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## Research Report

# The role of the anterior intraparietal sulcus in crossmodal processing of object features in humans: An rTMS study

Dorothee Buelte<sup>a,b,\*</sup>, Ingo G. Meister<sup>c</sup>, Mario Staedtgen<sup>a,b</sup>, Nina Dambeck<sup>a,b</sup>, Roland Sparing<sup>c,d</sup>, Christian Grefkes<sup>c,d,e</sup>, Babak Boroojerdi<sup>a</sup>

<sup>a</sup>Department of Neurology, RWTH Aachen University, Germany

<sup>b</sup>Interdisciplinary Centre for Clinical Research BIOMAT, RWTH Aachen University, Germany

<sup>c</sup>Department of Neurology, University Hospital Cologne, Cologne, Germany

<sup>d</sup>Institute of Neuroscience and Biophysics, Department of Medicine, Research Centre Juelich, Germany

<sup>e</sup>Neuromodulation and Neurorehabilitation Group, Max Planck Institute for Neurological Research, Cologne, Germany

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### ABSTRACT

Investigations in macaques and humans have shown that the anterior intraparietal sulcus (IPS) has an important function in the integration of information from tactile and visual object manipulation. The goal of this study was to investigate the special functional role of the anterior IPS in visuo-tactile matching in humans. We used the “virtual-lesion” technique of repetitive transcranial magnetic stimulation (rTMS) to test the functional relevance of anterior IPS for visuo-tactile crossmodal matching. Two crossmodal (visual encoding and tactile recognition and vice versa) and two unimodal delayed matching-to-sample tests with geometrical patterns were performed by 12 healthy subjects. We determined error rates before and after focal low-frequency rTMS applied over the left anterior IPS, right anterior IPS and vertex. During the manipulation of objects with the right hand, rTMS over the left anterior IPS induced a significant deterioration for visual encoding and tactile recognition, but not for tactile encoding and visual recognition. For the visual and tactile unimodal conditions, no significant alterations in task performance were found. rTMS application over right IPS when manipulating objects with the left hand did not affect crossmodal task performance. In conclusion, we have demonstrated an essential functional role of the left anterior IPS for visuo-tactile matching when manipulating objects with the right hand. However, we found no clear evidence for left IPS involvement in tactile encoding and visual recognition. The differential effect of rTMS on tactile and visual encoding and recognition are not consistently explained by previous concepts of visuo-tactile integration.

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## 1. Introduction

It is part of our daily life to find an object in a bag (for example a key) by tactile manipulation. This process is facilitated by the

knowledge of object features. Therefore, it seems reasonable to assume that for successful crossmodal object recognition, information from both senses, vision and touch, may be presented in a common area in the human brain. Object

\* Corresponding author. Department of Neurology, RWTH Aachen University, Pauwelsstr. 30, 52074 Aachen, Germany. Fax: +49 241 80 82444. E-mail address: [d\\_buelte@web.de](mailto:d_buelte@web.de) (D. Buelte).

recognition is based on visual or tactile features defined by basic contours and their spatial arrangement, and may ultimately involve tactile–visual integration (Amedi et al., 2001). Thus, object manipulation and recognition are multimodal processes involving both tactile and visual processing.

There is a long history of discussion about the relation between vision and touch. The Irish philosopher George Berkeley wrote as early as 1709 (Berkeley, 1732) that there is no essential conjunction of the visual and the tactile world. The speculation that there are no cortical areas where multimodal information for vision and touch converge has been supported by modern scientific work (Felleman and Van Essen, 1991; Singer, 1993; Singer and Gray, 1995; Young et al., 1992). Following this theory, different modalities must be processed by parallel functional streams (Gulyas et al., 1994; Haxby et al., 1991; Livingstone and Hubel, 1988; Zeki et al., 1991). Ettliger and Wilson (Ettliger and Wilson, 1990) assumed in a review on crossmodal abilities in human primates, that there is no polysensory crossmodal area. Instead, they favoured a neuronal system in which the senses can access each other directly from the sensory-specific network.

However, recent studies on visuo–tactile crossmodal integration have led to the hypothesis that the two sensory systems for the modalities vision and touch might indeed converge in particular cortical areas. Neurophysiological experiments with macaques have suggested that the posterior parietal cortex (PPC), and in particular the region around the intraparietal sulcus (IPS), constitute a polysensory region involved in the integration of neural signals for action in space (Andersen, 1997; Bremmer et al., 2001; Colby and Duhamel, 1996; Duhamel et al., 1998; Hyvarinen, 1981; Sakata et al., 1997). Some of these studies have indicated that the anterior part of the lateral bank of IPS is responsible for visuo–tactile integration and object-related action. Neurons of the anterior intraparietal area (AIP), for instance, have been demonstrated to be sensitive to 3D features of objects such as size, shape and orientation (Murata et al., 1996; Sakata et al., 1995). Object manipulation under visual control is an effective stimulus to lead to a discharge of AIP neurons (Murata et al., 2000; Taira et al., 1990). Furthermore, when presenting visual objects briefly, some neurons show ongoing activity in AIP (Murata et al., 1996), which might reflect short-term memory processes of visual 3D-object features (Murata et al., 1996).

Equivalent regions between macaque and human intraparietal cortex have been found in an increasing number of functional imaging studies (for a review see Grefkes and Fink, 2005). Based on the finding that visual and sensorimotor functions for 3-D object processing are represented in macaques anterior IPS, it has been hypothesized that the same area is involved in the integration of the visual and the sensorimotor system in the human brain too (Grefkes and Fink, 2005). Neuroimaging studies in humans have demonstrated the involvement of anterior IPS in tactile shape processing (Bodegard et al., 2001; Jancke et al., 2001) and the same region has also been implicated in the discrimination of the orientation of visual stimuli (Shikata et al., 2001). Based on this knowledge and on investigations in the macaque (Murata et al., 1996; Murata et al., 2000; Sakata et al., 1998, 1999), the functional activation of the IPS in visuo–tactile may indicate

that integration of tactile and visual object information is located in the anterior part of the IPS (Grefkes et al., 2002; Macaluso and Driver, 2001). However, a proof of the functional relevance of this area for this process is still missing.

Integration of visual and tactile information plays also an important role in the representation of peripersonal space, the space surrounding our body, particularly the sector of space that closely surrounds a certain body part. The perception of these immediate surroundings is distinguished from those of more distant space by our ability to interact with objects within peripersonal space (e.g. to reach and grasp an object).

In humans, most evidence for the multisensory representation of peripersonal space based on neuropsychological studies with patients suffering from crossmodal extinction after right hemispheric stroke (Farne et al., 2005). In those studies a visual stimulus presented near to the patient's ipsilesional (right) hand often extinguished the perception of a simultaneous tactile stimulus on the contralesional (left) hand. When the right visual stimulus was presented far from the hand, the degree of extinction was reduced (Ladavas et al., 1998). When hands were held in a crossed position, visual stimulation close to the right hand still induced pronounced extinction of left hand tactile stimulation. These results are consistent with electrophysiological findings from monkey studies suggesting that the representation of peripersonal space is body part centered (Farne et al., 2005). The aIPS seems to be a relevant neuronal structure in the multisensory representation of peripersonal space in humans (Makin et al., 2007).

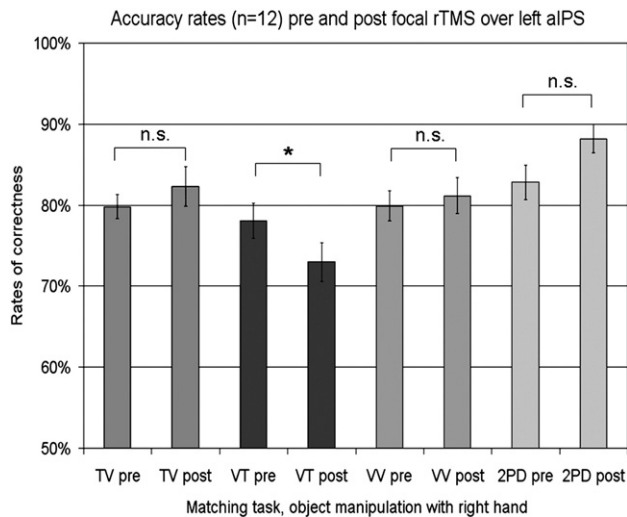
To elucidate the role and the functional relevance of anterior IPS for crossmodal object processing we used the "virtual-lesion" technique of repetitive transcranial magnetic stimulation (rTMS) (Pascual-Leone et al., 1999; Walsh and Cowey, 2000) by studying the potential deterioration in a crossmodal matching task. We hypothesised that the crossmodal function for visual and tactile transfer and vice versa would be suppressed with a measurable behavioural effect on performance of inhibiting low-frequency rTMS application to the anterior IPS.

## 2. Results

### 2.1. Crossmodal tasks

As main result, we found a significant alteration of performance for the crossmodal matching tasks following rTMS to the left anterior IPS. When manipulating objects with the right hand, focal rTMS over the left IPS induced a significant deterioration in crossmodal task performance for visual encoding and tactile recognition (VT) as compared with the baseline (mean relative increase of error rate  $4.24\% \pm 2.38\%$  (SE);  $p=0.016$ , see Fig. 1). For tactile encoding and visual recognition we found no significant influence on subjects performance (mean relative decrease of error rate  $2.48\% \pm 2.5\%$  (SE),  $p=0.363$ ).

rTMS application over right IPS (CP4) when manipulating objects with the left hand did not affect crossmodal task performance significantly (changes from baseline for TV condition was  $+5.39\% \pm 1.66\%$  (SE),  $p=0.09$  and for VT condition  $-1.36\% \pm 2.3\%$  (SE),  $p=0.52$ ) (see Fig. 2). Control-stimulation over Cz with crossmodal matching task showed no significant effects on

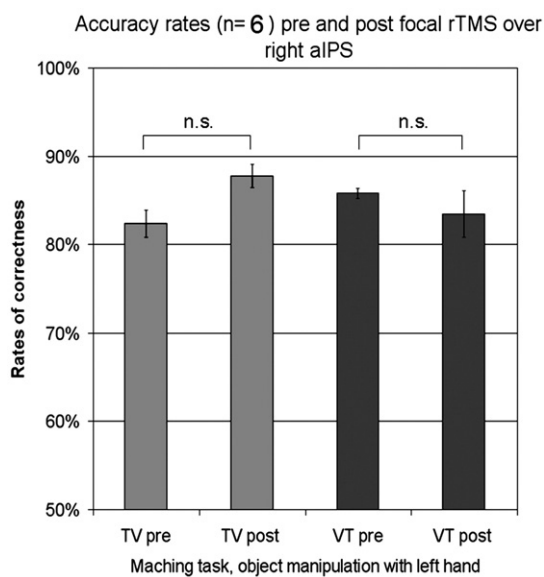


**Fig. 1** – Accuracy rates ( $n=12$ ) following focal rTMS applied over left anterior intraparietal sulcus (aIPS). Crossmodal (TV, VT) and unimodal (VV) matching task performed by object manipulation with the right hand, and two Point Discrimination task (2PD) performance. (\* $p<0.05$ ; n.s. non significant).

performance thereby excluding non-specific rTMS effects (changes from baseline for TV condition was  $4.98\% \pm 2.9\%$  (SE),  $p=0.13$  and for VT condition  $-4.27\% \pm 2.38\%$ ,  $p=0.11$ ).

## 2.2. Unimodal task

For visual (VV) and tactile (TT) unimodal conditions, no significant alteration of the performance was found (Changes from baselines for VV  $+1.27\% \pm 2.14\%$  (SE) and for TT  $-4.83\% \pm 5.02\%$  (SE),  $p=0.58$  and  $0.42$ , respectively). Simple tactile sen-



**Fig. 2** – Accuracy rates ( $n=6$ ) following focal rTMS applied right anterior intraparietal sulcus (aIPS). Crossmodal (TV, VT) matching task performed by object manipulation with the left hand. (n.s. non significant).

sory acuity was not influenced by rTMS (mean decrease of error rate  $5.39\% \pm 2.78\%$  (SE),  $p=0.09$ ). Control-stimulation over Cz with unimodal visual and sensory matching task showed no significant effects on performance, thereby excluding non-specific rTMS effects (mean decrease of error rate for VV condition  $3.06\% \pm 2.05\%$  (SE),  $p=0.18$  and for sensory acuity  $4.15\% \pm 2.49\%$  (SE),  $p=0.15$ ).

## 3. Discussion

The aim of the present study was to test the hypothesis whether the left human anterior intraparietal cortex is functionally relevant for object-related crossmodal information transfer between the two senses, vision and touch. We were able to demonstrate a significant deterioration of cross-modal matching performance after application of rTMS over left anterior IPS during manipulation of objects with the right hand. Do these findings support the hypothesis of anterior IPS being the key-interface for visuo-tactile transfer?

Macaluso and Driver (Macaluso and Driver, 2001) used fMRI to identify common effects in the anterior region of IPS for vision and touch by testing for the main effect after simple unilateral stimulation. Grefkes et al. (Grefkes et al., 2002) found an area activated in the left human anterior intraparietal cortex when healthy human volunteers performed a cross-modal visuo-tactile delayed matching-to-sample task with geometrical objects (identical to the objects in the present study) with their right hand. Shikata et al. (Shikata et al., 2003) used fMRI to demonstrate that the human AIP equivalent was activated both during discrimination of surface orientation and during subsequent spatial adjustment of the thumb and index finger position towards surface orientation. Tanabe et al. (2005) postulated an important role of human AIP in the sensorimotor transformation of crossmodal spatial information. They compared the activations between crossmodal conditions (eye movement triggered by somatosensory cues and finger movements triggered by visual cues) and intramodal conditions in an fMRI study. Though the parietal cortex was involved in all tasks regardless of sensorimotor combinations, the only region activated to a certain extent in the crossmodal conditions compared to the intramodal conditions was the anterior portion of the IPS. These results are supported by previous studies on the intraparietal sulcus and its electrophysiological properties in monkeys: a notable number of functionally relevant areas have been detected in macaque area IPS by means of their anatomical and electrophysiological properties. Anatomical studies have demonstrated that macaque area AIP has connections with premotor cortex (Matelli et al., 1986) and to somatosensory relevant areas such as secondary somatosensory cortex and unimodal somatosensory cortex (Lewis and Van Essen, 2000). These sensorimotor regions are strongly involved in generating grasping movements and tactile shape processing. Electrophysiologically, neurons in macaque area AIP are known to be involved in visually guided hand manipulation tasks and processing of 3D shapes (Gallese et al., 1994; Murata et al., 2000; Taïra et al., 1990). In monkeys, neurons which are active during fixation and manipulation of objects have been found in the anterior intraparietal area (Sakata et al., 1995). These

neurons in AIP are highly responsive for shape and size of objects (Murata et al., 2000). Furthermore, some neurons in AIP show sustained activity after a brief visual presentation of an object. This response pattern has been interpreted as a visual short-term memory processes for 3D object features to be incorporated in area AIP for the guidance of hand manipulation (Murata et al., 1996).

The deterioration of crossmodal performance after rTMS is not likely to result from differential spatial attention demands or nonspatial shifting of selective attention between visual and tactile features. These processes would not solely involve left anterior IPS and we found no alteration of crossmodal performance when stimulating right anterior IPS. Furthermore, the areas that are responsible for spatial attention tasks have been showing in fMRI and PET studies to be more posterior and superior (Corbetta, 1993; Fink et al., 2000) to those we targeted by rTMS. Attention related regions are typically found bilateral, or show right hemispheric dominance. Similarly, we found no effect on crossmodal performance when applying rTMS over right anterior IPS.

It is widely agreed that the posterior parietal cortex is involved in switching from touch to vision or vice versa. Areas of this region are implemented in networks associated with crossmodal attention, along with superior occipital gyrus, occipito-temporal junction and frontal cortex (DiGirolamo et al., 2001; Macaluso and Driver, 2001; Macaluso et al., 2002; Rushworth et al., 2001a,b).

In our study the verification of the location of magnetic stimulation was performed using a neuronavigation system to ensure to have stimulated the region encompassing the human equivalent of area AIP. Unspecific factors related to rTMS procedure (such as discharge noise of the coil or pain and discomfort induced by scalp stimulation) are unlikely to account for our results, as the control stimulation over the vertex showed no effect on this task.

The demonstrated behavioural effect on the performance cannot be interpreted as rTMS affecting the mental rotation requirement during crossmodal matching tasks. When designing the experiment, we made sure that mental rotation was included in all crossmodal and unimodal conditions. Thus, object orientation changed between encoding and recognition in all conditions. Moreover, regardless of stimulus properties during mental rotation, a bilateral involvement of both the superior and the inferior parietal lobules has been reported in several functional imaging studies (e.g. Jordan et al., 2001). Bestmann et al. (Bestmann et al., 2002) applied four pulses of 20-Hz rTMS to the left PPC, right PPC or vertex 100 ms after the presentation of an instruction cue for mental rotation. The reaction time was evenly prolonged by right or left parietal TMS compared with vertex-stimulation, but only for large angles of rotation, and without affecting the spatial accuracy of the final response. The authors suggested a bilateral involvement of the PPC in visuomotor mental rotation which increases with processing demands. In contrast, significant alteration of task performance was observed after rTMS over the left but not over the right anterior IPS.

The affection of visual encoding and tactile recognition (VT) in contact to tactile encoding and visual recognition (TV) is probably explained by the fact, that the visuo-tactile condition is more challenging than tactile-visual condition.

Actually, during debriefing retrospect our volunteers reported that visuo-tactile condition was more difficult than tactile-visual condition: 5 of the 12 volunteers needed more than 2 training sets to achieve an accuracy rate higher than 60%, whereas for the tactile-visual condition just one volunteer needed more than 2 training sets. This observation is supported by neuropsychological and functional studies which have demonstrated that VT is significantly more difficult than TV (Juurmaa and Lehtinenrilo, 1988; Kawashima et al., 2002; Reed et al., 2004; Stoeckel et al., 2003). We supposed that visual object recognition is much faster than the sequential object assessment during tactile manipulation, when comparing the object properties with the mental object image generated during the encoding phase. Thus as a condition encountered in our daily life, this condition might be more resistant to the influence of rTMS on performance. In line with our findings McNally et al. (McNally et al., 1982) found significant impairment when patients with parietal lesions performed a crossmodal transfer in the direction of vision to touch but not in the other direction. The authors suggested that the reason of the effect could be type or complexity of the material or differences in the modalities that were used.

Our data showed an effect of rTMS on the VT but not the TV condition. A possible explanation could be the presentation of the visual stimuli far from the acting hand on the computer screen (about 60 cm away). The results of Farne et al. (2005) suggest that visuo-tactile integration works better near the body (particularly near the hand or the face) than far the body.

The involvement of aIPS in building a multisensory representation of peripersonal space could be stronger when it starts with tactile perception. A recent fMRI study showed an involvement of aIPS in multisensory representing perihand space whereas posterior IPS and the lateral occipital complex represented hand-centred space in predominantly visual manner (Makin et al., 2007). Thus the order of presentation of the stimuli could have an effect on the cortical representation.

To exclude not to have selectively influenced tactile recognition by using rTMS, we also examined the unimodal tactile condition. rTMS did not affect the performance of unimodal tasks. To control for the influence of rTMS on tactile sensory acuity, a two-point-discrimination task was applied to the tip of the index finger and no effect of rTMS was found on the task. To test whether low-frequency repetitive transcranial magnetic stimulation (rTMS) of sensorimotor cortex has prolonged effects on somatosensory function, Satow et al. (Satow et al., 2003) tested eight subjects by giving 900 TMS pulses over the left hand sensorimotor cortex (0.9 Hz, 90% of the resting motor threshold). Tactile threshold of the right hand was increased for a short duration after rTMS over sensorimotor cortex and two-point discrimination and median nerve SEPs were unaffected after rTMS.

To study the functional relevance of right AIP for crossmodal visuo-tactile processing six subjects, who showed a severe effect of rTMS with visual encoding and tactile recognition, participated in both crossmodal conditions when stimulating CP4 (situated over right anterior IPS) and manipulating objects with the left hand. We found no significant effect of rTMS on the performance when focal rTMS was applied over right AIP when manipulating with the left hand. This indicates that visual-tactile crossmodal

processing may be lateralised to the left AIP. Butters et al. (Butters and Brody, 1968; Butters et al., 1970) compared performance of visuo–tactile matching task in patients with right hemisphere lesions with that of left hemisphere patients. It appeared that the left parietal region may be dominant for crossmodal associations, but that both the left and the right might be important for spatial reversible operations. However, our group of 6 volunteers may not have been enough to detect lateralization of crossmodal processing. Though the VT results following rTMS to the right hemisphere were not significant, an involvement of right aIPS in crossmodal processing, at least for object manipulation with the left hand, cannot be excluded. Further studies are needed to elucidate lateralisation of brain-activation during visual and tactile crossmodal processing. Interestingly, in the fMRI study by Grefkes et al. (Grefkes et al., 2002) only left but not right anterior IPS was activated during crossmodal transfer of object information when performing the task with the right hand. It should be noted that in this fMRI study 3 (of 12) subjects showed a bilateral fMRI activation during the task.

Taken together the results of the study of Grefkes et al. (2002) and of the present one, it can be concluded that crossmodal object-related activity seems to be a function rather of the left hemisphere. Similarly, Rushworth et al. (Rushworth et al., 2001a,b) reported a lateralisation for motor intention processes to the left supramarginal gyrus. Likewise, processing of spatial and temporal information are often lateralized to left parietal cortex (Assmus et al., 2003, 2005; Muhlau et al., 2005) and action-related deficits like apraxia preferentially occur after left parietal cortex lesions. Therefore, the implicated dominance of the left parietal cortex for object-related action is also reflected by the results of the present study for crossmodal visuo–sensorimotor aspects.

Our findings have demonstrated that anterior IPS is essential for visual and tactile crossmodal processing. Further studies are needed to disentangle the role of IPS within the cortical network for crossmodal object processing.

## 4. Experimental procedures

### 4.1. Participants

Twelve healthy right-handed volunteers (mean  $\pm$  SD age 26.9  $\pm$  2.6 years; 7 men and 5 women) participated in our study. All participants were right-handed (Edinburgh-Inventory Oldfield, 1971), had normal or corrected to normal vision. None of the subjects had a history of psychiatric or neurological disorders, including seizures. The protocol was approved by the local ethics committee and all subjects gave their informed consent. The study was performed in accordance with the declaration of Helsinki.

### 4.2. Matching task

The experiment was designed to investigate neural functionality of the human AIP in two crossmodal conditions in which 3D object features were encoded in one modality and had to be transferred into another modality for successful object recognition, in our particular case crossmodal transfer be-

tween visual and sensorimotor systems. The “unimodal” conditions which did not draw upon crossmodal transfer of object information served as control conditions for each of the two crossmodal tasks. Two crossmodal (visual encoding and tactile recognition [VT] and vice versa [TV]) and two unimodal (visual [VV] and tactile [TT] encoding and recognition) delayed matching-to-sample tests were used in our study (see Fig. 3 for time course of trial presentation in several experimental conditions).

### 4.3. Objects

Abstract objects with geometrical shapes, such as pyramids, triangles and squares, were presented to the subjects for tactile and visual encoding and recognition. A more detailed description of the stimuli are given elsewhere (Grefkes et al., 2002). In brief, the objects consisted of small wooden spheres (diameter 15 mm) with a smooth surface. The spheres were glued together yielding abstract objects. The smallest object consisted of three spheres and the largest object had 18 spheres. The size of the object never exceeded three spheres in two axes and two spheres in the third axis (maximum size 4.5  $\times$  4.5  $\times$  3.0 cm) enabling the object to be comfortably and completely explored by one hand.

Prior to the experiment, all visual and tactile stimuli were intensively tested for their suitability and difficulty on healthy volunteers ( $n=12$ ) who did not take part in the main part of the rTMS study.

For the visual encoding and recognition tasks each object was also photographed on a white background with a digital camera from two different points of view (camera distance about 30 cm).

### 4.4. Training

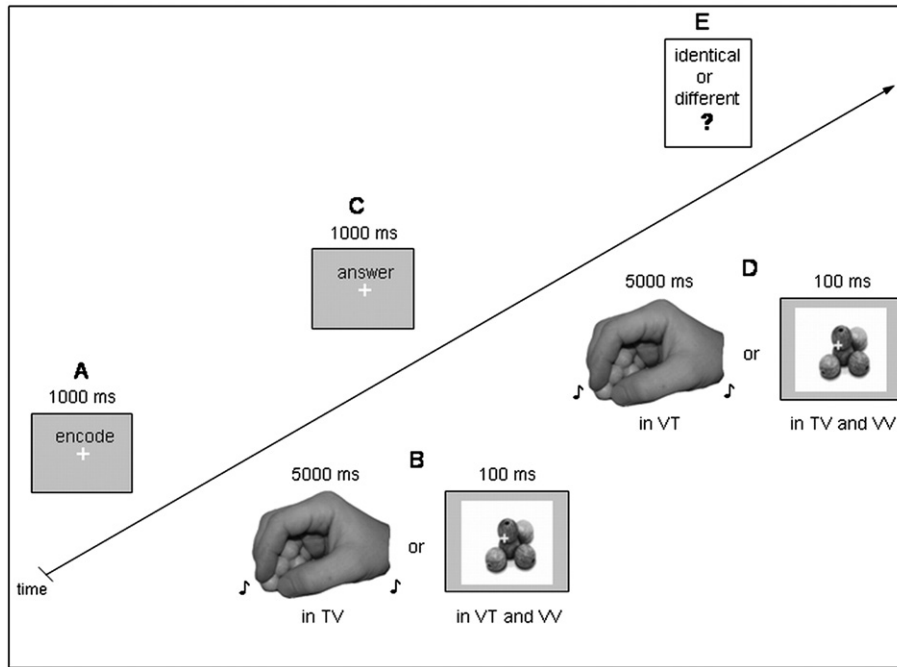
Participants were trained within each condition (at least two runs of 24 items) in order to familiarise them with the encoding and recognition procedures. The training was performed to minimise improvement through learning effects before creating the baseline of 34 items.

### 4.5. Time course and stimulus presentation

Participants were comfortably seated in a dimly illuminated room, facing a computer monitor (21 in.), placed 60 cm in front of them along the midsagittal plane and adjusted to eye level. Stimuli were presented and responses recorded using Presentation® software (NBS, Albany, CA).

There were two sessions with each of the twelve volunteers. The two crossmodal experimental conditions (VT, TV) and a control task (2PD, see below) were tested. Additionally six of the twelve subjects performed the TT condition. Both, the order of the conditions and the order of stimulation side were balanced. We used two sets of 34 different items with matched difficulty for each condition. The order of the two item lists was also balanced between subjects.

Before object encoding, the German command “Einprägen” (to encode) appeared on a light grey background for 1 s displayed above a white cross in the centre of the screen.. For tactile manipulation, subjects had to tactually explore the



**Fig. 3 – Time course of trial presentation in several experimental conditions of the delayed-match-to-sample task. After presentation of the word ‘encode’ (A) subjects were asked to manually explore an object of wooden spheres for 5000 ms in the TV or TT condition. Likewise subjects were required to visually explore a picture for 100 ms in the VT or VV condition (B). During the next 1000 ms the word ‘answer’ appeared on the screen (C). This time subjects explored an object (in the VT or TT condition) for 5000 ms or an picture of an object for 100 ms (in the TV or VV condition), respectively. Finally, they had to answer by pressing a mouse-button whether both explored objects were identical or not (E).**

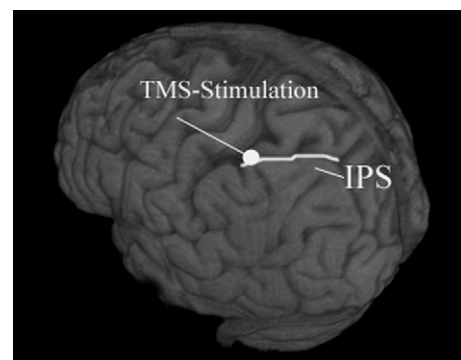
objects either with their right or left hand without visual control within 5 s. An acoustic signal indicated the beginning and the end (after 5 s) of the palpation period. The subject’s hand rested in a supine position under a white box to prevent the subjects from seeing the objects. The experimenter, who sat next to the volunteer, placed the object into the subject’s hand when instructed by the sound. The instruction was to actively palpate the object using all five fingers and the palmar surface of the hand. During object manipulation the volunteers had to fixate a white cross in the centre of the screen. We performed the same procedure for tactile recognition.

For visual encoding and recognition, photographs of the objects were shown briefly for 100 ms on a computer screen. During visual object presentation, the white cross was directly placed on the depicted object without hiding important features of the object.

1 s after encoding, the German command “Antworten” (to answer) was shown for 1 s above the white fixation cross. Subsequently, the object previously encoded had to be recognised either visually (VV, TV) or tactually (VT, TT). This time either the identical object or its similar but different counterpart was presented. In the visual recognition task, if the same object was presented, the latter was shown from a different point of view to ensure that all conditions involved mental rotation. Subjects were told to assess the figure either by tactile manipulation or visually, and to decide whether the second presented object was “identical” or “different” from the one previously encoded. Answers were given by pressing a mouse-button as accurately as possible.

#### 4.6. Control task

To control for the influence of rTMS on tactile sensory performance, a two-point-discrimination task (2PD) was applied using the tip of the right index finger (Touch Test®, North Coast Medical, USA). We applied stimuli with two spiky points separated by 2 to 8 mm distance with light pressure. For encoding, the experimenter gave a brief contact with the two laces of the two-point-discriminator on the tip of the right index finger when triggered by a sound and accompanied by a green circle with a black number “1” in the centre of the screen for 500 ms. After 2 s delay, the second stimulus was given



**Fig. 4 – The localisation of IPS on the left hemisphere and stimulation site on the left anterior intraparietal sulcus.**

signalled by a sound and accompanied with a red circle with a black number “2” in its centre for 500 ms. The separation of the second two-point-stimulus varied from the first stimulus by 2 mm. The volunteers were asked to decide whether the distance between the two points of the second stimulus was “identical” or “different” with the one before by immediately pressing a mouse-button.

#### 4.7. Transcranial magnetic stimulation

Low-frequency rTMS was used to test the functional relevance of anterior IPS for visuo-tactile crossmodal matching. Error rates were determined before (baseline) and after focal rTMS (1 Hz, 15 min, 60% intensity) investigating behavioural effects resulting in transient suppression of cortical excitability (Maeda et al., 2000; Mottaghy et al., 2003; Wassermann et al., 1998; Ziemann, 2004). rTMS at 1 Hz is known to reduce the excitability of the targeted region and so to interfere with cognitive processing beyond the duration of the train itself (Chen et al., 1997; Hilgetag et al., 2001; Koch et al., 2003; Pascual-Leone et al., 2000).

The intensity of magnetic stimulation was set to 60% of the stimulator output (maximum output 2 Tesla), since it has been argued that the motor threshold does not adequately represent the excitability of non-motor areas (Borojerdj et al., 2002; Dambeck et al., 2006; Robertson et al., 2003; Stewart et al., 2001).

Recent studies indicated a possible sufficient influence of neuronavigated rTMS over the anterior IPS on behavioural measurements (Rice et al., 2006; Tunik et al., 2005; Rushworth and Taylor, 2006). Magnetic pulses were generated using a Magstim super rapid stimulator (Magstim company, Dyfed, UK) connected to a 9 cm figure-of-8-coil.

In twelve subjects rTMS was applied over CP3 (situated over left anterior IPS) and Cz (vertex) according to the International 10–20 EEG system if objects were manipulated by the right hand. In addition, magnetic stimulation over CP4 (situated over right anterior IPS) if manipulating objects with the left hand was performed with six volunteers.

To control matching between 10–20 EEG system derived stimulation site and underlying anatomical structure (anterior IPS) we managed the localisation of the coil using a MRI-based neuronavigational system (Localite, Bonn, Germany) by online-navigation on the base of anatomical MRI-scans with 6 subjects (see Fig. 4). The definition of localisation acquired by the International 10–20-EEG system is known to be more for accurate for parietal areas than for other areas, i.e. frontal or central. A high correspondence of localisation of stimulation between the International 10–20-EEG system and the MRI-based neuronavigational system was found (for a review see Sparing et al., 2008).

#### 4.8. Statistical analysis

Accuracy rates of the baseline set of stimuli were compared with those of the responses of a new stimuli-set after rTMS application on CP3 and Cz or CP4 and Cz, using a paired two-tailed t-test. Significance was set to  $p < 0.025$  to correct for multiple comparisons. Evaluation of the reaction time was not performed, as this varied both with the volunteer and with the experimenter who placed the object in the subject's hand.

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