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# **The “Cognitive Oblique effect “ and its neural substrate**

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## **Abstract**

Previous studies have shown that visual direction reproduction results in two independent sources of anisotropy: a low level oblique effect, manifested in better accuracy in the reproduction of cardinal directions compared to oblique and a high level oblique effect, manifested in a distortion of directional space representation with space expansion around the cardinal directions and space contraction around the oblique directions. The low level oblique effect, known as “visual”, is strictly confined to vision. The high level oblique effect, known as “cognitive”, is caused by a systematic directional error introduced by the cognitive process of space categorization. It increases with decreasing amount of directional information and is observed in different sensory modalities (arm pointing movements, smooth eye pursuit movements). Although neuroimaging and electrophysiological studies so far have focused on the visual oblique effect, little is already known about the neural correlate of the cognitive or high level oblique effect. In this experiment, we investigated the cortical activation pattern during an arrow alignment task using an event-related fMRI model at high field. Directional error was measured categorically when normal individuals tried to align the direction of an arrow towards a peripheral target located in one of 3 directions/target angles (vertical and 11.25 degrees left and right to that). Task difficulty was manipulated by varying target distance (0.7, 1.4 and 2.1 degrees visual angle), while the arrow length was kept constant (0.7 degrees visual angle).

We hypothesized that in the diagonal orientations the increasing target distance (decreasing amount of directional information) would result in activation of brain areas involved in higher cognitive processing. Whole brain analysis and following exploratory ROI analysis results showed: 1) a significant main effect of target distance observed in frontal, parietal, visual areas bilaterally and a gradual increase of BOLD response with the increase of target distance including all the clusters, 2) a significant effect of target angle on activation restricted in visual associative areas. In these areas a greater activation was observed for the diagonal directions compared to cardinal. 3) a significant interaction of target

angle with target distance in right precuneus, left operculum, left superior temporal area and a brainstem region close to the right parahippocampal area. In the right precuneus, we showed a trend for higher activation with increasing task difficulty concerning only the diagonals. Our findings suggest a possible neural correlate of this oblique effect in brain areas involved in higher cognitive processing, in contrast to the classic oblique effect, which is represented in brain areas involved in primary visual processing.

**Keywords:** Oblique effect · Cognitive · Space categorization · Directional error · fMRI · Precuneus

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## Introduction

The oblique effect refers to the well-established fact that our discriminability of orientation or direction is significantly better around the cardinal (horizontal or vertical) axes compared to an oblique axis (**Mach 1861; Appelle 1972; Howard 1982**). Whereas this orientation bias is known for more than a century, its origin remains still an issue of controversy in perception research. A theoretical model proposed by **Essock (1980,1992,1997)** suggests the existence of two classes of oblique effect, a purely visual one (class 1) related to low level visual processing, that is observed using measures of visual spatial resolution (acuity) and contrast sensitivity and a higher level oblique effect that is evoked in several sensory modalities (visual, vestibular, kinesthetic, haptic), consistent with the idea that this effect stems from a bias of “higher-level” representation, memory, and/or recall of orientation information. In a previous work of our team, we investigated the oblique effect in the reproduction of visual direction in 2-D space using an arrow alignment behavioral task (**Smyrnis et al. 2014**). We showed the existence of two independent sources of anisotropy in visual direction reproduction, a low level oblique effect and a high level oblique effect.

The first source of anisotropy was measured by the variance of directional error and resulted in less variance, thus better accuracy in the reproduction of cardinal directions compared to oblique. This effect has not been observed in other modalities, such as the representation of direction of motion (**Krukowski and Stone 2005**) or haptic representation of direction (**Gentaz et al. 2008**) or representation of direction for a pointing movement (**Smyrnis et al. 2007**), indicating that the source of this oblique effect is strictly confined to vision. The second oblique effect was measured by the mean directional error (DE) and the change in mean DE with change in target direction, namely the gain (**Smyrnis et al. 2007**). This second source of anisotropy manifested with a trend of subjects to direct their movements away from the cardinal and toward the oblique directions in 2-D space. Thus, it resulted in a distortion of directional space representation with space expansion in the surrounding area of cardinal

directions and space contraction in the surrounding area of oblique directions. We also demonstrated that only the second oblique effect increased with increasing task difficulty (decreasing amount of directional information), whereas the oblique effect measured by the variance of directional error remained unchangeable. **(Krukowski and Stone 2005; Smyrnis et al. 2007)**. The pattern of this oblique effect, measured by the systematic directional error, is identical to that observed in other sensory modalities, such as representation of direction in fast and slow arm pointing movements **(van der Graaff et al. 2014; Baud-Bovy and Viviani 2004; Smyrnis et al. 2000; Gourtzelidis et al. 2001; Smyrnis et al. 2007; Mantas et al. 2008)**, motion perception and smooth eye pursuit movements **(Krukowski and Stone 2005)**, saccades **(Koehn et al. 2008)**, haptic representation **(van der Graaff et al. 2014)** and even verbal encoding of direction in space **(Spencer et al. 2006)**.

This directional anisotropy has been explained by theoretical models proposing the existence of two representations of the direction of stimulus in 2-D space: a veridical representation based on vision and a categorical representation in which oblique directions **(Essock and Siqueland 1981; Quinn and Bomba 1986; Huttenlocher et al. 1991; Huttenlocher et al. 2004)** or cardinal and oblique directions **(Baud-Bovy and Gentaz 2012)** serve as categories. The initial category adjustment model suggests the existence of four primary categories representing the four quadrants of 2-D directional space centered in the oblique directions **(Huttenlocher et al. 1991, 2004)**. The revised version of the model of **(Baud-Bovy and Gentaz 2012)** proposes the existence of eight categories: four broad corresponding to the categories of the previous model and four narrow centered on the cardinal directions. According to these models, the reproduced direction depends on the amount of available information. Thus, when the veridical directional information degrades by increasing the cognitive load between visual stimulus presentation and response (for example by introducing a memory delay or by increasing task difficulty), then the system relies more on the category and less on the veridical direction information. This results in the described space distortion and the corresponding oblique effect. An alternative theoretical framework, that was proposed to explain systematic biases in the perception of orientation was the Dynamic Field Model **(Spencer et**



**al. 2006**). Basic assumption in this model was that directional signal decays in time. In a previous work of **Balikou et al. (2015)**, applied increasing memory delay did not produce increase in mean directional error, as predicted by this model.

Research on the oblique effect has been interested in providing evidence on its underlying neural mechanisms. There is robust evidence nowadays that the class 1 oblique effect most likely originates from the visual cortex. Early neurophysiological studies revealed orientation detectors in the visual cortex of cats and monkeys by **Hubel and Wiesel (1959, 1977)**, and **Pettigrew, Nikara and Bishop (1968)**. Since then, a great deal of studies has shown that in the visual cortex of animals there are more cells responding to horizontal and vertical than to oblique orientations (**DeValois, Yund, & Hepler 1982; Kennedy, Martin, Orban, & Whitteridge 1985; Mansfield & Ronner 1978; Coppola, White, Fitzpatrick, & Purves, 1998; Keil & Cristobal 2000**). Differences in orientation tuning specificity have also been studied. Neurons in V1 with horizontal or vertical preferences have been reported to exhibit narrower orientation tuning widths (**Kennedy and Orban 1979; Nelson et al. 1977; Orban and Kennedy 1981; Rose and Blakemore 1974**). As far as neuroscience is concerned, using event-related potentials (ERP) unequal responses have been obtained to cardinal and oblique orientations in steady state potentials (**Maffei and Campbell 1970; Skrandies 1984; Moskowitz and Sokol 1985**), transient ERPs (**Yoshida et al. 1975; Arakawa et al. 2000; Proverbio et al. 2002**), and MEG (**Koelewijn et al. 2011**). **Maffei and Campbell (1970)** found an oblique effect in humans by means of visual evoked potential. They showed that the visual evoked response, thought to derive from primary visual cortical activation and measured from the scalp recorded electroencephalogram, is larger for visual stimuli presented at cardinal orientations compared to that for stimuli presented at oblique orientations. This could not be observed in the electroretinogram, implying that the oblique effect arises somewhere between the site of origin of the electroretinogram and the cortical evoked potential. Consistent with this, results from an fMRI study by (**Furmanski and Engel 2000**) demonstrated that the BOLD response in the primary visual cortex (V1) is larger for stimuli at cardinal orientations

compared to stimuli at oblique orientations. Some recent fMRI studies have failed to find differences in mean BOLD responses to different orientations, while others have demonstrated a reverse oblique effect, named horizontal effect, finding that mean BOLD responses are greater for oblique than for cardinal orientations in early visual areas (**Serences et al. 2009, Swisher et al. 2010**). Other fMRI studies have revealed a radial bias instead (**Clifford, Mannion, & McDonald, 2009; Sasaki et al. 2006**), which is tightly localized with the angular-position component of the retinotopic map in V1 (**Freeman, Brouwer, Heeger, & Merriam 2011**). These discrepancies in the findings of functional neuroimaging studies concerning the class 1 oblique effect could be the result of differences in the exact stimuli used, the attentional task demands and the different methodologies for neuroimaging data analysis. This is confirmed in a very recent study by **Pratte et al. (2016)**, in which novel, non-parametric approach to fMRI pattern similarity analysis revealed robust oblique effects in activity patterns in early visual areas (V1-V3) with more sharply tuned pattern responses around cardinal orientations. This advantage in tuning precision for cardinal orientations was observed even when mean BOLD responses revealed a reverse oblique effect, suggesting that neural locus of the oblique effect measured by the variance of directional error includes early visual cortex.

In contrast to the classic visual oblique effect, the neural substrate of the class 2 oblique effect has not been explored in such an extent, though it definitely occurs higher in the visual processing stream, as it is affected by scene processing. Some researchers have looked at the parietal cortex as a possible location, as it is known to process spatial information. In an orientation categorization task, **Mikhailova et al. (2015)** found a delayed response in the occipital cortex after original signal differences in the parietal cortex (possible feedback).

What is the origin then of this systematic directional error observed in such diverse tasks both in terms of input (visual, kinesthetic), output (fast or slow movements, isometric forces, pointing with a pointer) and cognitive demands (memory movements, movements toward a visual target)?

To address this question, we present this fMRI study, which explores brain activation during a visual reproduction task that emerges the two

orientation anisotropies. We used an alternative version of an arrow alignment task similar to that of **Smyrnis et al. (2014)**, modified in a way that activation in the motor cortex is avoided. Subjects were instructed to mentally align the direction of an arrow to point to a visual target at different directions (one cardinal and two oblique) in 2-D space. We manipulated the amount of available directional information and thus the difficulty of the task by introducing three target distances.

We planned to assess the underpinnings of class 2 oblique effect with a factorial ANOVA design exploring the effect of target angle, the effect of target distance (amplitude) and the interaction between these two effects. Our specific hypothesis was that the interaction between target angle and target distance would activate brain areas involved in cognitive processing of orientation and located beyond visual processing. Based in categorical models, we expected that in these areas BOLD activation would increase with decreasing directional information (increasing target distance) only for oblique directions, representing an increase in the magnitude of the cognitive, “class 2” oblique effect. In contrast, the same experimental factors (decreasing directional information) should not have a significant effect on the activation of visual areas representing the “class 1” oblique effect.

## **Materials and Methods**

### **Participants**

Forty-four healthy adults performed the fMRI arrow alignment experiment (age span 20 – 40 years, men). From the behavioral data analysis, one subject was excluded due to incomplete performance. From the fMRI analysis 17 subjects were excluded: 5 were excluded due to brain lesions, 5 due to poor EPI sequence quality and presence of scanner artifacts, 6 due to excessive head movement during EPI acquisition and one dropout. As a result, a total of 26 subjects was included in the fMRI data and behavioral data analysis.

All participants had normal or corrected to normal vision, and none reported neurological, psychiatric or cardiovascular disorders. All subjects were right-handed and performed the tasks with their preferred right hand. The experimental protocol was approved by the Eginition Hospital Scientific and Ethics Committee.

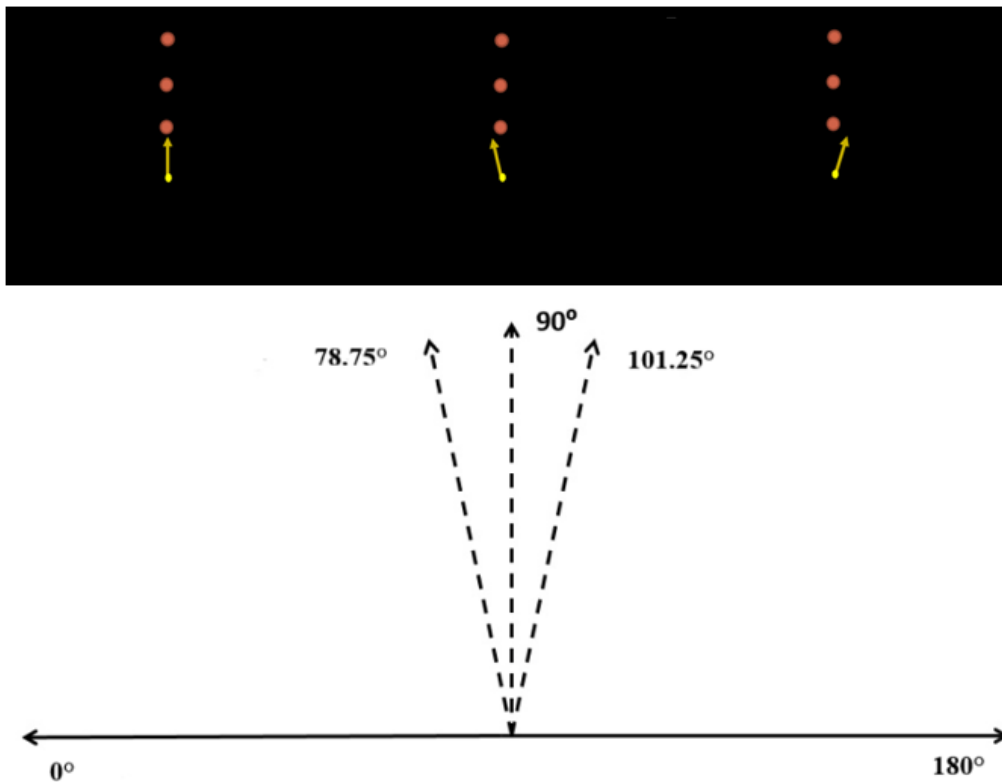
### **Set up – Procedure**

#### **Behavioral Task Design**

All subjects performed an arrow – alignment task while measuring their BOLD response. A few trials were also administered prior to scanning, in order to familiarise participants with the task procedure. The stimuli presentation program was written in Embarcadero Delphi. Stimuli were presented with a computer and projected to a back-projection screen (0.68 m width) at a distance of approximately 2.90 m from participant's eyes. Antialiasing techniques were used to draw targets and arrows. The visual angle for all stimuli (starting point of arrow to target) was < 2.5 degrees, in order to avoid saccades. The subjects used two fingers of the right hand to press the left or right arrow key on the computer keyboard. Participants were instructed to maintain fixation at all times.

In each trial, an arrow of constant length (40mm) appeared, starting at the center of the screen and a peripheral target at 3 different distances from the

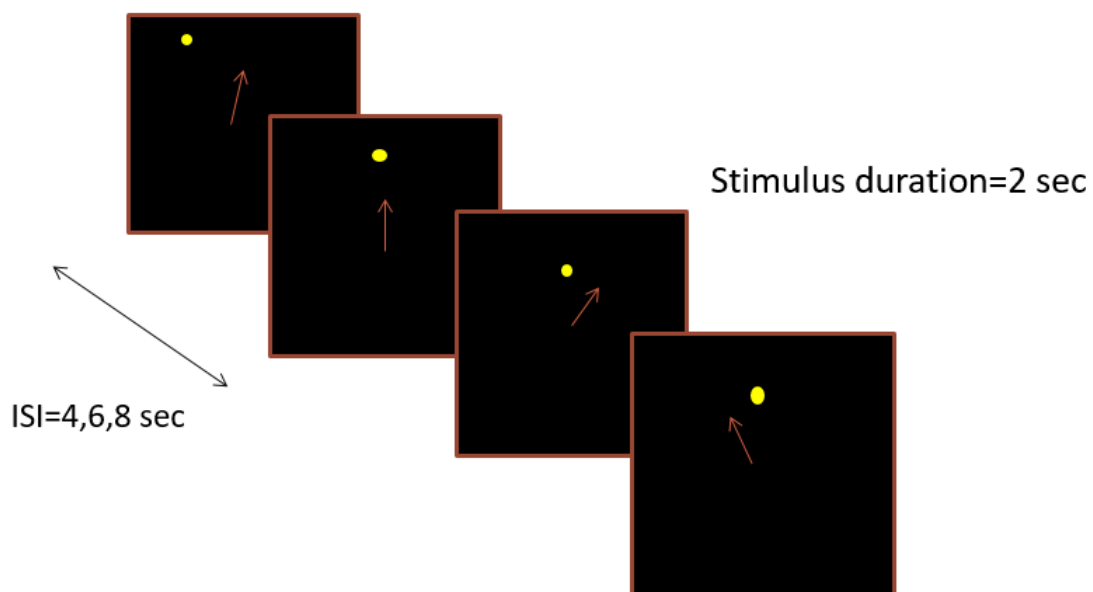
center of the screen (40, 80 and 120 mm). The targets were presented in 3 different directions relative to the center (vertical and 11.25 degrees away from it, clockwise and counterclockwise). The arrow pointed exactly to the target or 2 degrees away, clockwise or counterclockwise. The subject was instructed to align the arrow to the direction of the target using the arrow buttons of the keyboard. By pressing the right button, he chose to turn the arrow clockwise, by pressing the left, counterclockwise. When pressing both buttons, he chose not to move the arrow at all (already aligned). The arrow didn't actually turn, the subject just showed his/her intention. All different trial conditions (target angle, target distance and arrow pointing error) were randomly presented. **(Fig. 1).**



**Figure 1: Arrow alignment task**

## fMRI design

We used an event related fMRI design consisted of four blocks with a total duration of 40 minutes (16 minutes per block). In each block, the subject performed 3 repetitions for every target distance and target direction in a randomized sequence, for a total of 81 trials (3 repetitions x 3 target distances x 3 target directions x 3 different arrow pointing angles). The inter-trial time varied randomly 4, 6 or 8 sec and trial duration time up to 2 sec. **(Fig 2)**.



**Figure 2: Event Related fMRI Design**

## Analysis

### Behavioral Data Analysis

Mean error was calculated for each target distance (amplitude 1,2,3), for each target angle (78.75, 90, 101.25) and each subject, as the sum of the arrow angle difference and the answer angle difference in degrees. Variable error was the standard deviation of the mean error. We excluded trials where the latency was < 70 or > 3000ms. After application of these exclusion criteria we retained of the

trials for all subjects. Then a 2 factor ANOVA was performed for mean and variable error with distance and angle as the independent factors.

## **f MRI Data Acquisition and Analysis**

Participants were scanned in a Philips Achieva 3.0 Tesla TX MRI scanner equipped with 36 channel –head coil; 3 mm thick axial slices were acquired in a descending sequential order using an echo planar sequence. (TR=2000 ms, TE=60 ms, 36 slices covering most of the cerebral cortex, voxel size 3x3x3). An anatomical image of high resolution (T1 image, voxel size 1x1x1) was acquired for each participant. DICOM files were converted to NIFTI data image files using dcm2nii in MRICron. Prior to preprocessing, we applied artifact correction with ArtRepairToolbox. Detection and repair of bad slices was performed with Art\_Slice and detection of bad volumes with Art\_Global. Runs with great number of slice/volume artifacts were excluded from the analysis. Preprocessing and GLM Analysis was then performed using SPM12 Toolbox (Wellcome Trust Centre for Neuroimaging, London, UK) for MATLAB. Procedures consisted of realignment of the functional images for motion correction and slice time correction. Trials with head-movements greater than 3 mm or 3 degrees of movement were removed from the analysis. The high-resolution anatomical image was used to perform tissue segmentation into gray and white matter and cerebrospinal fluid (CSF). Images were next normalized to standard MNI space and smoothed with an 8 mm FWHM (full width at half maximum) Gaussian kernel.

### **1. Whole Brain Analysis**

GLM was then conducted for the functional scans from each participant by modelling the observed event-related BOLD signals and regressors to identify the relationship between the task events and the hemodynamic response.

In our experiment, we have 3 different target angles (90angle, 78.75angle,101.25angle) and three different target distances in each angle

(Amplitude 1, Amplitude 2, Amplitude 3). Our statistical model is a 3x3 ANOVA with two independent variables (Target Angle, Target Distance). A schematic representation of the design matrix is provided in Supplementary material.

The first level general linear model analysis contained nine regressors (90angle A1, 78.75 angle A1, 101.25angle A1, 90angle A2, 78.75 angle A2, 101.25 angle A2, 90 angle A3, 78.75 angle A3, 101.25angle A3) from all the possible combinations between the conditions of the two variables. Six parameters generated during motion correction were entered as covariates, along with a constant column for each session, modeling the baseline voxel activation.

In order to avoid cost in activation for our factorial ANOVA we used the "Partitioned Error Method". We created simple contrasts from the first level analysis (subject-specific). Then, the first level contrast images from all participants were entered into a second-level group analysis, where we applied t and F contrasts. Then T statistical maps were created for the Main effect of Target distance, Main effect of Target angle and Interaction effect.

Results for the main effects were thresholded at cluster-level to  $p < 0.05$  corrected for familiar wise error, extent  $k > 10$ . For the interaction effect, the most lenient voxel-wise threshold of  $p < 0.001$  uncorrected was used, as we expected the interaction effects to be notably smaller. Small volume correction in 10 mm spherical volume centered on the peak activations was applied in areas of a priori interest.

Results are reported in MNI space, ordered by decreasing z-coordinate. The anatomical labels were taken from AAL atlas (Tzourio -Mazoyer et al. 2002) incorporated in the WFU PICK Atlas Tool (Maldjian et al. 2003).

## 2. ROI Analysis

After the whole-brain analysis was completed, we conducted a region of interest (ROI) analysis to explore specific contrasts using MarsBaR Toolbox for SPM (<http://marsbar.sourceforge.net/>). Spherical ROIS of 5mm diameter were defined from coordinates showing significant activation for each effect in the second level analysis. Mean beta values were extracted for simple contrasts derived from the first level analysis, for each participant for each ROI. The



parameter estimates were then entered into ANOVA and t -tests to test for differences in each ROI.

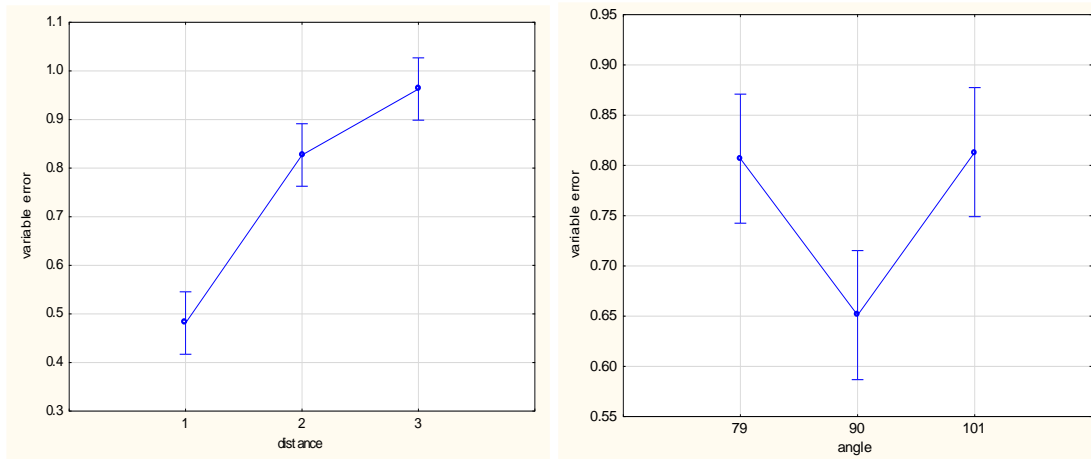
## Results

### Behavioral Data Results

**Figure 3** shows the modulation of the standard deviation of the Mean error (Variable Error) for different target distances and directions. The variance of the direction error (DE) increases significantly with increasing target distance ( $F_{2,378} = 57.8, p < 0.00$ ). It is also significantly affected by target angle ( $F_{2,378} = 7.9, p < 0.000$ ). Variable Error is larger for 78.75 and 101.25 deg. angles compared to the 90 deg. angle, replicating the classic oblique effect (larger accuracy for cardinal axis angle compared to oblique axis angles). This oblique effect scales for different distances and there is no distance by angle interaction ( $F_{4,378} = 0.61, p = 0.65$ ) showing that the modulation of variance with direction is not affected by target distance. The same results are observed when excluding the smallest distance 1. Table 1 displays the results of the ANOVA.

**Figure 4** shows the modulation of the Mean error with target direction for all subjects for the three different target distances. There is no significant effect of target distance on mean direction error ( $F_{2,384} = 2.16, p = 0.12$ ), while the effect of target angle is highly significant ( $F_{31,384} = 45.89, p < 0.00$ ). The mean error varies with target angle and is positive for 101.25 deg, negative for 78.75deg and 0 for 90deg replicating the oblique effect towards the diagonals. The variation though of mean error with angle (diagonal oblique effect) is larger with increasing distance, as shown by the significant distance by angle interaction. ( $F_{31,384} = 20.83, p < 0.000$ .) This interaction remains significant even when excluding distance 1 (smallest distance). **Tables 2 and 3** display the results of the ANOVA.

In brief, our behavioral data results demonstrated for the Mean error: significant main effect of angle, no main effect of distance, significant distance by angle interaction and for the Variable error: significant main effect of angle, significant main effect of distance, no distance by angle interaction.



**A.**

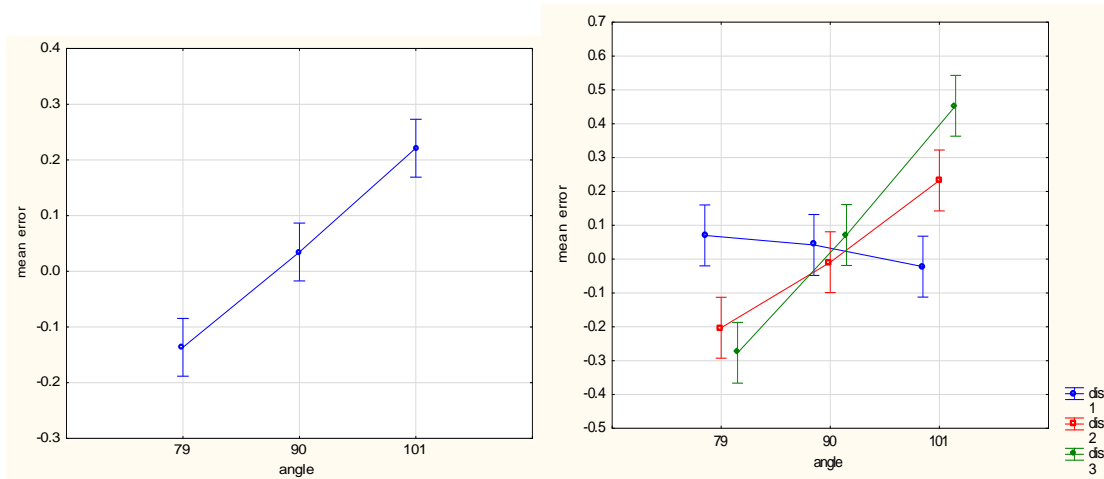
**B.**

**C.**

**Figure 3:** Plot of mean of the SD of DE for arrow endpoints for all subjects **A.** for each Target distance. **B.** for each Target angle **C.** for each Target distance and each Target angle. Separate symbols and line patterns represent the values for the three different target distances.

**Table 1:** ANOVA Results for the Variable Error

Effect	Univariate Tests of Significance for variable (data_subj.sta) Sigma-restricted parameterization Effective hypothesis decomposition				
	SS	Degr. of Freedom	MS	F	p
Intercept	<b>221.7725</b>	1	221.7725	<b>1611.857</b>	<b>0.000000</b>
distance	<b>15.9057</b>	2	7.9529	<b>57.802</b>	<b>0.000000</b>
angle	<b>2.1757</b>	2	1.0878	<b>7.907</b>	<b>0.000433</b>
dist*angle	0.3401	4	0.0850	0.618	0.649907
Error	52.0083	378	0.1376		



**A.**

**B.**

**Figure 4:** Plot of mean of DE for arrow endpoints for all subjects **A.** for each Target angle **.B.** for each Target angle and Target distance. Separate symbols and line patterns represent the values for the three different target distances.

**Table 2:** ANOVA Results for the Mean Error using all distances

Effect	Using all distances				
	SS	Degrees of Freedom	MS	F	p
Intercept	<b>0.61197</b>	1	0.611967	<b>6.80502</b>	<b>0.009451</b>
Distance	0.38901	2	0.194504	2.16287	0.116416
Angle	<b>8.25327</b>	2	4.126634	<b>45.88779</b>	<b>0.000000</b>
dist*angle	<b>7.49249</b>	4	1.873122	<b>20.82895</b>	<b>0.000000</b>
Error	33.99309	378	0.089929		

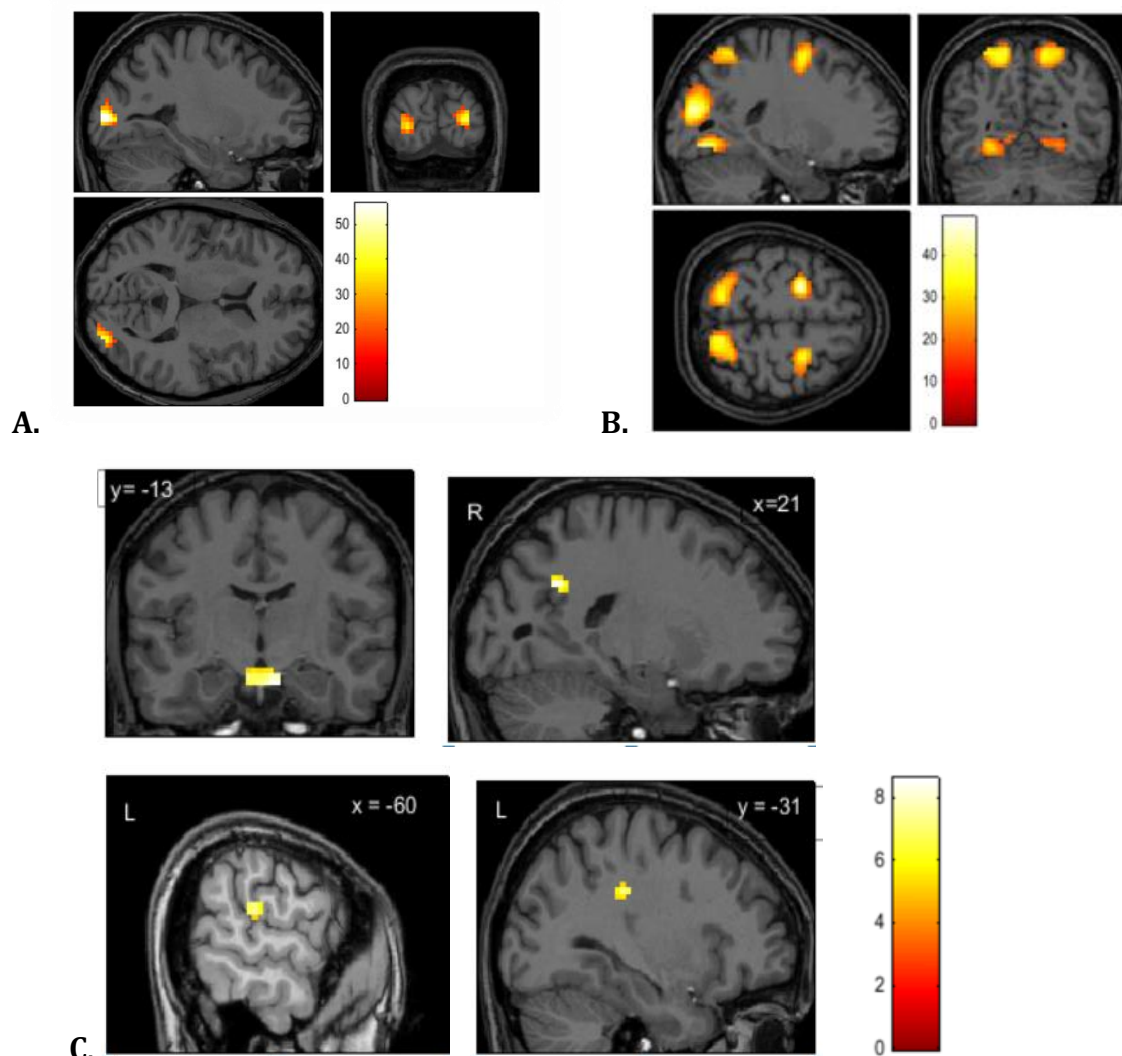
**Table 3:** ANOVA Results for the Mean Error using only distances 2 and 3

Effect	Only for distances 2 and 3				
	SS	Degrees of Freedom	MS	F	p
Intercept	<b>0.51579</b>	1	0.515789	<b>4.23827</b>	<b>0.040550</b>
distance	0.37007	1	0.370071	3.04090	0.082410
angle	<b>14.61754</b>	2	7.308769	<b>60.05671</b>	<b>0.000000</b>
dist*angle	<b>0.93583</b>	2	0.467915	<b>3.84489</b>	<b>0.022655</b>
Error	30.66784	252	0.121698		

## Neuroimaging Data Results

### 1. Whole Brain Task Results

The 2 way - ANOVA revealed a significant main effect of Target Distance in occipital, parietal and frontal lobes bilaterally (at p-value < 0.05 FWE corrected). Main effect of Target Angle was found significant in regions restricted in the occipital lobe (at p-value 0.05 FWE corrected). For the interaction effect: Target Distance x Target Angle small regions were activated, when we applied a p<0.001 uncorrected threshold. These regions include the right precuneus, the left parietal operculum, the left temporal gyrus and a brain stem region near to the right parahippocampal area. No Interaction effect was found at the stricter threshold of p < 0.05 FWE corrected. (Fig. 5, Tables 4,5).



**Figure 5:** Whole-Brain ANOVA results. **A.** Main effect of Target Angle **B.** Main effect of Target Distance. **C.** Interaction effect. Results were thresholded at p< 0.05 FWE corrected for the two main effects. For the Interaction effect results are displayed at p<0.001 uncorrected.

**Table 4:** Whole-brain task fMRI for the two main effects

H	Regions	Cluster size	p(FWE)	Z	B.A.	x, y, z
<b>Main effect of Target Distance</b>						
L	Calcarine	1709	0.000	6.96	Visual Assoc (18)	-6, -88, -8
	Superior frontal gyrus	131	0.000	6.84	BA6	-24, -4, 52
	Superior parietal lobule	146	0.000	6.26	BA7	-18, -64, 58
R	Superior frontal gyrus	144	0.000	6.26	BA6	27, -1, 58
	Superior parietal lobule	163	0.000	6.25	BA7	12, -64, 55
<b>Main effect of Target Angle</b>						
L	Medial occipital gyrus	35	0.002	6.51	Visual Assoc (18)	-18, -97, -2
	Lingual gyrus	12	0.045	5.89	Visual Assoc (18)	-21, -88, -11
R	Medial occipital gyrus	94	0.000	7.14	Visual Assoc (18)	27, -88, 7
	Right inferior occipital gyrus	25	0.006	5.55	BA19	45, -73, -5

H, hemisphere; L, left; R, right; Z, Peak Z - score; B.A., Brodmann's area; x, y, z, MNI coordinates; P, p-value < 0.05 corrected for family -wise error.

**Table 5:** Whole-brain task fMRI for Interaction effect

H	Regions	Cluster size	p*	p**	Z	B.A.	x, y, z
<b>Interaction effect: Target Distance x Target Angle</b>							
L	Superior Temporal gyrus	23	0.094		4.01	BA40	-60, -31, 19
	Rolandic operculum	28	0.067		3.87	-	-30, -31, 31
R	Precuneus / Post Cingulate	13	0.198	0.009	4.24	BA31	21, -58, 31
	Para hippocampal area	48	0.021		4.39	-	9, -13, -23

H, hemisphere; L, left; R, right; Z, Peak Z-score; B.A., Brodmann's area; x, y, z, MNI coordinates; p-value P\* voxel level uncorrected p<0.001, p-value P\*\*, p < 0.05 small volume correction with 10 mm sphere for regions of a priori interest.

## 2. ROI Results-Simple effects

In order to explore which contrasts drove the effects in our whole brain analysis, we used spherical ROIS of 5mm radius defined by the peak – activations in our second level analysis. We then analyzed the simple differential effects of interest both for the main effects and the interaction effect.

### Target Distance

For the Main effect of Target Distance (Amplitude) 5 ROIS were created from the 5 clusters that showed significant activation in group analysis :1) the calcarine ( CalC; peak MNI coordinates -6 -88 -8 [ x y z] ) ; (2) the left superior frontal gyrus ( L\_SFG ; peak MNI coordinates -24 -4 52 [ x y z] ) ; (3) the right superior frontal gyrus (R\_SFG; peak MNI coordinates -18 -64 58 [ x y z] ) ; (4) the left superior parietal lobe (L\_SPL ; peak MNI coordinates -18 -64 58 [ x y z] ) ; (5) the right superior parietal lobe (R\_SPL; peak MNI coordinates 12 -64 55 [ x y z] ).

In these ROIS, we examined simple contrasts of Amplitude A1, A2, A3 (derived from the 1<sup>st</sup> level analysis). Beta values from each person were extracted for A1, A2, A3 contrast and entered a repeated measures ANOVA with 3 variables.

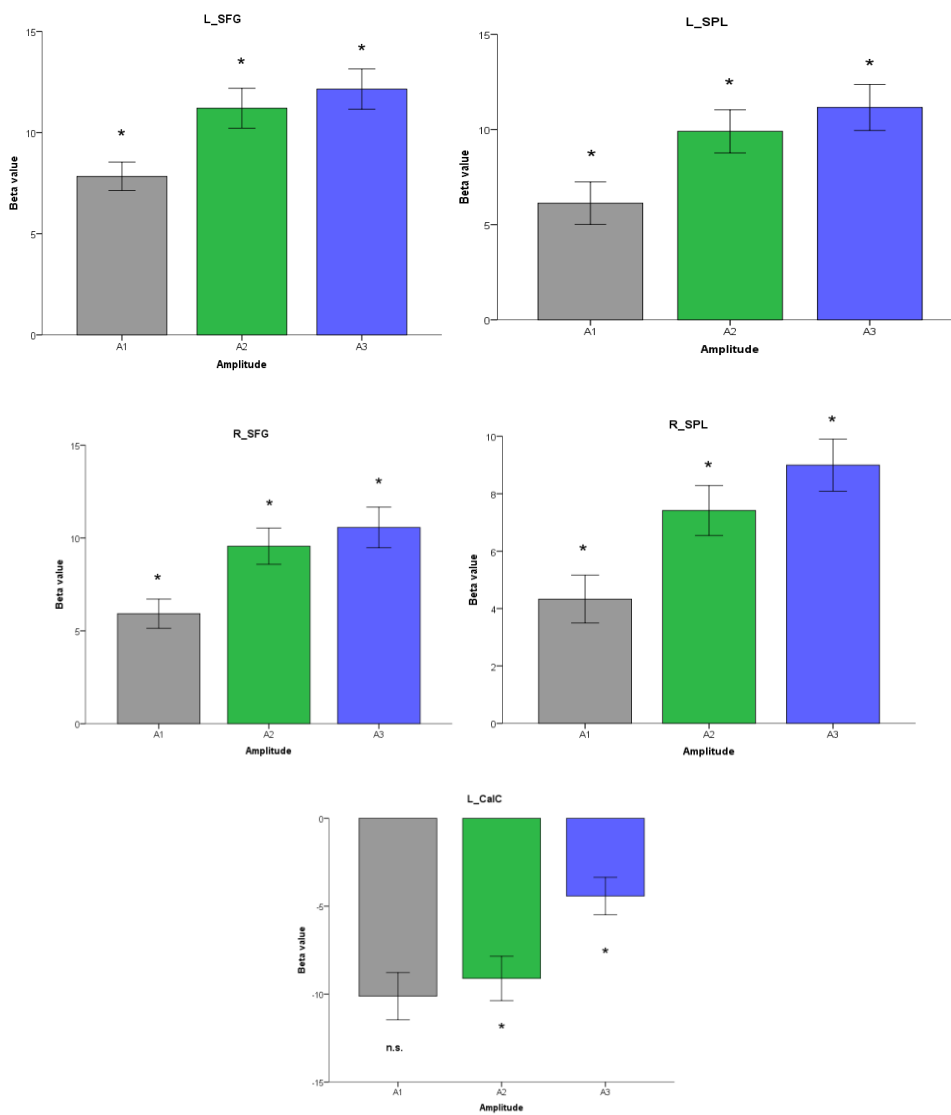
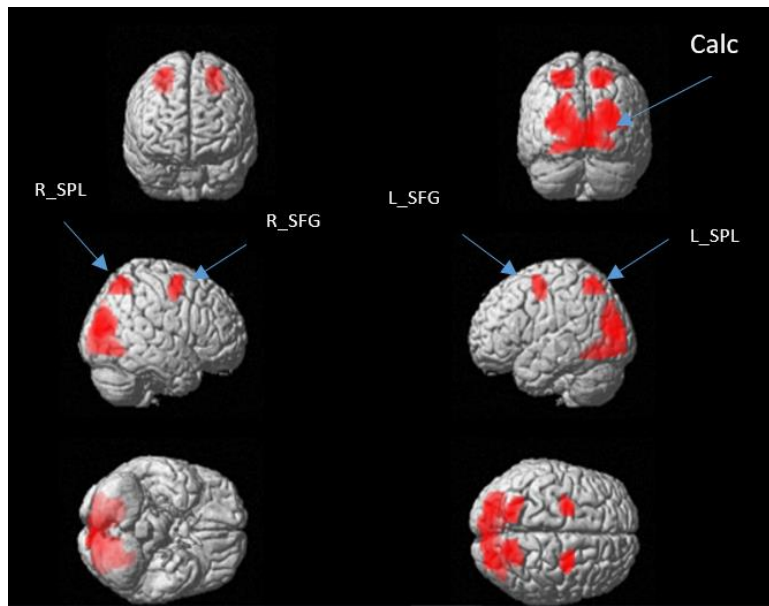
Our specific hypothesis was an overall increase in signal (both at peak-level and at cluster- level) with an increase in amplitude (distance of the target), including all the areas that are involved in the main effect of amplitude.

In ROI L-SFG, a repeated measure ANOVA with a Greenhouse - Geisser correction determined that mean beta value differed significantly between the 3 levels of Amplitude [ $F(1.346, 33.360) = 46.146, p < 0.001$ ]. Post - hoc testing using the Bonferroni correction revealed that beta value increased by an average of 3.369 units from Amplitude A1 to A2 ( $p < 0.001$ ) and then increased by an additional 0.944 units from A2 to A3. ( $p < 0.001$ ). Similar results were observed in the other ROIS of Amplitude in frontal, parietal and visual areas (**Fig. 6, Table 6**).

In each different cluster, the BOLD signal was higher for the condition A3-A1 comparing to the condition A2-A1. Thus, we conclude that there is a modulation of signal (both in intensity and magnitude) with the gradual increase of the target distance ( $A3 > A2 > A1$ ).







**Figure 6:** Results from the ROI analysis, calculated for the main effect of Target Distance (Amplitude). **A.** Top, rendered brain images showing the cortical ROIs of Target Distance. **B.** Bottom, Bar plots represent mean beta values for the three conditions.

**Table 6:** ANOVA results and Post hoc differences between levels of Target distance in ROIs of Target distance.

ROI	N	Mean	SD	F	p	Post-hoc
Difference						
<b>L_SFG</b>				F(1.346,33.360)	0.000	
	26	4.31	0.6	46.146**		A3 > A1*
	26	3.37	0.44			A2 > A1*
	26	0.94	0.32		0.02	A3 > A2*
<b>L_SPL</b>				F(1.2,30.01)	0.000	
	26	5.03	0.83	36.21**		A3 > A1*
	26	3.77	0.54			A2 > A1*
	26	1.26	0.41		0.016	A3 > A2*
<b>R_SFG</b>				F (1.33,33.3)	0.000	
	26	4.65	0.64	46.97**		A3 > A1*
	26	3.63	0.5			A2 > A1*
	26	1.00	0.31		0.01	A3 > A2*
<b>R_SPL</b>				F (1.47,36.64)	0.000	
	26	4.66	0.60	49.12**		A3 > A1*
	26	3.09	0.45			A2 > A1*
	26	1.58	0.35			A3 > A2*
<b>Calc</b>				F(1.47,36.84)	0.000	
	26	-5.70	0.80	45.97**		A3 > A2*
	26	-4.69	0.58			A2 > A1*
	26	-1.00	0.49		0.144	A3 > A2

\*\*p<0.001, \*p<0.05 Bonferonni correction for multiple comparisons.

### Target Angle

For the Main effect of Target Angle 3 ROIS were created from the 3 clusters that showed significant activation in group analysis: (1) the right medial occipital gyrus (R\_MOG ; peak MNI coordinates 27 -88 7 [ x y z ] ) ; (2) the left medial occipital gyrus ( L\_MOG; peak MNI coordinates -18 -97 -2 [ x y z ] ) ; (3) the left lingual gyrus ( L\_ LgG ; peak MNI coordinates -21 -88 -11 [ x y z ] ).The right

inferior occipital gyrus ( R\_IOG ; peak MNI coordinates 45 -73 -5) area was excluded from ROI analysis because it included voxels at the edge of the brain.

In these ROIS we examined simple contrasts of Target Angle 90angle, 78.75angle and 101.25angle (derived from the first level analysis). Beta values from each subject were extracted for these 3 contrasts and entered a repeated measures ANOVA with 3 variables. Our analysis intended to compare the BOLD response between cardinal and diagonal directions exploring the classic visual oblique effect.

In ROI R\_MOG, a repeated measures ANOVA with a Greenhouse-Geisser correction showed that mean beta value differed significantly between the three target angles [F (1.444,36.112) = 40.612,  $p < 0.001$ ]. Bonferroni post-hoc tests showed significantly higher beta value for 78.75 angle (mean = 7.29; SD= 6.2) compared to 90 angle (mean = 5.03; SD=5.98,  $p=0.00$ ) and significantly higher beta value for 90 angle (mean = 5.03; SD=5.98) compared to 101.25angle (mean = 3.66; SD=6.04,  $p=0.00$ ). In ROI L\_MOG, a repeated measures ANOVA with a Huynh-Feldt correction revealed a significant main effect of Target Angle in activation [ F (1.633,40.817) =26.9,  $p=0.00$ ]. Bonferroni post hoc tests showed significantly higher beta value for 101.25 angle (mean =2.4; SD= 5.05) compared to 90 angle (mean = 0.35; SD=4.56) and significantly higher beta value for 90 angle (mean = 0.35; SD=4.56) compared to 78.75angle (mean = -0.85; SD=4.78). In ROI L\_LgG , a repeated measures ANOVA with a Huynh-Feldt correction showed that mean beta value differed significantly between the three target angles [ F (1.862,46.539) =25.7,  $p < 0.001$ ]. Bonferroni post hoc tests showed significantly higher beta value for 78.75 angle (mean = 2.64; SD=6.05) compared to 90 angle (mean = 1.6; SD=6.03,  $p=0.00$ ) and significantly higher beta value for 90 angle (mean = 1.6; S D=6.03) compared to 101.25angle (mean = 0.8; SD=6.00,  $p=0.007$ ). **(Fig. 7, Table 7).**

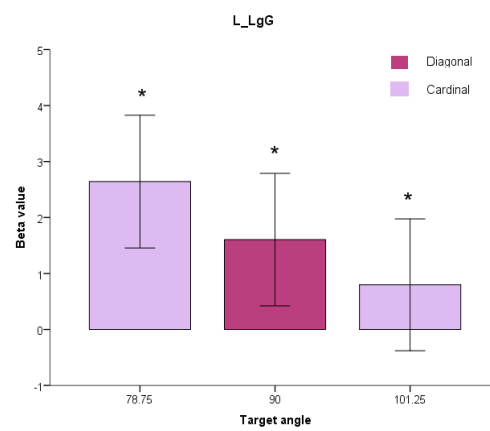
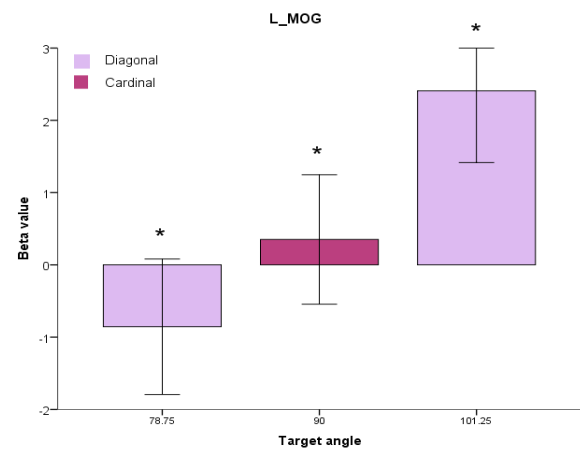
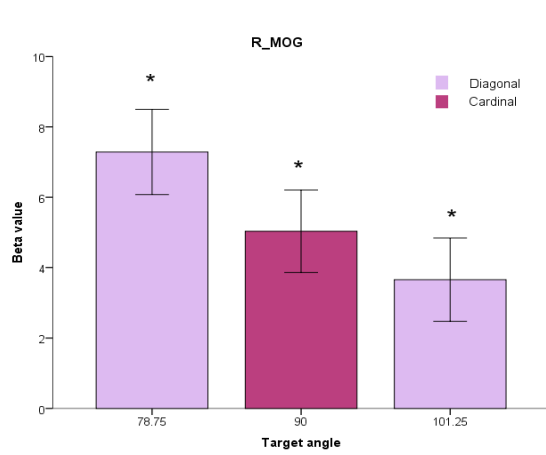
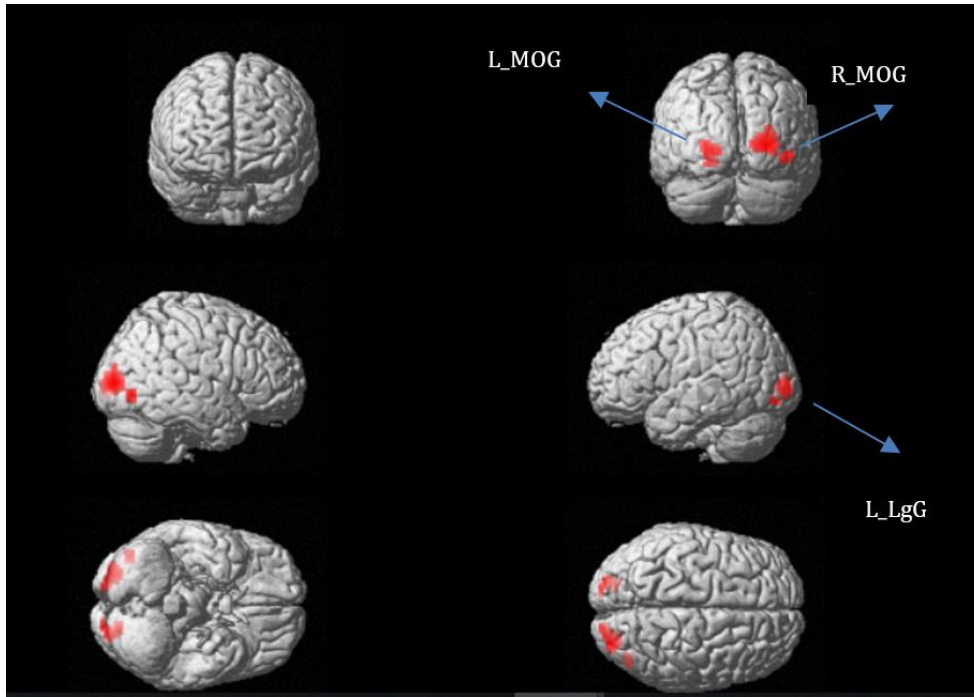
In summary, we demonstrated that in the right middle occipital gyrus the activation was driven by the 78.75 angle (left diagonal), whereas in the left middle occipital gyrus the activation was driven by the 101.25 angle (right diagonal). In the left lingual gyrus, a lateral visual area close to the fusiform gyrus, the BOLD response was driven by the 78.75 angle (left diagonal). In order to explore the differences between diagonal and cardinal directions in the

primary visual cortex we performed another ROI analysis using anatomically defined ROI. We observed a shift in activation towards the diagonal, although the results did not reach statistical significance. (For this extra analysis, see supplementary material).

**Table 7:** ANOVA results and Post hoc differences between levels of Target angle in ROIs of Target angle

ROI	N	Mean Difference	SD	F	p	Post-hoc
R_MOG				F( 1.44,36.11)	0.000	
	26	2.25	0.33	40.61**		78.75angle > 90angle**
	26	1.38	0.34		0.001	90angle > 101.25angle
L_MOG				F (1.63,40.82)	0.000	
	26	2.06	0.34	26.9**		101.25angle > 90angle**
	26	1.20	0.44		0.032	90angle > 78.75angle
L_LgG				F ( 1.86,46.5)	0.000	
	26	1.04	0.23	25.7**		78.75angle > 90angle**
	26	0.81	0.24		0.007	90angle > 101.25angle*

\*\*p<0.001, \*p<0.05 Bonferonni correction for multiple comparisons



**Figure 7:** Results from the ROI analysis, calculated for the main effect of Target Angle. **A.** Top, rendered brain images showing the cortical ROIs of Target angle. **B.** Bottom, Bar plots represent mean beta values for the three conditions 78.75angle, 90angle, 101.25 angle.

### **Interaction: Target Distance x Target Angle**

For the Interaction effect 4 ROIS were created from the 4 regions that showed significant activation in group analysis : (1) a brainstem region close to the right parahippocampal area (R\_SN pr ; peak MNI coordinates 9 -13 -23 [ x y z ] ); (2) the right precuneus (R\_Precuneus ; peak MNI coordinates 21 -58 31 [ x y z ] ); (3) the left superior temporal gyrus (L\_STG ; peak MNI coordinates -60 -31 19 [ x y z ] ); (4) a region close to left Rolandic operculum (L\_ ROL ; peak MNI coordinates -30 -31 31 [ x y z ] ).

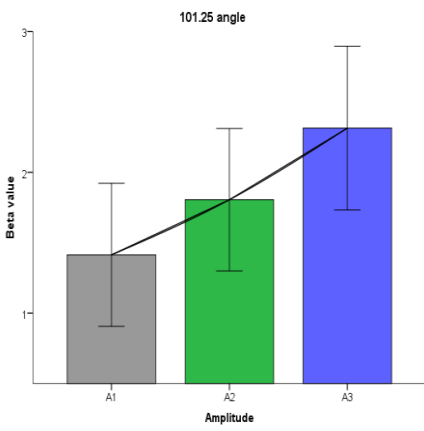
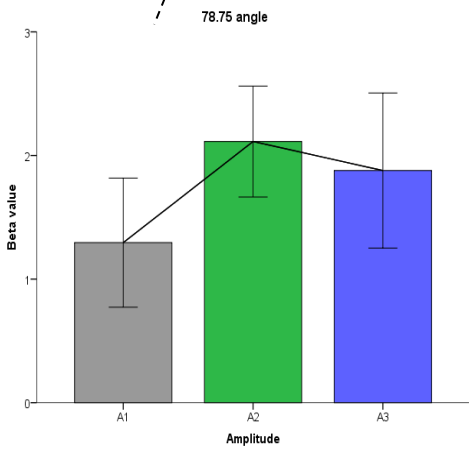
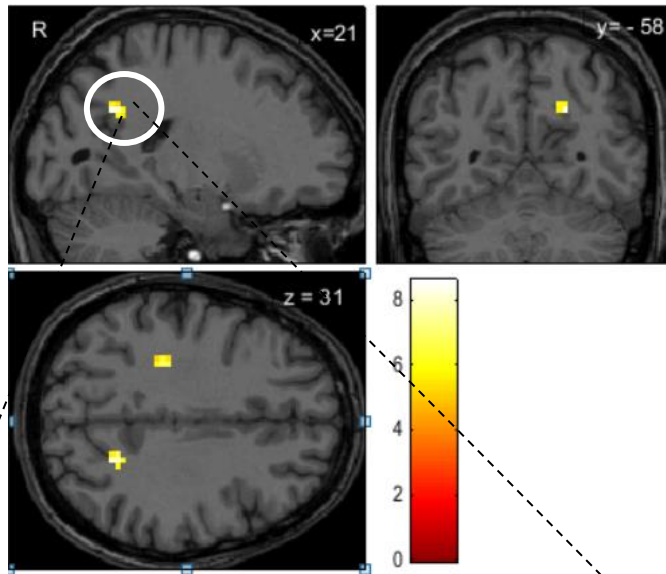
In these ROIS we examined simple contrasts of Interaction effect: 90angleA1, 90angleA2,90angleA3,78.75angleA1,78.75angleA2,78.75angleA3,101.25angleA1, 101.25angleA2,101.25angleA3. Beta values from each subject were extracted for these contrasts. Then we performed a repeated measures ANOVA with two within independent variables Target Angle and Target Distance and Mean beta value as the dependent.

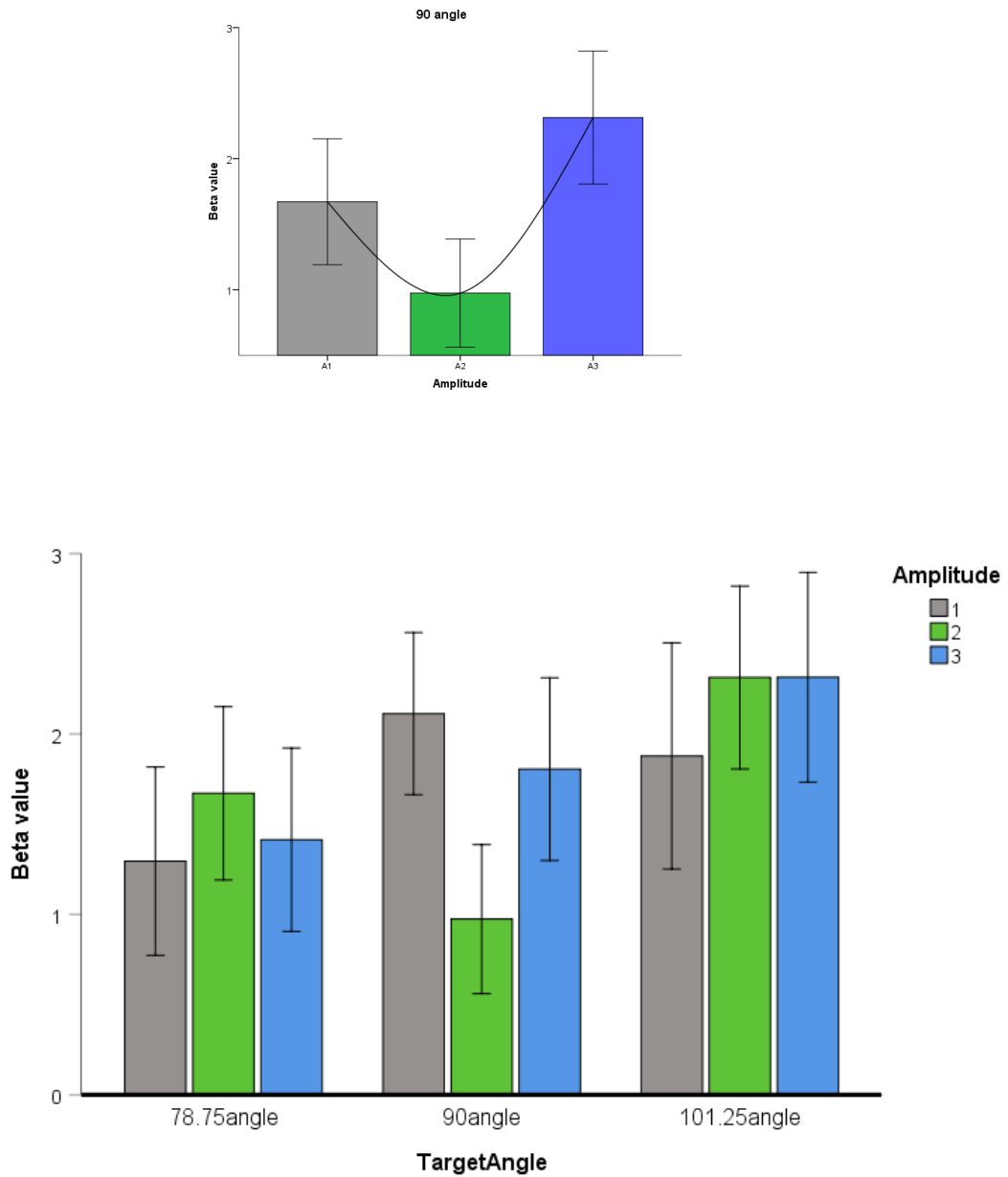
Our specific hypothesis was that there is an area in which the signal increases with the increase of target distance (amplitude) for the two diagonal orientations (78.75 and 101.25 degrees), but not for the cardinal (90 degrees).

The ANOVA of beta coefficients in right precuneus revealed a significant interaction of Target Distance with Target Angle  $F(4,100) = 3.12$ ,  $p < 0.05$ . When evaluating the simple contrasts, we observed a trend of gradual increase of beta with the increase of target distance ( $A3 > A1$ ) in both diagonal directions. We did not observe any specific pattern in the cardinal direction. However, the results from post-hoc differences did not reach significance. **(Fig. 8).**

From the analysis in the other ROIS of Interaction, no significant effects were found and not similar results as in the precuneus. Besides, beta values extracted from these areas had abnormal negative values showing deactivation effects. (see supplementary material).

# Right Precuneus





**Figure 8:** Results from the ROI analysis, calculated for the Interaction effect in R\_precuneus. **A.** Top, Axial, coronal and sagittal brain images showing the cortical ROI of R\_Precuneus. **B.** Bottom, Graphs plot mean beta values extracted from the three conditions.



## **Discussion**

The current study was set up to explore the neural processing underlying the class 2 oblique effect in the reproduction of visual direction in 2D space.

We expected the regions activated by this oblique effect to be clearly dissociated from regions activated by the class 1 oblique effect. We also predicted that class 2 oblique effect would emerge activation in brain regions engaged in higher cognitive processing, whereas class 1 oblique effect would activate areas of early visual processing. We specifically hypothesized that areas replicating the class 2 oblique effect would exhibit greater BOLD activation with decreasing amount of directional information only for the diagonal directions.

Our observations generally verified our initial hypothesis. The interaction effect of target angle with target distance did activate regions beyond visual cortex. What is more, the single differential effects between the three target distances ( $A3 > A2 > A1$ ) for the diagonals in right precuneus indicated a possible neural correlate of this effect.

### **An inverse oblique effect in visual cortex**

In our experiment, differences between the cardinal and oblique directions resulted in activation of areas restricted in the visual cortex, mainly in V2 association cortex. We observed larger responses for oblique directions compared to cardinal in two large clusters in V2 association area and one smaller in the left lingual gyrus, a V2/V3 area. We observed the same pattern of activation oblique > cardinal in V1 primary visual cortex to a smaller extent (extra analysis using anatomical ROI).

Taking into consideration that the two large clusters in the left and right middle occipital gyrus are located near the V1 primary visual cortex, our findings are best explained by the inverse oblique effect. As mentioned in the introduction, more recent fMRI studies have demonstrated a reverse oblique effect, named horizontal effect, finding that mean BOLD responses are greater for oblique than for cardinal orientations in early visual areas V1, V2, V3 and V3A/B

(Serences et al. 2009; Swisher et al. 2010; Mannion, McDonald and Clifford 2010). Here, it is noteworthy mentioning, that conventional orientation decoding from fMRI scans don't actually reflect individual orientation columns, but are instead due to larger-scale orientation maps in V1 (Freeman, Brouwer, Heeger and Merriam 2011). Therefore, it is possible that orientation biases found in the above fMRI studies including ours may be due to these coarse orientation maps and not individual orientation columns. In support to this, studies using methods that measure smaller areas and perhaps individual orientation columns tend to find an orientation preference for cardinal vs oblique in early visual areas. (Yacoub et al. 2008; P. Sun et al 2013; Pratte et al. 2016). Future studies including novel methods like fMRI pattern similarity analysis or unconventional spin echo are needed to shed light to this issue.

Notably, we also found that in the right middle occipital gyrus the activation was driven by the left diagonal, whereas in the left middle occipital gyrus the activation was driven by the right diagonal. On the contrary, in the left lingual gyrus, a lateral visual area close to the fusiform gyrus, the BOLD response was driven by the left diagonal. These results are consistent with the general idea that visual input is processed predominately in the contralateral hemisphere. This characteristic is very strong in the primary visual cortex but decreases at higher levels of the object vision pathway in ventral visual cortex (in both the lateral occipital gyrus, lingual, and fusiform gyrus). (Serenio et al. 1995; Kanwisher et al. 1997).

### **Dissociable effects of Class I and Class II oblique effect**

One of the most important findings in our study was the clear separation of the two oblique effects in terms both of brain activation and behavioral performance.

In our visual reproduction task, subjects' performance revealed the two independent anisotropies in striking resemblance with a previous work of our team (Smyrnis et al. 2014; Balikou et al. 2015). Class I oblique effect

manifested in better accuracy, or less variance in the reproduction of cardinal directions compared to oblique. Class II oblique effect resulted in a distortion of directional space representation, with space expansion in the vicinity of cardinal directions and space contraction in the vicinity of oblique directions. Only the high level oblique effect increased with increasing target distance, as predicted from a theory proposing that this oblique effect is caused by a cognitive process of space categorization.

As far as neuroimaging results are concerned, main effect of Target Angle resulted in 3 big clusters of activation restricted in the early visual cortex: 2 clusters in the V1/ V2 association cortex and one in the left lingual gyrus near the V2/V3 boundary (**Clarke 1994; Sereno et al., 1995; Shipp et al. 1995**). V1, V2 areas are involved at the very early stage of visual processing containing cells responsive to color, form and differences in orientation and shape. V3 areas contain cells responsive to form but not color. All these areas process stimuli early in the visual streaming (**Zeki 1993, Self, M. W., & Zeki 2005**). Considering that main effect of Target Angle represents differences between diagonal directions and cardinal, the above mentioned clusters of activation represent neural loci of visual/class I oblique effect.

On the contrary, Interaction between Target Angle and Target Distance activated small areas beyond the visual cortex: the right precuneus, the left parietal operculum, the left superior temporal gyrus and a brain stem region close to the right parahippocampal area. Notably, all these regions are engaged in higher, more demanding cognitive processes of multisensory integration and certainly they do not consist part of the primary sensory cortex (**Lynch 1980**). Assuming that interaction represents modulation of direction by target distance, the above mentioned areas represent possible loci for class II oblique effect. In accordance with our hypothesis, interaction between orientation/target angle and target distance did not produce any signal in the visual cortex.

While in the literature, “the oblique effect” is used as a unified term and many authors refer to this as a “whole”, there is more and more evidence for a clear distinction between the two effects. To our knowledge, this is the first fMRI study that attempted to show the distinct regions involved in each anisotropy. Most neuroimaging studies investigating orientation bias have focused on visual

oblique effect, using tasks that measure low level vision properties: line detection, intensity discrimination, two-line resolution, Vernier acuity and line-orientation discrimination (**Furmanski and Engel 2000; Sasaki et al. 2006; Mannion et al. 2009, 2010; Freeman et al. 2011**). The first neuroimaging evidence that other superior areas beyond visual cortex may be involved in orientation bias was that of **Nasr and Tootel (2012)**. Via an fMRI paradigm using indoor/outdoor or non-scene stimuli, they showed a preference for cardinal orientations in an area of the medial temporal cortex (ventral stream), known as parahippocampal area. This difference in PPA activity shows that the oblique effect is not simply a result of activity in the striate cortex, but it also involves extrastriate areas such as the dorsal and ventral pathways of visual processing. However, in this study the task used does not emerge a class II oblique effect, as it is defined in ours; measured by the change of mean directional error. What is more, in their paradigm orientation bias did not provoke any signal in the visual cortex, something that was attributed to their less sensitive technique of averaging activity across multiple orientation columns.

### **A magnitude frontoparietal circuitry**

Differences in the magnitude of target distance ( $A3 > A2 > A1$ ) resulted in activation of left visual association area, superior motor area (SMA) and superior parietal lobe (SPL) bilaterally. Whereas not the main purpose of this study, we observed that these results represent a network of brain regions similar to that involved in controlling attention to visual targets.

Humans use cognitive information to direct attention to relevant objects (targets) in a visual scene. Information such as the target's color or location (in our experiment) is represented as a 'perceptual set'. Similarly, advance information about the required response to a target is represented as a 'motor set'. These can be considered together as an 'attentional set', which aids the detection of and response to targets. Such top-down control of attentional

processes activates dorsal posterior parietal and frontal regions of the brain bilaterally in both monkeys and humans. This dorsal frontoparietal system is responsible for the generation of attentional sets (**Corbetta et al. 2002**). Under some conditions, the preparatory activation of the dorsal frontoparietal network extends to visual cortex, presumably reflecting the top-down modulation of sensory representations (**Giesbrecht et al. 2006; Hopfinger et al. 2000; Kastner et al. 1999; Serences et al. 2004; Silver et al. 2007; Sylvester et al. 2007**).

### **Interaction Results**

The main purpose of our study was to identify the neural substrate of class II oblique effect. As mentioned in the introduction, we addressed this issue by using a task of visual reproduction in 2D space, in which the anisotropy attributed to this effect emerges well. Our core hypothesis was that modulation of target angle with target distance would reveal activation in areas involved in a high-level cognitive processing, representing the nature and properties of class II oblique effect. Our specific hypothesis was that the brain region we are seeking not only would arise from the interaction between target angle and target distance, but also it would exhibit greater BOLD activation with decreasing amount of directional information exclusively for the oblique directions.

The results of our whole brain analysis data support this core hypothesis, as ANOVA revealed a significant interaction effect of the two variables in the right precuneus, the left superior temporal gyrus, the left parietal operculum and a brainstem region close to the right parahippocampal area. Notably, these regions were significant at voxel wise error threshold but were not large enough to create statistically significant cluster. Whereas voxel-based correction for multiple comparisons is regarded as less powerful than cluster-based correction (**Friston et al. 1996**), with this reduced power comes greater spatial precision on the location of effects. In our case, in which we are seeking for a very specific effect, this was expected. In order to compensate for multiple comparisons

problem, we applied small volume correction to region of right precuneus, as a region of a priori interest.

The precuneus anatomically belongs to the medial aspect of the parietal cortex **(Foville 1844; Critchley 1953)**. Recent functional imaging findings in healthy subjects suggest a central role for the precuneus in a wide spectrum of highly integrated tasks including visuo-spatial imagery **(Kawashima et al. 1995; Wenderoth et al. 2005)**, episodic memory retrieval **(Dorfel et al. 2009; Lundstrom et al. 2005; Lundstrom et al. 2003 )**, self-processing **(Kjaer et al. 2002; Lou et al. 2004)** and consciousness **(Fransson and Marrelec 2008; Cavanna, 2007)**. In our task, we predicted from our core hypothesis that interaction effect represents generally highly integrated cognitive process. From the nature of our experiment, visuospatial processing is certainly involved. Besides this, our more specific hypothesis for a modulation in class II oblique effect by increasing cognitive load only for the diagonal directions, interpreted by a categorical model, suggests the engagement of subjects in self-referential processing and consciousness. Moreover, as mentioned in the introduction paragraph, we had some a priori neuroimaging evidence for the possible implication of parietal lobe generally in the class II oblique effect. **(Mikhailova et al. 2015)**.

The selective activation of the right and not the left precuneus may be better attributed to the engagement of subjects in a visuospatial orientation task, since it is known that visuospatial processing is lateralized predominately to the right hemisphere **(Vogel et al. 2003)**. However, it is worth mentioning that the reviewed studies provide no evidence of interhemispheric specialization for the precuneus **(Cavanna and Trimble 2006)**.

To further support our predictions, we conducted exploratory ROI analysis to the right precuneus, a functional ROI with peak coordinates [21 -58 31], originated from the results of second level analysis. Via this analysis, we confirmed our more specific hypothesis for this brain region.

## **The Precuneus and its potential role in Class II oblique effect**

The precuneus, along with the adjacent areas within the posteromedial parietal cortex may have an interesting association with Class II Oblique effect.

The precuneus is located in the medial posterior parietal cortex (**Foville 1844; Critchley 1953**). It is considered as a major associative cortical area because of its broad connectivity with numerous cortical and subcortical structures (**Buckwalter et al. 2008; Colby et al. 1988; Leichnetz 2001; Morecraft et al. 2004; Pandya and Seltzer 1982**). Comparative anatomical studies of the cytoarchitecture and connectivity, in parallel with more recent functional studies have demonstrated activity within the medial parietal areas during certain forms of complex behaviors. These studies suggest that the precuneus plays an important role in a diverse array of highly integrated functions that can no longer be regarded as a simple extension of the visuo-spatial processes subserved by the lateral parietal cortices. It has also been suggested that these different processes may selectively involve distinct regions within the precuneus that participate in distinct functional networks (**Cavanna and Trimble 2006; Margulies et al. 2009; Cauda et al. 2010**).

This central role of the precuneus in cognition is in accordance with the cognitive nature of the class 2 oblique effect that we investigate. The modulation of the systematic directional error with manipulations on cognitive demands confirms a highly integrated basis for this effect. Besides this, the generalization of this orientation bias in different sensory modalities and different tasks suggests a neural loci located in multisensory or major associative cortices.

Looking more specifically into the hypothesis of the origins of the class II oblique effect, we have stated that the most prominent theories assume the representation of orientation in terms of categories (**Essock and Siqueland 1981; Quinn and Bomba 1986; Huttenlocher et al. 1991; Huttenlocher et al. 2004; Baud-Bovy and Gentaz 2012**). According to these Category –Adjustment models, there is a double representation of the orientation of visual stimuli: a veridical one confined to vision and a categorical one at a later stage of processing, where both representations are combined with possible different weights to produce the response. In this theoretical framework, the double

representation of visual stimuli provides an advantage when the reliability of the low-level representation decreases (decreasing amount of directional information). Under these conditions, the system relies more on categories - an internal representation of orientation and introduces orientation bias.

**Damasio in 1999** first suggested that medial parietal areas together with the secondary somatosensory cortices and insula help subserve the primitive representation of the self in relationship with the outside world (proto-self). Numerous neuroimaging studies nowadays have revealed a central role of the precuneus in a variety of highly-integrated tasks, including visuo-spatial imagery (**Kawashima et al. 1995; Suchan et al. 2002; Astafiev et al. 2003; Wenderoth et al. 2005; Kjaer et al. 2002; Lou et al. 2005**), episodic memory retrieval and self-processing operations (**Kjaer et al. 2002; Lou et al. 2005**). In addition, the precuneus as part of the Default Mode Network is engaged in processes such as retrieval or consolidation of episodic memory, conscious representation of information in the form of mental images and spontaneous thoughts, and manipulation of this information for problem-solving and planning (**Mazoyer et al. 2001; Fransson and Marrelec 2008**). Interestingly, these diverse functions overlap in certain ways and share a common unifying factor: a conceptual processing operating on internal stores of information (endogenous signals), rather than 'perceptual' functions (concerned with sources of information external to the brain). This notion is totally compatible with the theories of categorization processing mentioned above.

Taking all these together, we suggest an association between the function of the precuneus and the neural process that implements categorization process and gives rise to the class II oblique effect.



## **Summary**

We presented evidence for the existence of a neurophysiological correlate of class 2 /cognitive oblique effect, representing a meaningful set of small brain regions. These areas are clearly dissociated from regions engaged in low level visual processing. Our observations confirm previous behavioral findings suggesting that this orientation bias results from a high level cognitive neural process. In addition, we provided extra evidence for the potential role of the intriguing area of the precuneus in the class 2 oblique effect. Future research is needed to deepen our understanding of orientation bias. To our knowledge, this is the first neuroimaging study that is attempting to dissociate the neural loci of the two well separated effects. These preliminary findings are encouraging and may serve as an impetus for further research.

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