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## Vestibular integration in human cerebral cortex contributes to spatial remapping

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### Abstract

The process of visuo-spatial updating is crucial in guiding human behaviour. While the parietal cortex has long been considered a principal candidate for performing spatial transformations, the exact underlying mechanisms are still unclear.

In this study, we investigated in a patient with a right occipito-parietal lesion the ability to update the visual space during vestibularly guided saccades. To quantify the possible deficits in visual and vestibular memory processes, we studied the subject's performance in two separate memory tasks, visual (VIS) and vestibular (VES). In the VIS task, a saccade was elicited from a central fixation point to the location of a visual memorized target and in the VEST task, the saccade was elicited after whole-body rotation to the starting position thus compensating for the rotation. Finally, in an updating task (UPD), the subject had to memorize the position of a visual target then after a whole-body rotation he had to produce a saccade to the remembered visual target location in space. Our main findings was a significant hypometria in the final eye position of both VEST and UPD saccades induced during rotation to the left (contralesional) hemisphere as compared to saccades induced after right (ipsilesional) rotation. Moreover, these deficits in vestibularly guided saccades correlated with deficits in vestibulo-ocular time constant, reflecting disorders in the inertial vestibular integration path. We conclude that the occipito-parietal cortex in man can provide a first stage in visuo-spatial remapping by encoding inertial head position signals during gaze orientation.

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### 1. Introduction

Space constancy for a moving subject is realised through the remapping of visual information taking place in a cortical network distributed between the occipito-parietal and frontal regions (Pisella & Mattingley, 2004). Such remapping processes implicate multisensory and motor integration in different reference frames (e.g. object-, hand-, body- and gravity-centered) depending on the current motor behaviour (Bremmer, Klam, Duhamel, Ben Hamed, & Graf, 2002; Galati, Committeri, Sanes, & Pizzamiglio, 2001; Graziano & Gross, 1998; Klier, Angelaki, & Hess, 2005; Merriam, Genovese, & Colby, 2003; Van Pelt, Van Gisbergen, & Medendorp, 2005; Wilson, Woldorff, & Mangun, 2005). In the context of gaze orientation, the visual scene should be constantly updated using the eye and head position signals

in order to provide a coherent and stable space representation independent of and compensatory for the subject's motion. One major cortical site for multimodal convergence and spatial updating is represented by the parietal cortex. In monkey, the receptive fields of parietal neurons move along with eye movements yielding a constantly remapped visual space (Duhamel, Colby, & Golberg, 1992; Medendorp, Goltz, Vilis, & Crawford, 2003; Merriam et al., 2003). The corollary discharge of the eye movement command is supposed to trigger this neuronal transformation. Accordingly, a similar process encoding head motion signals should take place to insure a stable representation of space during subject's displacements. In monkey, electrophysiological recordings in parietal cortex have identified neural coding of head rotation velocity integration as well as large visual field displacements (indicative of frontal, forward or backward self-motion) (Andersen, Shenoy, Snyder, Bradley, & Crowell, 1999; Bremmer et al., 2002; Kawano, Sasaki, & Yamashita, 1984). The implication of vestibular inputs in visual updating has been mainly suggested in human by behavioural studies of visual-

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vestibular memory contingent saccades (Blouin, Gauthier, van Donkelaar, & Vercher, 1995; Israël, Ventre-Dominey, & Denise, 1999; Klier et al., 2005; Nakamura & Bronstein, 1995). However, understanding of the neural mechanisms and anatomical substrates of computations on visual and vestibular cues that underlie stable space representation during gaze orientation remains incomplete (Israël, Rivaud, Gaymard, Berthoz, & Pierrot-Deseilligny, 1995). In brain-damaged patients, we have demonstrated a co-occurrence of vestibulo-ocular time constant deficits and visuo-spatial disorders suggesting a functional link between the representation of space and the integration of inertial vestibular information in cortex (Ventre-Dominey, Nighoghossian, & Denise, 2003, 2005). Based on this result, we postulate that spatial integration of inertial vestibular signals is computed in the parietal cortex, as distinct from the gain control process that would require other cortical or sub-cortical structures. In contrast to numerous monkey studies, there are only few reports investigating the cortical mechanisms related to the contribution of head motion signals in visuo-spatial remapping in humans.

In the current study we address this question in a patient with a right occipito-parietal lesion by using different visual and vestibular memory contingent saccade paradigms. We demonstrate for the first time in human the crucial role of the occipito-

parietal cortex in the spatial integration of vestibular cues that are combined with visual cues to achieve visual space remapping during head motion.

## 2. Material and methods

We investigated visual spatial updating during vestibularly guided saccades in a 28-year-old right-handed male patient (JF) with partial hemianopia due to a right occipito-parietal cortical lesion (Fig. 1). Three years before the examination, JF underwent cortical surgery for a stroke due to an arterio-venous malformation. As shown in Fig. 1, the anatomical MRI images reveal that the cortical lesion involved the middle and inferior occipital cortex (Brodmann areas: BAs 17–18–19) spreading medially in the cuneus and anteriorly in the temporal gyrus (BA 37) and in the inferior parietal lobe (BA 39). At the time of the examination, the patient had completely recovered from any motor (hemiplegia) and sensory (hemiparesia and neglect) deficits except for the left visual field that was spared in the parafoveal region up to about 10° on the horizontal meridian. Apart from his cerebral stroke, JF had no history of ophthalmological, vestibular and psychiatric disease. He was alert and had returned to a normal daily working life. The patient's performance was compared to a group of six age-matched and right-handed normal subjects (mean age, 26.5 years; S.D., 3.5; two males and four females). The patient and the control subjects had given their informed consent to participate in the study.

During the test, the subject was seated in the dark on a rotatory chair that supported a LED panel located at a distance of 50 cm in front of the subject. Horizontal and vertical eye movements were recorded by DC electrooculography (EOG). The EOG calibration was performed on 10° and 20° visually guided

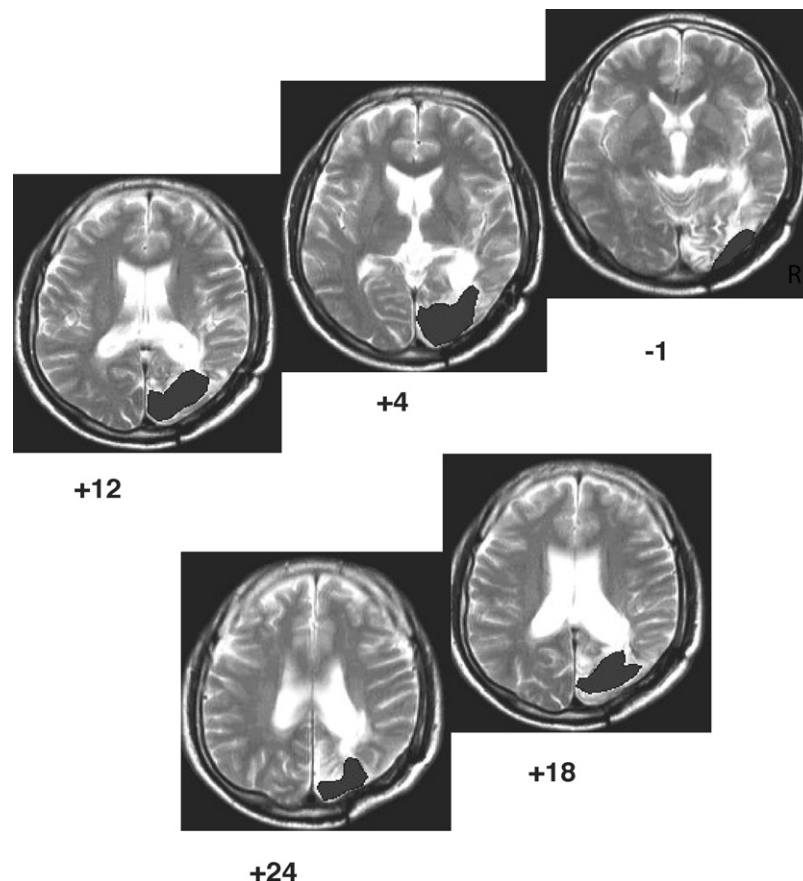


Fig. 1. Location of the right cortical lesion (black area) in the occipital and inferior parietal lobes on transverse sections localized in Talairach and Tournoux (1988). R: right side.

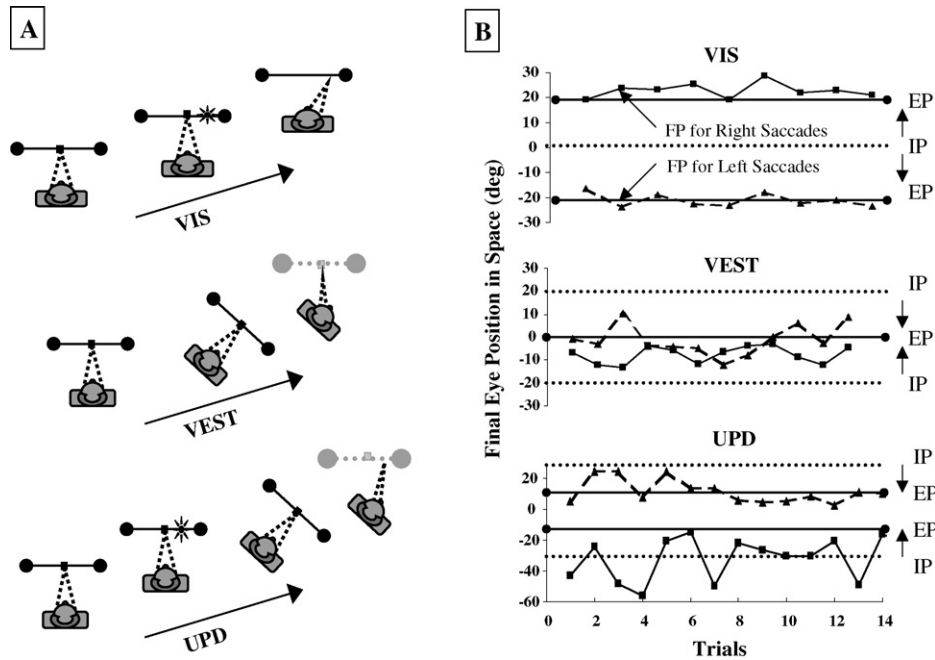


Fig. 2. Final eye position in space and the corresponding task. (A) Sequence of events in the different memory tasks: VIS, visual memory saccades; VEST, vestibular memory saccades; UPD, visual-vestibular saccades. Note: target and chair displacement amplitudes are arbitrary examples in this cartoon representation. (B) Final eye position plotted over the trials and for each task, in patient JF. IP, initial eye position; EP, expected eye position; FP, final eye position. The arrows indicate the expected directions of the saccades from IP to EP. Positive values, right visual space; negative values, left visual space. In each task, the solid lines indicate the rightward saccades and the dotted lines the leftward saccades. In VEST task, the hypometric rightward saccades (solid line) due to a left rotation never reach the expected central (0) position. In the UPD task, note that while the leftward saccades (dotted line) due to a right rotation become progressively more accurate to reach EP, the rightward saccades (solid line) remains more variable with misdirected movements.

saccades. To quantify the possible deficits in visual and vestibular memory processes, we first studied the subjects' performance in two separate visual (VIS) memory tasks and vestibular (VEST) memory tasks. In the VIS task, a saccade was elicited from a central fixation point to the location of a visual memorized target ( $10^\circ$ ,  $20^\circ$  right or left) and in the VEST task, the saccade was elicited after whole-body rotation ( $10^\circ$ ,  $20^\circ$  right or left, constant chair velocity =  $10^\circ \text{ s}^{-1}$ ) to the starting position thus compensating for the rotation (Fig. 2). Finally, in an updating task (UPD) that combined both visual and vestibular memory tasks, the subject had to memorize the position ( $10^\circ$  right or left) of a visual target then after a whole-body rotation ( $10^\circ$  or  $30^\circ$ , right or left, constant chair velocity =  $10^\circ \text{ s}^{-1}$ ) he/she had to produce a saccade to the remembered visual target location in space (Fig. 2). The memorized visual target was presented during 1 s and the memorisation time was randomized between 5.5 and 7.5 s. In VIS and VEST conditions, the trials could require  $10^\circ$  or  $20^\circ$  saccades while in the UPD condition, only  $20^\circ$  saccades were required on the basis of the following possible stimuli combination: trials with  $10^\circ$  right visual target and either: (1) a left  $10^\circ$  or (2) a right  $30^\circ$  rotation and trials with  $10^\circ$  left visual target and either (3) a right  $10^\circ$  or (4) a left  $30^\circ$  rotation. In each condition, each trial was repeated 10 times. At each VEST and UPD trial, the subject had to maintain the gaze on the central visual point moving with the chair in order to prevent any eye movements. On each trial, the subject was instructed to produce a saccade the most accurately as possible once the central point was switched off. After the saccadic movement was completed, the desired target was reilluminated to allow the subject to correct for any mislocation (visual feedback). JF was permitted to release fixation in order to localize and to memorise the most eccentric targets ( $20^\circ$ ) in the hemianopic field, which occurred only in the VIS task. We quantified the subject's performance by the number of misdirected saccades (percentage of errors), the horizontal saccade amplitude and maximal velocity. The horizontal saccade amplitude was measured at the final position before the visual feedback that reflects the final goal and thus the internal spatial encoding. In addition, using sinusoidal (0.02, 0.05, 0.1 Hz at maximal velocity =  $60^\circ \text{ s}^{-1}$ ) and constant velocity rotations ( $60^\circ \text{ s}^{-1}$ ), the vestibulo-ocular reflex (VOR) was analysed for the gain, phase and time constant. For the VOR and the VEST and

UPD vestibular memory saccades, the percentage of asymmetry between the two sides of rotation was calculated by the directional preponderance (DP) of performance as following:

$$DP = \frac{[R - L]}{[R + L]} \times 100$$

where  $R$  is the performance during right rotation and  $L$  is the performance during left rotation. The performance of the patient was analysed by rmANOVA using as the within-subject factors: the tasks (VIS, VEST and UPD) and the side of body rotation (right and left). Specific comparisons between the different within-subject factors were established by using the post hoc Scheffé test. The significance level was accepted at a 95% confidence interval. Moreover, a normal range of performance was established from the control group for each parameter as  $NR = \text{mean value} \pm 2S.D.$  A linear regression analysis was performed on the saccade amplitude versus velocity plot (the so-called saccade main sequence) for further comparison between tasks.

### 3. Results

The saccade final position was significantly task- and direction-dependent in patient JF (task  $\times$  side interaction:  $F(1, 3) = 12.5$ ,  $p < 0.001$ ). While the final position of VIS saccades elicited at the different eccentricities was in the normal range of amplitude with no significant difference between the two hemispaces (post hoc Scheffé,  $p > 0.05$ ) (Fig. 3), the final eye position of VEST saccades was significantly hypometric (post hoc Scheffé,  $p = 0.0013$ ) during rotation to the left (contralateral) space ( $12.4^\circ$  versus NR: 14, 27) as compared to the right (ipsilateral) space ( $21.2^\circ$  versus NR: 11, 24). As illustrated in Figs. 2 and 3, JF was unable to update either right or left retinal

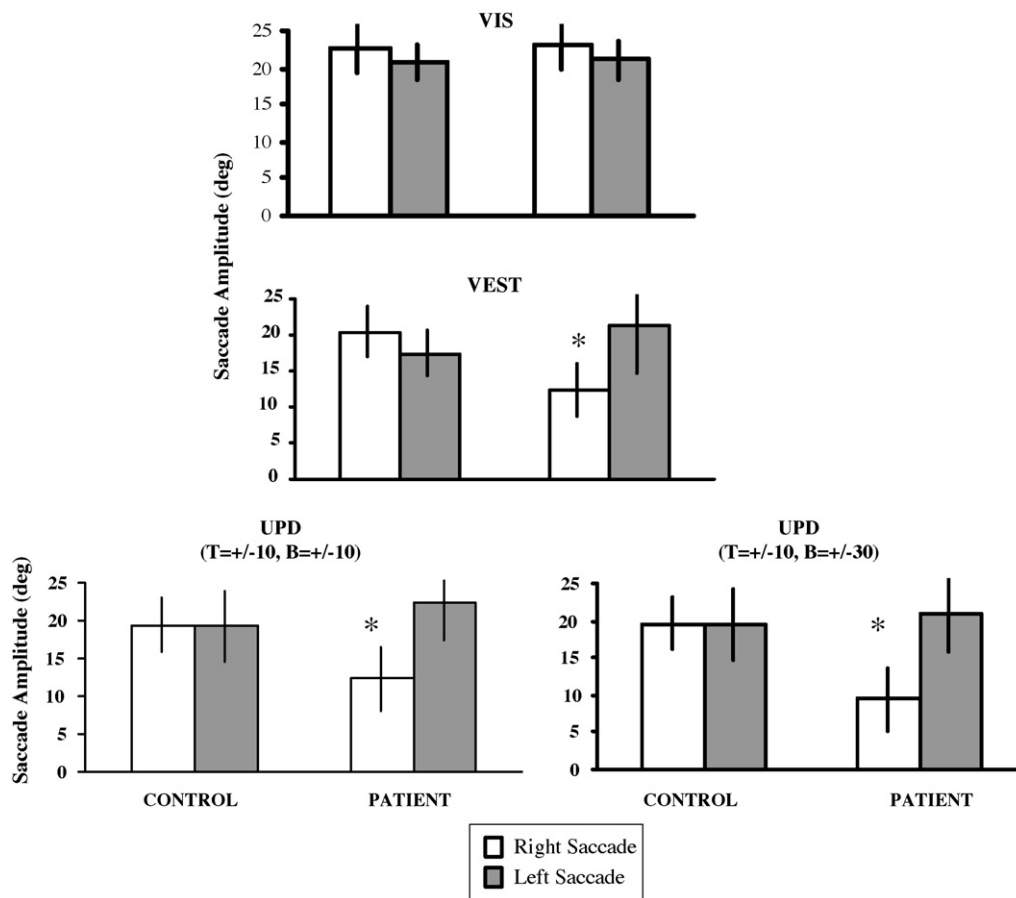


Fig. 3. Mean amplitude of right and left saccades and standard deviation in control group and in patient JF. *T*, visual target eccentricity; *B*, amplitude of the whole-body rotation in degrees; \*, saccade amplitude outside the normal range as defined in Section 2.

errors only when the head was rotated to the left (contralesional) hemispace as demonstrated by: (1) a significant increase of misdirected UPD saccades (40%) compared to the opposite side (6%) and (2) significantly hypometric UPD saccades (rightward saccades) induced after left (contralesional) body rotation as compared to saccades (leftward saccades) induced after right (ipsilesional) rotation (post hoc Scheffé,  $p < 0.01$ ). As represented in Fig. 3, in the UPD task, only the amplitude of the leftward saccades ( $20.8^\circ$ ) induced after right body rotation of patient JF was in the normal range (NR = 10–29). Interestingly, the accuracy of leftward UPD saccades clearly improved over time yielding precise saccade endpoints after the five first trials (Fig. 2). We characterized this asymmetry for vestibular related saccades in terms of directional preponderance using the above formula. This yields abnormal DP of 26 in the VEST task and of 33 in the UPD task. Interestingly, this asymmetry in vestibular integration was reflected in the vestibulo-ocular parameters as a strong asymmetry in VOR time constant (DP = –26), but not in the VOR gain (DP = 2). The saccade asymmetry in both vestibular saccadic tasks likewise reflects this VOR time constant asymmetry. Finally, the saccade amplitude/velocity main sequence was not significantly different between JF and the control group in any tasks (the slopes of the regression lines were included in the normal range).

#### 4. Discussion

Thus, in a patient with a right occipito-parietal damage (including the extrastriate Brodmann areas 18–19–37 and 39), the use of the vestibular signals in visual remapping is impaired only when they are issued from a body motion into the defective visual space. This effect was independent of a pure visual and/or memory defect as the memorized visual saccades (final position) without head motion were normal in both the spared and defective visual fields. Likewise, the normality of the saccade main sequence obtained in the three different tasks allows us to exclude any saccadic motor deficits.

This study demonstrate for the first time that the vestibular integration previously described in the parietal cortex is crucially involved in visual space remapping. Interestingly, in our patient we observed a learning effect revealed by the improvement of the accuracy of updated saccades induced after whole-body rotation into the normal hemispace. This learning behaviour was never present in the other direction suggesting a failure to compute visual and vestibular integration subtending visual remapping after body rotation towards the defective hemispace. In a previous work using memory contingent saccades in normal subjects, we demonstrated that such a learning effect was closely dependent on the presence of visual feedback that allows the subject

to correct for mislocalization errors (Israël et al., 1999). We postulate that in contrast to vestibular memory saccades, the visual/vestibular updated saccades requires a more complex computational process that needs a short phase of learning.

Finally, another point of particular interest concerns the comparison of the saccadic performance to the vestibulo-motor performance that points out the vestibular mechanisms subtending the spatial updating process. We know that the vestibulo-ocular system is operating on the basis of two components: one related to an inertial vestibular storage mechanism characterized by a time constant and the other related to a gain control mechanism (Katz, Vianney de Jong, Buettner-Ennever, & Cohen, 1991). Interestingly, the vestibulo-ocular deficits observed in our patient revealed a clear dysfunction in the slow inertial vestibular path often described as a multimodal integrator subtending spatial representation (Ventre-Dominey et al., 2003, 2005; Wearne, Raphan, & Cohen, 1997). When analysing the directional preponderance of our patient's performance, while the vestibular gain was near normal, the magnitude of the inertial vestibular deficits (time constant directional preponderance) was strikingly comparable to the magnitude of those in the visual-vestibular saccades. Accordingly, in right brain-damaged patients the co-occurrence of vestibulo-ocular time constant deficits and visuo-spatial disorders (neglect) suggests a functional link between the representation of space and the integration of inertial vestibular information (Ventre-Dominey et al., 2003). In accordance with our previous observation, the current results suggest that the inertial vestibular cues might be combined with visual cues in the occipito-parietal cortex for purpose of space constancy of gaze orientation during body displacement. Interestingly, Galati et al. (2001) demonstrated that the occipital cortex is engaged in body-centered judgements with spatial pre-processing of visual cues upstream from the parieto-frontal network. Based on Galati's and our observations, we suggest that the occipital and the posterior parietal cortices damaged in our patient are likely involved in the first stages of a bottom-up process of multimodal transformations, including integration of dynamic head position cues necessary for the craniotopic encoding of gaze orientation.

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