the experiment, the subjects watched the movement of a white square (visual angle = 3.5°) on a black LCD display (visual angle = 32 × 23°) and felt the passive movement of their right index finger on the rectangular field (size 30 × 24 mm) of a mouse-like device (Felix, Altra). The mouse was fixated in the horizontal plane on a support which rested on the subject's thigh. The subject's wrist and the other fingers were immobilized with velcro straps on the mouse support, and the index finger was fixated with tape onto the mobile piece of the mouse. An experimenter (DB) stood beside the scanner and moved the mobile piece of the mouse, and hence also the subject's finger (Fig. 1*A*). The trajectory of finger movement was arbitrarily chosen and covered the entire rectangular field. In the congruent condition, the screen cursor displayed the actual movement of the finger. In the incongruent condition, the subjects saw a playback of cursor movement recorded during the congruent condition, so that finger and cursor locations were randomly associated. The playback solution was preferred to computer generated motion in order to fully match motion speed and trajectory across conditions. In order to reduce the possibility that the subjects remembered the patterns of cursor movement across conditions, this playback was constructed for each presentation of the incongruent condition by choosing a cursor movement sequence at random from previous same-session congruent condition recordings and playing this recording in reverse (Fig. 1*B*). For instance, if the presentations of the congruent condition within one session are numbered from 1 to 8, then an example of the order of presentation in the incongruent condition could be 1r 2r 1r 3r 3r 5r 4r ('r' meaning 'reversed'). The recorded sequence was padded with up to 1 s of computer generated cursor movement that brought the cursor from the actual mouse position to the first cursor position in the playback, and from the last cursor position in the playback to the actual mouse position. This was done in order to avoid a sudden cursor movement at the transition between conditions. The computer recorded finger and cursor location every 0.05 s.

To ensure that the subjects attended to both sensory modalities, they were instructed to press a key with the left thumb whenever they detected a transition between conditions.

Before the scanning session, the subjects were familiarized with both experimental conditions and practiced the detection task.

Data Acquisition

Gradient echo echoplanar images at a resolution of 3.75 × 3.75 × 3.75 mm were acquired with T_R = 4.1 s, T_E = 66 ms, flip angle = 90° with a 1.5 T Siemens, Vision scanner. A total of 24 slices, covering a field of view = 89 mm, were positioned obliquely, between the coronal and axial plane, so as to cover optimally the parietal lobe, leaving out the anterior temporal and anteroinferior frontal lobes. High-resolution T_1-weighted anatomical scans covering the entire brain were acquired at 1 × 1 × 1 mm resolution. Each subject completed two sessions of functional data acquisition giving a total of 2 × 73 volumes. The first three images in each session were discarded to allow for equilibrium in the magnetization. The two conditions were presented alternately, in blocks of 20 s. Each session consisted of 15 blocks, starting with the congruent condition. Because the sequences of cursor movement in the incongruent condition were constructed using recorded sequences from the congruent condition, it was not possible to randomize the order of condition presentation.

Data Analysis

Using SPM99 (http://www.fil.ion.ucl.ac.uk/spm/spm99.html), data were realigned, co-registered to the subject's structural image, normalized to the space of the Montreal Neurological Institute (MNI) brain template and smoothed with a Gaussian filter of 8 mm FWHM (full-width, half maximum). The difference between conditions was estimated on group data using the general linear model as implemented in SPM99 (random-effects model). The design matrix for each individual subject included one covariate of interest for the difference between conditions, modelled with a boxcar convolved with a standard haemodynamic response function, six nuisance covariates containing realignment parameters and one nuisance covariate containing the left-hand key press events modelled with the standard haemodynamic response function. Additionally, a high-pass filter with a cut-off period of 80 s, implemented in SPM99, was applied to the BOLD signal in order to remove low-frequency noise. To better estimate the temporal autocorrelation in the fMRI data the signal was smoothed with a Gaussian filter of 4 s FWHM. The difference between conditions was estimated voxelwise for each individual subject, and then tested across subjects using a one-sample *t*-test. Clusters of contiguous voxels (extent threshold = 0 voxels, height-threshold $P < 0.001$ uncorrected) are reported at a significance threshold of $P < 0.001$ at the cluster-level, corrected for multiple comparisons (Friston *et al.*, 1996).

Results

Behavioral Data

The average finger velocity calculated *post hoc* was 29.33 ± 3.57 mm/s (mean ± standard deviation) for the congruent condition and 28.51 ± 2.59 mm/s for the incongruent condition. There was no statistical difference between conditions in the average finger- (paired *t*-test, $P = 0.242$) or cursor-speed ($P = 0.395$). This confirms that finger and cursor movement were well-matched across conditions.

In the incongruent condition, the subjects were able to detect correctly 79.31 ± 9.16% of the transitions with a reaction time in milliseconds of 2749.73 ± 1214.38. In the congruent condition, the transition to the incongruent condition was detected correctly in 81.16 ± 9.72% cases with a reaction time of 2250.36 ± 957.73 ms. The difference in reaction times between conditions was not significant (paired *t*-test, $P = 0.123$). The long reaction times and the high number of errors support previous results showing limited awareness of the correspondence between visual and motor spaces (Fourneret and Jeannerod, 1998).

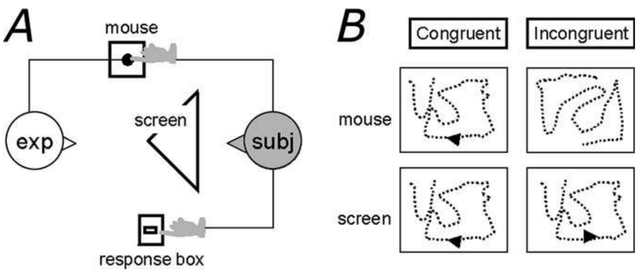

Figure 1. Diagram of the experimental set-up and behavioral conditions. (*A*) The experimenter (Exp) stood beside the scanner moving the subject's right index finger on a mouse field. The subject (Subj) lay in the scanner facing an LCD screen and responded with the left hand by pressing the response box key. (*B*) In the congruent condition finger and cursor movement followed the same trajectory. In the incongruent condition, the movement of the cursor was played from a memory buffer recorded during a previous trial of the congruent condition. The arrowhead indicates the direction of movement.

fMRI Data

Compared with the congruent condition, the incongruent condition was associated with higher neural activity bilaterally in the premotor cortices/supplementary motor area and in the right temporoparietal junction (Fig. 2 and Table 1).

Discussion

This experiment identified brain areas that responded to the spatial disagreement between visual and proprioceptive

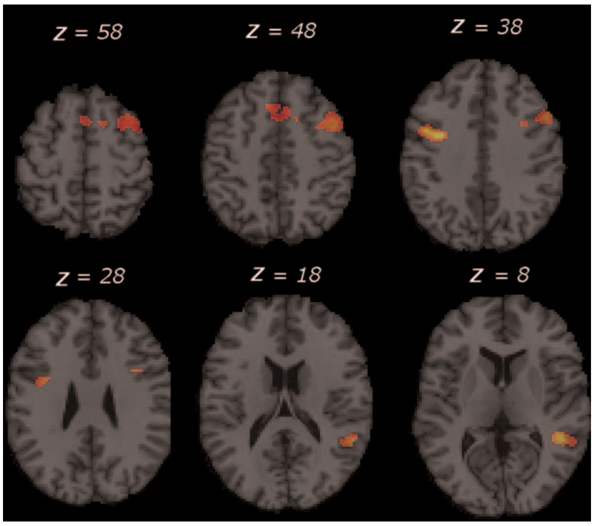

Figure 2. Brain areas with higher activity in the incongruent compared with the congruent condition. The congruent condition was subtracted from the incongruent condition and the result is showed as a parametric map of the *t*-statistic. The map is thresholded at a corrected *P*-value < 0.001 at the cluster level (random-effects analysis). For the purpose of anatomical localization, the map is superposed on a single-subject T_1-weighted image in corregistration with the stereotactic space of the MNI template. The *z*-value for each transversal slice is the stereotactic coordinate in vertical direction in the MNI space. The left side of the brain is shown to the left.

Table 1

Clusters of voxels showing significant activity increase in the incongruent compared with the congruent condition

Anatomical location of the cluster	No. of voxels	Coordinates at peak activation (*x y z*)	*z*-Value at peak activation	Cluster-level *P*-value (corrected)
L precentral gyrus/frontal lobe	304	−38 0 40	4.91	<0.001
R temporoparietal junction	369	48 −42 8	4.66	<0.001
R precentral gyrus/frontal lobe + SMA	1170	52 14 38	4.07	<0.001

L, left; R, right; SMA, supplementary motor area; (*x*, *y*, *z*), lateral, sagittal and vertical coordinates in the stereotactic space of the MNI brain template.

feedback by comparing the brain's haemodynamic response across two conditions. These conditions differed by the congruence of the movement trajectory conveyed by the visual and proprioceptive sensory channels. The subjects were exposed to similar sensory stimuli and performed the same task across conditions. The main finding of this experiment was the higher level of activity in the right temporoparietal junction and the premotor cortices in the incongruent condition compared with the congruent condition. Previous studies have demonstrated increases in brain activity in these areas when subjects covertly shift their attention or overtly move their eyes from one location to another (Corbetta *et al.*, 1998). Right temporoparietal and sometimes premotor lesions are associated with visuospatial neglect (Vallar, 2001), a disorder in which deficits in orienting attention in space are common (Bartolomeo and Chokron, 2002). The right temporoparietal junction is also active when subjects detect visual targets at unexpected locations (Corbetta *et al.*, 2000). The increased activity in the right temporoparietal junction in the incongruent condition in the present study may thus reflect spatial disorientation when the visual and proprioceptive feedback point towards incompatible locations.

Besides responding during shifts in spatial attention, the right temporoparietal junction also reacts to stimulus novelty, regardless of location (Downar *et al.*, 2000; Corbetta and Shulman, 2002). It is, however, unlikely that the differential activation in the right temporoparietal junction found in the present study is related to the novelty of the incongruent condition. First, the subjects were exposed to both conditions during the practice trials and were thus familiar with the incongruent visuo-proprioceptive stimulation at the beginning of the scanning session. Secondly, if this were the case, then the difference between conditions would have been expected to decrease over time as the subjects became accustomed to the incongruent condition. To identify brain areas where the difference between the incongruent and the congruent condition decreased over time, we repeated the statistical analysis after inserting a covariate that modeled a linear time-by-condition interaction. This comparison did not yield any statistically significant voxels, even when the threshold was decreased to $P = 0.01$, uncorrected and the search volume was limited to the right temporoparietal cluster.

No temporoparietal junction activation was identified in a previous PET experiment where a condition with visuo-proprioceptive mismatch induced by wearing prism goggles was compared with a control condition with no sensory-sensory conflict (Clower *et al.*, 1996). The disagreement between the results of these apparently very similar studies could be explained by a putative activation of the right temporoparietal junction during the control condition of the previous experiment. In this control condition a visual target jumped to an unexpected spatial location while the subjects were performing target directed movements. Because the right temporoparietal junction is activated when subjects detect stimuli at unpredictable locations in the visual field (Corbetta *et al.*, 2000), the control condition may have recruited this brain area.

In the present study, we used passive rather than active movement in order to separate peripheral proprioceptive inflow from central signals related to action planning and initiation (Sperry, 1950; Von Holst and Mittelstaedt, 1950). Thus, the difference in brain activity between the incongruent and the congruent condition reflects specifically the sensory–sensory mismatch. During active movements performed with incongruent visual feedback the inferior parietal lobe of the right hemisphere and the left premotor area are activated (Farrer and Frith, 2002). Our findings suggest that the presence of a visuo-proprioceptive conflict is sufficient for activating these brain regions.

In this study a qualitative paradigm was used in order to optimize the sensitivity for detecting a change in the fMRI signal across conditions. A further experiment with a parametric paradigm that systematically varies the angle between the direction of finger movements and the direction of cursor movements can be used to test whether the activity of the right temporoparietal lobe correlates with the degree of spatial incongruence between the visual and proprioceptive input.

The limited size of the visual field and the limited neural capacity for information processing restricts the number of spatial locations from where sensory stimuli can be sampled and analyzed. There is now a large body of evidence for perceptual connections between the visual space and other unimodal sensory spaces such as the auditory (Spence and Driver, 1997; McDonald *et al.*, 2000) or the tactile (di Pellegrino *et al.*, 1997; Mattingley *et al.*, 1997; Spence *et al.*, 2000) space. This interplay between modalities is believed to facilitate an orienting response that increases the efficiency with which incoming sensory stimuli are processed (Driver and Spence, 1998a,b). The question whether a similar attentional link exist between the proprioceptive hand space and the visual space where hand movements are monitored has, to our knowledge, not being addressed yet. The present results suggests that such a connection may exist.

Notes

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Proprioceptive modulation of visuo-spatial orienting

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Abstract

Vision and proprioception are the main modalities that convey location and movement direction for the hand. Whereas the fusion of visual and proprioceptive information into a single, more robust percept is now well documented, it is still unclear whether these modalities also interact in the spatial allocation of stimulus processing resources, which has been demonstrated for other modality pairings. The aim of this study was to test whether spatially congruent as opposed to spatially incompatible proprioception speeds up visual processing. Healthy subjects discriminated the vertical component (upwards or downwards) of the visual movement of a cursor in the presence of an uninformative and orthogonal proprioceptive distractor. Proprioceptive stimuli were given by moving the subject's right index finger passively along a horizontal line in the left or right direction. Synchronous cursor movement was produced on a computer screen using the input from a mouse onto which the subject's right index finger was fixated. The horizontal component of the cursor movement was either in the same direction (compatible) or in the opposite direction (incompatible) to that of the proprioceptive distractor. The reaction time for upwards/downwards discrimination was increased when the horizontal component of the cursor movement was incompatible with the direction of proprioceptive stimulus compared to when it was compatible. This suggests that proprioception influences the allocation of processing resources in the visual space.

Introduction

Feedback information about the direction of hand movement comes to the brain via two sensory modalities: vision and proprioception. In general, the mechanisms by which the brain combines multimodal spatial information fall into two categories: multisensory integration and crossmodal spatial attention.

Multisensory integration is the fusion of the multimodal information into a single, more robust, percept (Ernst and Bulthoff, 2004;van Beers et al., 2002). Visuoproprioceptive integration has been clearly demonstrated by experiments in which a discrepancy between visual and proprioceptive spaces led the subjects to perceive their hand in-between the visually- and proprioceptively-cued locations (Welch and Warren, 1986;Rossetti et al., 1995).

The interaction between modalities in spatial attention is the facilitation of stimulus processing when the stimulus is sampled from a location highlighted by a stimulus in a different modality (Spence and Driver, 1994). For instance, a visual stimulus is perceived faster and more accurately when presented in spatial proximity as opposed to further away from a sound (Spence and Driver, 1997) or a touch on the skin (Spence et al., 1998). Crossmodal interactions between sensory modalities in which a salient, non-predictive cue in one modality facilitates or inhibits the processing of a target in another modality have been found for all modality pairings that have been tested within vision, touch and audition (Spence et al., 2004). It is unclear whether vision and proprioception also interact in this way. Previous studies suggest that this may be the case. First, exposure to spatially conflicting visual and proprioceptive information activates the temporoparietal cortex (Balslev et al., 2005), a brain area involved in stimulus-driven spatial attention (Corbetta and Shulman, 2002). However, because this area has also been activated by tasks with no spatial component, such as for instance during perception of oddball sensory stimuli (Downar et al., 2000), its activation suggests, but does not prove this interaction. Second, a previous study found that visual movement discrimination is slower and less accurate in the presence of passive finger movement going in opposite rather than similar directions (Klein, 1977). In this study however, the decrease in the efficiency of visual discrimination may have been the result of the incompatibility relationship between the direction of movement of the proprioceptive distractor (passive finger movement oriented to the left or to the right) and the required response (left or right).

The aim of the present study was to test whether proprioception influences the allocation of processing resources in visual space. To this end we used a variation of the “orthogonal” paradigm invented by Spence and Driver (Spence and Driver, 1997). The advantage of this paradigm is the independence, or “orthogonality”, of the proprioceptive distractor and the required response. We presented visual movement going in four possible directions (up-left, down-left, up-right and down-right) in the presence of passive finger movements in the left or right direction on a horizontal line. The visual cursor always moved on a trajectory that made an angle of 30 degrees with the horizontal. The subjects were asked to discriminate the vertical direction of cursor movement, “up” or “down”, which was independent on the direction of finger movement. Reaction times were compared across two conditions that differed by the compatibility between the visual and the proprioceptive direction of movement. In the compatible condition, the horizontal component of the cursor movement was in the same direction as the proprioceptive stimulus and in the incompatible condition the horizontal component of the visual movement was in the opposite direction of the proprioceptive stimulus. We hypothesized that visual discrimination would be slower in the incompatible as compared with the compatible condition.

Proprioceptive stimuli were given by passive finger movement performed by an examiner (see Figure 1). While watching cursor movement, the subjects were allowed to move their eyes freely, engaging both overt and covert components of visual attention.

To dissociate visual and proprioceptive stimuli in space we used a computer set-up with a screen and a finger-operated mouse. All subjects included in the study were familiar with the directional correspondence between hand and cursor movement from their daily use of a computer mouse. Experience-induced mapping between the somatosensory hand space and the visual space in which a tool operates has previously been documented at a behavioural (Maravita et al., 2002; Maravita et al., 2001; Farne and Ladavas, 2000; Berti and Frassinetti, 2000) and neurophysiological (Iriki et al., 1996; Iriki et al., 2001) level. These links appear to be short-lived, persisting only a few minutes after the active tool use has been discontinued (Iriki et al., 1996;Farne and Ladavas, 2000). In the light of these observations the duration of a test block in the present experiment was limited to 72 seconds and each test block followed immediately after a training block in which subjects traced a screen target using the computer mouse actively.

Methods

Subjects

9 subjects (5 female, aged between 20 and 44 years, median age 32.5), right-handed by self-report, gave their informed consent and participated in the study. All subjects used a computer mouse daily. The study was conducted according to Helsinki II declaration and approved by the Ethical Committee of Copenhagen (KF01-028/02).

Study design

There were two conditions that differed by the compatibility between the direction of finger movement and the horizontal component of cursor movement. The horizontal component of cursor movement was compatible with the proprioceptive stimulus in half of the trials and incompatible in the other half (see Figure 1). The vertical component of the cursor movement and the direction of finger movement (left or right) were varied randomly, independent of the two experimental conditions and with equal probability. Each condition was repeated 6 times within a block of 12 trials. The order of condition presentation was randomized within and between subjects. Each subject completed 4 blocks of trials. The first block was considered practice and was not analysed further.

Apparatus and procedure

Subjects were seated at a table, facing a computer display (size 330 x 240 mm, visual angle 36.5 x 27 degrees, refresh rate 60 Hz) at a viewing distance of 50 cm. The right forearm rested on the table, in a comfortable position at the right side of the screen. The index finger of the right hand was fixated with tape on the mobile piece of a sliding ”mouse” (FELIX Pointing Device, Altra, Rawlins, WY) which moved in an active area of the size 30 x 24 mm. The mouse was placed horizontally on the table behind a screen that prevented the subject to see the movements of the right finger directly (see Figure 1).

Insert Figure 1

Proprioceptive stimuli in the form of passive finger movement were given by an examiner seated at the opposite side of the table. The examiner was unaware of whether the trajectory of the cursor was compatible or not with the trajectory of the finger. For each trial, the subject’s finger was moved 15 mm along a horizontal line from an initial position located at the middle to a final position, located at the left or right corner of the active mouse area. The total duration of a trial was 6 seconds. The trial was started by an auditory signal given to the examiner in the headphones. The pitch of this signal indicated the direction – left or right – for finger movement. The examiner moved the subject’s index finger to the final lateral position and stopped. There was a short rest period at this lateral position. Three seconds after the first signal, a second auditory signal instructed the experimenter to return the finger to the initial position and prepare for a new trial. The position of the mouse was recorded every 20 milliseconds. Post-hoc calculations showed that the finger was moved with an average velocity of 16.1± 0.86 mm/second (mean ± standard error).

Visual cursor movement was produced on the screen using the mouse input, so the velocity of the cursor was proportional to the velocity of the finger. For each trial, the cursor (a white square, 3.9 degrees visual angle) moved from the centre of the screen along an oblique line, rotated 30 degrees from horizontal in the same (compatible) or the opposite (incompatible) direction to that of the finger. The visual cursor was presented only during the first 4.7 mm of the 15 mm finger deflection. After that, the cursor was hidden until the beginning of the next trial. The motivation for showing a visual trajectory of predefined length corresponding to the initial part of mouse movement was to equal the length of visual cursor trajectory across trials regardless of the length of mouse trajectory. Cursor position was recorded every 20 milliseconds. The parameters of cursor movement calculated post-hoc (mean and standard error) were: distance = 46.5 ± 0.3 mm (5.3±0.02 degrees visual angle), velocity = 159.3±8.09 mm/second and duration of presentation = 0.33±0.02 seconds.

The task was to discriminate the up-down direction of cursor movement. Subjects responded with their left hand by pressing key 1 for up and key 2 for down. The response was collected using a computer keyboard placed at the left side of the computer screen. The keyboard was turned at 90 degrees (key 1 front, key 2 back) as shown in Figure 1. The subjects used the index (down) and middle (up) fingers to respond. The reaction time was defined as the time elapsed between the start of cursor movement and the subject's key press. In order to avoid spurious cursor movements due to small oscillations of the finger around the initial position, the screen cursor started to move only after a mouse deflection of at least 0.5 mm from its initial position. Using the average finger speed and the refresh rate of the display, we calculated that the stimulus onset asynchrony between proprioceptive and visual motion to be between 30 - 46.6 milliseconds. There was no perceptible delay between the start of visual and proprioceptive movement.

Subjects were told that the cursor was equally likely to move in the same or in the opposite direction to that of the finger. They were instructed to ignore the movements of their finger and to perform the visual task as fast as possible.

Stimulus presentation and data collection was performed using a laptop computer running E-prime (Psychology Software Tools, Inc., Pittsburgh, PA, 2002) in MS Windows 2000.

Before each test block, the subjects completed a 60 seconds-training session. During this session the subjects used the mouse actively to move a screen cursor to targets that appeared every 750 milliseconds at random locations on the screen. The purpose of the training blocks was to re-enforce the correspondence between visual space of the computer screen and the proprioceptive space of the hand.

Results

Reaction time and error data for the compatible and incompatible conditions are presented in Table 1.

Insert Table 1

The difference in reaction time and response accuracy between conditions was assessed using a one-tailed paired-samples *t*-test and a Wilcoxon signed-rank test, respectively. Two-tailed paired-samples *t*-tests were also run in order to check whether stimulus presentation variables such as the velocity of finger movement or the amplitude, velocity and duration of cursor movement were well matched between conditions.

The subjects performed the discrimination task correctly in 98% of the trials in the compatible condition and 97% of the trials in the incompatible condition. No significant difference in discrimination accuracy was found between the two conditions ($p = 0.375$).

The analysis of reaction time data was based on the mean reaction time for each subject and condition. The reaction time for discriminating the direction of visual motion was 440 ± 66 milliseconds (mean ± standard deviation) in the compatible condition and 481 ± 90 milliseconds in the incompatible condition. The difference between conditions was significant ($t(8) = 2.65$, $p < 0.05$). Only reaction times for correct responses were included in this analysis.

None of the stimulus presentation variables differed significantly between conditions (finger movement velocity, $t(8) =- 0.915$, $p = 0.387$; cursor movement amplitude, $t(8) = 0.424$, $p = 0.684$; cursor movement velocity, $t(8) = -1.04$, $p = 0.328$ and cursor presentation time, $t(8) = 0 .465$, $p = 0.654$).

Discussion

This study showed that the reaction time of visual discrimination depends upon the spatial compatibility between the direction of movement of the visual stimulus and the direction of movement of a task-irrelevant proprioceptive stimulus. Visual discrimination was faster in the compatible as compared with the incompatible condition. Previous studies have demonstrated faster reaction times for visual discrimination when a sound or a touch on the skin were presented in proximity of, as opposed to further away from, the visual stimulus (Spence et al., 1998; Spence and Driver, 1997). The present result extends these findings by observing a similar effect for visual trajectory discrimination in the presence of proprioceptive movement.

We measured the effect of visuo-proprioceptive compatibility on visual discrimination indirectly using the reaction time of a motor response. This opens the possibility that the increase in reaction time in the incompatible condition reflects a disruption of the response rather than of visual perception. This could arise if, for instance, the proprioceptive stimulus preactivates a response or if the subject's surprise at the visuo-proprioceptive incompatibility delays their response. None of these confounds are likely to be responsible for the difference in reaction times observed in the present experiment. First, the orthogonal paradigm (Spence and Driver, 1994;Spence and Driver, 1997) ensured that the required response (upwards/downwards discrimination) was completely independent from the direction of finger movement (to the right or to the left, on a horizontal line). This manipulation rules out the confounding effect of the proprioceptive distractor on the motor response, independent of the visual stimulus. Second, if the increase in reaction times in the incompatible condition reflected a response disruption caused by the subjects' surprise, then one would have expected a decay over time in this difference in reaction time between conditions, as the subjects were becoming accustomed with the large incompatibility angle. To test for a time-by-condition interaction, reaction time data were re-analysed by a within-subjects repeated-measures two-way ANOVA with factor 1 - condition and factor 2 - block number. Neither this interaction ($F(2,16) < 1$) nor the main effect of time/block number ($F(2,16) = 1.041$, $p = 0.376$) were statistically significant. The main effect of condition was again found to be statistically significant ($F(1,8) = 8.069$, $p < 0.05$, Figure 2.).

Insert Figure 2

This difference in reaction time between conditions cannot be explained by the fusion of visual and proprioceptive information into a single percept. If this were the case, then the subjects would perceive cursor trajectory as being deviated towards the proprioceptively cued direction. The weight of proprioception in the visual estimate of hand position has been calculated to be between 3% and 69% (Welch and Warren, 1986; Rossetti et al., 1995; Sober and Sabes, 2003). In the compatible condition (vision at 30 degrees, proprioception at 0 degrees) the cursor would thus be perceived to move on a trajectory between 29.10 and 9.3 degrees from horizontal, whereas in the incompatible condition (vision at 30 degrees, proprioception at 180 degrees) - between 34.5 and 133.5 degrees from horizontal. The larger angle in the incompatible condition would make the vertical direction of movement easier to spot, so the reaction time for up/down discrimination in the compatible condition would be expected to increase relative to the incompatible condition. This is the opposite of our finding, ruling out visuoproprioceptive integration as the explanation of the present result.

This study demonstrates that proprioception influences the processing of visual stimuli. Further studies can investigate this interaction in more detail by looking for instance at i) how the magnitude of the spatial discrepancy (angle) between the visual and proprioceptive trajectories influences the difference in reaction times, ii) whether the subject's experience with active mouse use has an effect on the interaction between finger proprioception and cursor movement, iii) whether this interaction is symmetrical, i.e. whether vision influences the processing of proprioceptive stimuli as well, or iv) whether the difference in reaction time reflects a facilitation in the compatible condition or an inhibition in the incompatible conditions.

It is general consensus within the literature on visual attention that visual processing is capacity limited (e.g. Bundesen, 1987; Shibuya and Bundesen, 1988; Sperling, 1963; Townsend, 1983). To effectively deal with the incoming visual stimuli, visual attention enables us to prioritise objects or locations in the visual field. Thus, when a visual stimulus is presented at an attended location, it is processed more efficiently than stimuli presented elsewhere. Salient sensory stimuli can attract attention in their direction improving the perceptual quality or facilitating the decision processes for sensory data sampled from that location (Luck and Thomas, 1999) at the expense of a reduced efficiency of processing for sensory stimuli presented further away (Chun and Marois, 2002). It is tempting to extrapolate from this effect of visuo-proprioceptive incompatibility on visual perception to its effect on motor control during visually guided movement. During visually guided movements visual feedback is essential for trajectory control (Miall et al., 1995; Sheth and Shimojo, 2002; Brown et al., 2003). The visual scene is usually complex, so mechanisms that allow the brain to favour the processing of visual feedback over other visual objects may be called upon.

The facilitation of visual processing for stimuli sampled from a proprioceptively congruent location may serve this purpose.

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Table 1. Reaction time (mean and standard deviation) and response accuracy (percentage) as a function of visuoproprioceptive compatibility, direction of finger movement and correct response.

	Finger direction – Left		**Finger direction – Right**	
	Response - Up	**Response-Down**	**Response- Up**	**Response- Down**
Compatible	430 (69)	467 (75)	439 (96)	439 (81)
	100%	100%	92.59%	97.77%
Incompatible	483(108)	474 (100)	446 (83)	515 (140)
	94.60%	95.55%	97.22%	97.77%

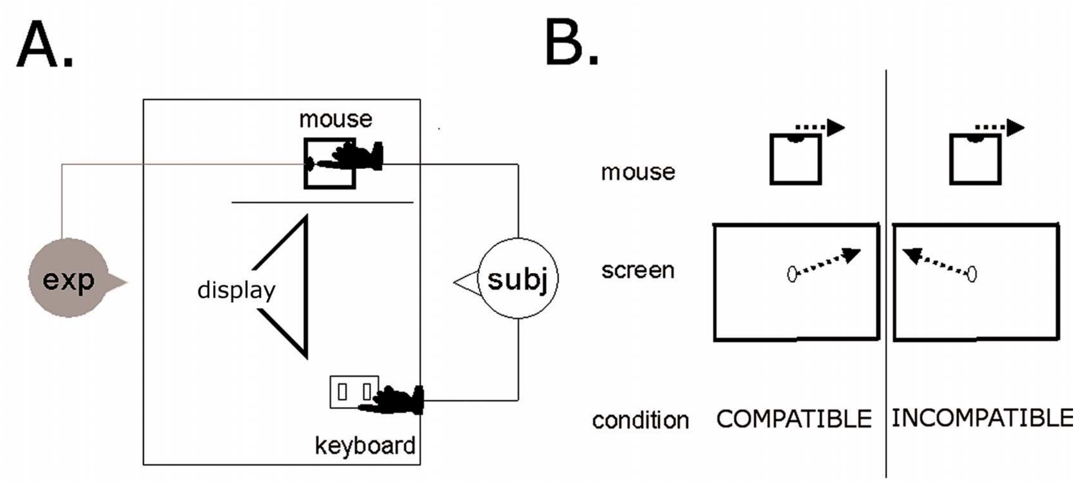

Figure 1. Diagram of the experimental set-up and behavioural conditions. A. The experimenter (Exp) moved the subject's right index finger on the mouse field. The subject (Subj) watched visual cursor movement presented on a computer display and responded with the left hand by pressing a key on a keyboard. **B.** For each trial, the finger was moved on a horizontal line, to the left or to the right. The horizontal component of the movement of the cursor was either in the same direction (compatible) or in the opposite direction (incompatible) relative to the trajectory of the mouse.

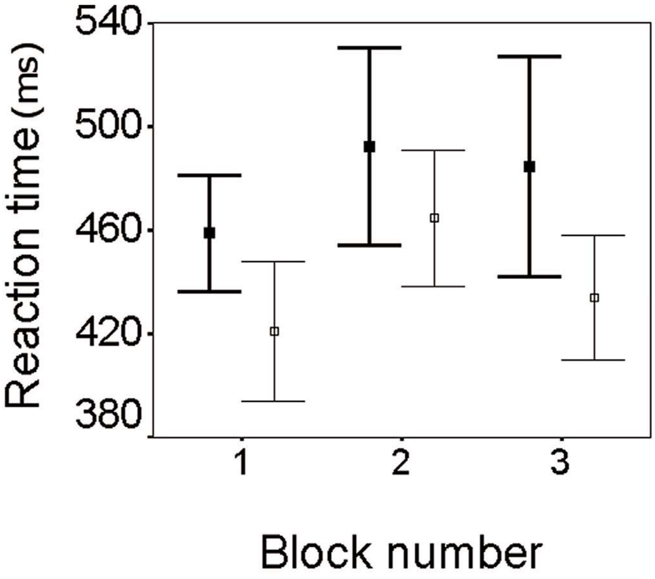

Figure 2. Time-course of the reaction time (mean ± SE) for visual discrimination. Filled squares - incompatible condition, empty squares - compatible condition. There was no significant time x condition interaction (within-subjects repeated-measures ANOVA, *F* < 1, N = 9 subjects)

Subject:
Daniela Balslev: Statement from coauthors about the PhD- student's contribution to the papers included in the PhD disertation.

Paper 1:
Daniela Balslev, Lars O.D. Christensen, Ji-Hang Lee, Ian Law, Olaf B. Paulson, R. Christopher Miall. (2004). Enhanced accuracy of mirror-drawing after rTMS induced proprioceptive deafferentation. J Neurosci 24:9698-702.

Daniela Balslev suggested the idea for this study, contributed to the design of the experiment, collected and analyzed the data and was the main author involved in writing the manuscript.

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Paper 2:
Daniela Balslev, Finn Årup Nielsen, Olaf B. Paulson, Ian Law (2005) Right Temporoparietal Cortex Activation during Visuo-proprioceptive Conflict. Cereb Cortex 15: 166-9

Daniela Balslev suggested the idea for this study, contributed to the design of the experiment, collected and analyzed the data and was the main author involved in writing the manuscript.

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Paper 3:
Daniela Balslev, Søren Kyllingsbæk, Olaf B. Paulson, Ian Law. Proprioceptive modulation of visuospatial orienting. Experimental Brain Research (submitted aug. 2004, revisions submitted jan. 2005)

Daniela Balslev suggested the idea for this study, contributed to the design of the experiment, collected and analyzed the data and was the main author involved in writing the manuscript.

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