Refuting the hypothesis that a unilateral human parietal lesion abolishes saccade corollary discharge

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This paper questions the prominent role that the parietal lobe is thought to play in the processing of corollary discharges for saccadic eye movements. A corollary discharge copies the motor neurons’ signal and sends it to brain areas involved in monitoring eye trajectories. The classic double-step saccade task has been used extensively to study these mechanisms: two targets (T1 and T2) are quickly (40–150 ms) flashed sequentially in the periphery. After the extinction of the fixation point, subjects are to make two saccades (S1 and S2), in the dark, to the remembered locations of the targets in the order they appeared. The success of S2 requires a corollary discharge encoding S1’s vector. Patients with a parietal lobe lesion, particularly on the right, are impaired at generating an accurate S2 when S1 is directed contralesionally, but not ipsilesionally, thought due to an impaired contralesional corollary discharge. In contrast, we hypothesize that failure on the classic double-step task is due to visual processing and attentional deficits that commonly result from lesions of the parietal lobe and imperfect data analysis methods. Here, we studied parietal patients who fail in the classic double-step task when tested and data analysed according to previously published methods. We then tested our patients on two modified versions of the double-step task, designed to mitigate deficits other than corollary discharge that may have confounded previous investigations. In our ‘exogenous’ task, T2 was presented prior to T1 and for longer (T2: 800–1200 ms, T1: 350 ms) than in the classic task. S1 went to T1 and S2 to T2, all in the dark. All patients who completed sufficient trials had a corollary discharge for contralesional and ipsilesional S1s (5/5). In our ‘endogenous’ task, a single target was presented peripherally for 800–1200 ms. After extinction of target and fixation point, patients made first an ‘endogenous’ S1, of self-determined amplitude either to the left or right, before making S2 to the remembered location of the previously flashed target. To be successful, a corollary discharge of endogenous S1—generated in the dark—was required in the calculation of S2’s motor vector. Every parietal patient showed evidence of using corollary discharges for endogenous S1s in the ipsilesional and contralesional directions (6/6). Our results support the hypothesis, based on our previous studies of corollary discharge mechanisms in hemidecorticate patients, and electrophysiological studies by others in monkey, that corollary discharges for left and right saccades are available to each cortical hemisphere.

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Abbreviations: contral = contralesional; FEP1 = final eye position after first saccade; FEP2 = final eye position after second saccade; ipsil = ipsilesional

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Introduction

We scan our visual surrounds by frequently (~3/s) displacing the high resolution fovea using fast eye movements called saccades. The motor command for a saccade is copied and distributed to many brain areas via a ‘corollary discharge’ or ‘efference copy’ (Sperry, 1950; von Holst and Mittelstaedt, 1950) that enables the nervous system to, for example: (i) distinguish between self-generated and externally-generated visual events on the retina; (ii) maintain an updated internal representation of the position of the eyes in the orbit; and (iii) track salient locations in the visual world when the eyes move (Guthrie et al., 1983).

A tool commonly used to study corollary discharges is the classic double-step paradigm (Hallett and Lightstone, 1976; Becker and Jurgens, 1979; Mays and Sparks, 1980; Goldberg and Bruce, 1990). In a typical experiment, a subject fixates a central light spot while two targets (T1 and T2) are rapidly flashed sequentially in the periphery. The subject is required, upon extinction of fixation point, T1 and T2, to make a sequence of two saccades (S1 and S2) in the dark to the remembered location of each target, in the order they were presented. To perform this task correctly and make an accurate S2, the location of T2 initially defined relative to fixation point, must be updated after S1. It is thought that the motor command of S1—i.e. S1’s corollary discharge—is used together with the retinotopic visual vector of fixation point to T2, to calculate S2 (Quiaia et al., 2010).

Influential studies of patients with a lesioned parietal lobe (Duhamel et al., 1992; Heide et al., 1995) showed a significant impairment in completing an ipsilesionally-directed second saccade if it followed a contralesionally-directed first saccade. These authors argued that S1’s corollary discharge, generated by the lesioned hemisphere—particularly a right-side lesion—is not transmitted to the visuomotor areas of the intact hemisphere that generate S2.

Evidence suggests that these reported deficits (Duhamel et al., 1992; Heide et al., 1995) in the double-step task may not be strictly due to a corollary discharge impairment, but rather to visual processing deficits common after lesions of the parietal lobe (Vallar, 1998). In classic double-step sac- cade studies, the targets are flashed very briefly and in quick succession, less than 100 ms apart and in close proximity to each other, within or across hemisfields. In similar situations, patients with parietal lesions cannot distinguish the temporal sequence of stimuli presented in different hemisfields: an ipsilesional stimulus is reported to have been seen first unless a contralesional stimulus precedes it by more than 200 ms (Rorden et al., 1997; Ro et al., 2001; Baylis et al., 2002). Furthermore, parietal patients show an ‘extinction’ phenomenon in which only one of two stimuli is detected when both are presented in the contralesional hemisfield (Vuilleumier and Ralaf, 2000; Baylis et al., 2002). Clearly, these impairments render problematic the determination of the cause of failure on the classic double-step task.

We investigated how hemispherectomy patients track bilateral eye movements via corollary discharge (Rath-Wilson and Guitton, 2015). These patients, who by definition lack all cortex in one hemisphere including the parietal lobe, are able to monitor bilateral S1s via corollary discharge, and generate accurate S2s. This led us to further question the conclusions of previous studies investigating corollary discharge: how could hemispherectomy patients have preserved bilateral corollary discharges, while patients with unilateral lesions of the parietal lobe lack contralesional corollary discharges? Evidence from neurophysiological and lesion experiments in monkeys (Colby et al., 2003; Heiser and Colby, 2006), as well as imaging studies in humans (Medendorp et al., 2003, 2006) support the hypothesis that corollary discharges of bilateral saccades are available to each cortical hemisphere. We hypothesized that patients with parietal lesions may retain the ability to monitor bilateral saccades via corollary discharges, but previous tests failed to reveal this.

In monkeys, lesions of the lateral intraparietal area lead to ‘disrupted metrics’ in saccades to memorized targets (Li et al., 1999). Li and Andersen (2001), realizing that this could explain failure in the classic double-step task, modified the task. Targets were now presented in the reverse order: T1 flashed after T2 such that only the memory of T2 was required, the first saccade in the dark being directly visually triggered. We hypothesized that this variation on the classic task would be more resistant to the negative effects of visual neglect associated with parietal lobe lesions. We used an additional task, dubbed ‘endogenous’, wherein we flashed a single target and asked the patients to make a first saccade, of self-determined amplitude in the dark, before making a second saccade to the previously seen single target.

When our patients were tested using the classic double-step task and analysis methods described in the Duhamel et al. (1992) and Heide et al. (1995) studies, we obtained very similar results, suggesting impaired corollary discharges. However, using the modified version of the double-step task, coupled with an analysis that accepted multiple-step saccades and long (2500 ms) trial duration, we found, in contradiction to the literature, that our parietal patients were able to monitor—via corollary discharge—both ipsilesionally- and contralesionally-directed saccades whether driven by external cues or the self.

Materials and methods

Participants

Six patients with parietal lobe lesions (four left, two right) and two healthy control subjects participated in our study, approved by the Montreal Neurological Institute and Hospital Research Ethics Committee. Participants gave informed and voluntary consent, in accordance with the Declaration of Helsinki. The lesions of our patients...

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(Fig. 1A–E) match quite precisely the lesions of the patient population in Heide et al. (1995): compare their Fig. 1A (black shaded area) and our Fig. 1E (yellow/red area for left and green area for right patients). The lesioned area of Patient PR1 in our study is almost identical to that of the single patient in Duhamel et al. (1992) except that Patient PR1’s lesion does not extend as fully into the frontal lobe. Figure 1F provides further details about each patient, including Posner task scores (normal score = 0); the Posner effect was highest in Patient PL4 and lowest in Patient PR2. Our patients were studied 6–18 years post-injury compared to an average 10 months in Heide et al. (1995). We show here that differences in performance could not be attributed to compensatory strategies developed over time.

Stimuli and apparatus

A participant was seated in a dark room with head restrained by a bite bar. Visual stimuli (MATLAB, Psychophysics Toolbox) were back-projected (Electrohome Marquee 8000 projector, 85 Hz, resolution: 1024 × 768 pixels) onto a screen located 57 cm from the participant. Monocular eye position was recorded by a video eye-tracker (EyeLink 1000, SR research) with 1000 Hz sampling.

Visual stimuli consisted of 0.6° circular light spots. The fixation point, at screen-centre, and all different colour targets were isoluminant and flashed on a black background. In the control and endogenous tasks, fixation point was red and the single target was green. In the exogenous task, fixation point was red and, to help subjects distinguish the order in which targets were to be foveated, T1 green and T2 white. In the classic double-step task, the fixation point and the targets were white.

Experimental design

Figure 2A–G summarizes, for all tasks, the timing information, expected saccadic eye movement sequences, and an example eye movement trace. All blocks contained 60 trials; in the exogenous task, ipsilesional (ipsiL) blocks contained ipsiL-ipsiL and ipsiL-contraL trials and contralesional (contraL) blocks contained contraL-contraL and contraL-ipsiL trials; in the endogenous task, each trial type was run in separate blocks; in the classic task, all trial types were interleaved. For the exogenous and endogenous double-step tasks, the targets were in the horizontal plane and the eye opposite the targets was patched. The classic double-step task was as in Duhamel et al. (1992) and the patient chose which eye to patch. Before each block, the camera was calibrated. Between each trial, the screen was briefly illuminated to prevent dark adaptation. Importantly, subjects were given 2500 ms to complete each trial. IpsiL and contraL define saccades in the ipsilesional and contralesional directions.

In separate blocks, we ran a control task (Fig. 2): after the fixation point was on for 750 ms, a single target (T) appeared for 800, 100, or 1200 ms; fixation point and T were extinguished and a saccade in the dark to T was required (Supplementary Fig. 2 and Supplementary Box 1).

Patients were tested in several different sessions lasting a total of ~12 h, spread over a 3–4 day period with frequent breaks. One right parietal patient (Patient PR2) could not attend all sessions and completed about half the tasks. In two patients (Patients PL1 and PL3) we presented targets at 15° instead of 20°.

Data analysis

For each trial, the target location, target onset, target offset, fixation point onset, fixation point offset and the horizontal and vertical eye position signals were stored online for further offline analysis.

Accepted trials

Data from all trials were inspected visually. Trials were rejected because: (i) there were significant blink/noise artefacts; (ii) initial eye position deviated more than 2° from fixation point; (iii) S1 latencies were <100 ms or >2000 ms from the GO signal; (iv) the first saccade was in the wrong direction; or (v) there was only a single saccade in a double-step task. Supplementary Tables 1–7 show the breakdown of the number of trials accepted in each trial type.

When we replicated Heide et al.’s (1995) analysis, we rejected additional trials on top our own ‘accepted trials’ pool and only looked at the first 1000 ms of each trial. Supplementary Table 8 shows the breakdown of the additional rejected trials.

Accepted multiple-step saccade sequences

Eye position was obtained by digitally differentiating the filtered eye position trace. A saccade was accepted if its amplitude exceeded 1° and peak velocity reached 80°/s; onset when eye velocity first exceeded 30°/s. Saccade reaction time was the time between the GO signal (fixation point-off) and first saccade onset.

In all trial types, parietal patients frequently generated multiple-step saccades to reach a single goal. Each ‘step’ onset and offset times and initial and final eye positions were tabulated. We defined S1 and S2 to be the sum, in a single trial, of the amplitudes of all saccades used to reach T1 and T2, respectively. ΣS1 and ΣS2 could include up to four saccades (S1.1–S1.4 and S2.1–S2.4) although there were no trials in which ΣS1 had four saccades. For every trial, the final eye position (FEP) at the end of the last saccade in each sequence (ΣS1, ΣS2) was dubbed FEP1 and FEP2, respectively. Figure 2G shows an example eye position trace of right parietal patient, Patient PR1, performing the endogenous double-step contraL-ipsiL-X task. Patient PR1 made two endogenous contralesional saccades (ΣS1) and then two saccades (ΣS2) to the remembered location of T, overshot by ~5°.

To ensure consistency in our analyses, it was important to determine reliably the end of ΣS1 and beginning of ΣS2. To do this, we followed Rath-Wilson and Guitton (2015) and used a combination of saccade direction and intersaccadic time interval to determine which saccades were aimed at which targets. We found consistently across patients and trial types that time interval duration provided a good measure of the end of ΣS1 (FEP1) and the beginning of the first saccade in ΣS2 (S2.1). Thus ‘S1 Int. 2’ in Fig. 2G was longer than the time between the two saccades in ΣS1 (‘S1 Int. 1’, Fig. 3B). In any one trial, we used the longest intersaccadic interval to mark the end of ΣS1 and beginning of ΣS2. To validate this empirical criterion, we looked at all the trials in those tasks in which ΣS1 and ΣS2 were in different directions such as in the contraL-ipsiL condition. This provided two methods for
defining the interval which marked the end of $\Sigma S1$ and the start of $\Sigma S2$: (i) the longest intersaccadic time interval as just explained; and (ii) the interval that preceded the reversal of saccade direction. We found congruency between these two approaches in 98.5% of trials. When incongruent, saccade direction reversal was used to distinguish between $\Sigma S1$ and $\Sigma S2$.

Accounting for multiple-step saccades improved patients’ accuracy (see ‘Results’ section). Furthermore, allowing
Patients were tested monocularly, by patching eye opposite target presentation for the modified tasks, and of the patients’ choice for the classic task. (A and B) Exogenous double-step task: T1 and T2 flashed before the sequential saccades in the dark first to T1, then T2. T2 was presented first (800–1200 ms) and T1 second (350 ms). This arrangement provided two advantages: (i) it maximized the accuracy of S1 because it was aimed at T1 that had just been presented; and (ii) T2 was presented for a relatively long time, a feature that countered the effects of neglect. Two exogenous trial types were interleaved within each block: ipsilesional blocks consisted of ipsiL-ipsiL and ipsiL-contral trials; contralateral blocks consisted of contral-contral and contral-ipsiL trials. Targets could appear at 5°, 10°, 20° or 25° in various combinations depending on the trial type. We also ran blocks, interleaved with the others, of visually-guided versions of the exogenous task (not illustrated) in which the target(s) remained illuminated throughout a trial. (C and D) Endogenous double-step task: after simultaneous extinction of the fixation point and single target T, participants were required to generate a first saccade (S1) of self-determined amplitude in the direction indicated by the experimenter, followed by a second saccade (S2) to the location of the previously-seen T (which could appear at 5°, 10°, 20° or 25° or 30°, depending on the trial type). Six block types were run each with a specific trial type. (E and F) Classic double-step task similar to that in Duhamel et al. (1992). After the fixation point (FP) extinguished, two targets (T1 and T2) were flashed in sequence. Targets were off before first saccade began. The patient was required to look, in the dark, to locations T1 and then T2, where targets had been presented. All trial types interleaved. T1 could appear only at ±6° or ±3°, and T2 could only appear at ±2° or ±3°, depending on the trial type, and were sometimes offset by 1.5° down as outlined in Duhamel et al. (1992). We also ran blocks of a visually-guided version of this task (not illustrated) in which the targets were kept visible for 500 ms each; if T1/T2 were not acquired by the time they were extinguished, the trial was discarded, ensuring that these were visually-guided saccades. (B, D and F) Schematic movement sequences depicted by arrows for an example left parietal patient. Dashed lines indicate a saccade that is endogenously-driven, i.e. of self-determined amplitude. A control, memory-guided saccade task in which a single target was presented was also conducted; not shown here, but available in Supplementary Fig. 2A and B and described in the ‘Materials and methods’ section. (G) Sample horizontal eye position trace (filtered with a 20Hz low-pass band filter) for Patient PR1 performing the endogenous contral-ipsiL-X task with target at 25°. The initial endogenous displacement (S1) contained two saccades: S1.1 and S1.2. There were also two saccades in S2 to the target: S2.1 and S2.2, which she overshot by about 5°.
multiple-step saccades did not impede our evaluation of corollary discharge because, for multiple-step saccades to be accurately made, the vector of each step (saccade) must itself be monitored, presumably via corollary discharge. Supplementary Tables 9–15 give the number of saccades generated by each subject to reach a target location expressed as a percentage of each trial type: most subjects on most tasks performed between one and two saccades in $C_6S_1$ and $C_6S_2$. In the analysis of our data using the Heide et al. (1995) approach, we allowed multiple-step saccades, as they did, the first two saccades of each trial, called S1 and S2.

**Corollary discharge**

To determine the performance of subjects across trial types, we performed a series of regression analyses that are further explained in the ‘Results’ section. We only accepted a regression analysis when there were more than six data values available in a given condition. We used a Bonferroni correction to control for multiple comparisons within patients and across trial types.
To verify whether failure on the classic double-step flashed task was due to corollary discharge impairment or visual processing deficits, we assessed each patient’s performance on a visually guided version of the task (Part 3).

Results

We studied the ability of patients with a parietal lesion, to perform modified and classic versions of the double-step task. Each task required the use of corollary discharges that encoded S1’s amplitude, whether S1 was exogenously-driven by a previously seen visual target or endogenously driven (self-determined amplitude). Although the classic double-step literature indicates that parietal patients have a strongly impaired contralesional corollary discharge, we show here that this view is incorrect: using our modified tasks and analysis method, we show that parietal patients could generate and use accurate bilateral corollary discharges. In Parts 1 and 2, we demonstrate the use of corollary discharge in our exogenous and endogenous (first saccade self-generated, not visually-triggered) double-step tasks. In Part 3 we show that our patients have similar deficits to those described by Duhamel et al. (1992) and Heide et al. (1995) when our data are analysed using their methods.

Control, memory-guided saccade task

All patients were accurate in the control, memory-guided saccade task (Supplementary Fig. 2A and B and Supplementary Box 1). The linear relation between overall saccade amplitude and target position, had regression coefficients between 0.6 (Patient PL1) and 0.9 (Patient PR1), indicating that patients could encode target locations, retain these in memory for the long duration (Fig. 3A) of their saccade reaction times (400–800 ms) and make accurate multi-step saccades in the dark (Supplementary Tables 16 and 17). Importantly, this analysis validated our acceptance of multiple-step saccade for estimating S1.

Part 1: Exogenous double-step flashed task

Accepted versus rejected trials

In the exogenous double-step task experiment, out of 2809 trials in six patients across all tasks (Supplementary Tables 2 and 3), we accepted 1554 (55%). We rejected trials principally because subjects generated either only one saccade or made false starts and, in fewer cases, either generated saccades in the wrong order, never initiated the first saccade, or used more than three saccades to reach T1.

The critical paper of Heide et al. (1995) established that parietal patients have impaired contralesional corollary discharges largely on the basis of their failure to generate S2 when S1 was directed contralesionally. Our data suggest this view is incomplete. Two of our left parietal patients, Patients PL2 and PL3, on the contraL-ipsiL trial type, often generated only the first contralesional saccades, S1, with no S2 to T2. Here, we rejected such trials, but both of these patients used a contralesional corollary discharge in the remaining accepted trials.

In our exogenous double-step task, trials in which the targets were shown on the ipsilesional side were, in all patients, more successful than trials in which the targets were shown on the contralesional side (accepted ipsilesional: 66%, contralesional: 44%). This is likely due to the fact that more contralesional trials were rejected due to false starts, indicating a problem suppressing reflexive saccades in the contralesional direction.

Note that the Posner effect score (Fig. 1F) did not correlate with any of the measurable behavioural features of the exogenous double-step task: rejected trials, number of saccades used to reach a target, saccade reaction time, S1 or S2 accuracy.

One subject (Patient PL3) had consistent difficulty interpreting the colours of the targets. Despite repeated explanations and a seemingly thorough understanding of the task, he would look consistently to the T2 location first and the T1 location second. Thus, when presented with an ipsiL-ipsiL condition (Fig. 2B), he made the required movements for an ipsiL contraL condition and vice versa. He also inverted T1 and T2 for the contraL-contral and contral-ipsiL trial types. This behaviour was so consistent that we categorized his trials into the trial types that he was actually performing as opposed to the ones he was asked to perform. Indeed, as these eye movements were performed in the dark, after the targets were extinguished, a corollary discharge was still required to successfully foveate the previously shown target locations (they were simply executed in the wrong order). As his performance on the exogenous task was comparable with that of the other patients (and better than his classic double-step task performance when analysed using previously described methods, as seen in Part 3 below), we hypothesize that longer target presentation times during the exogenous task were sufficient to allow Patient PL3 to overcome possible visual processing and/or attentional deficits that were impeding his performance on the classic double-step task.

Saccade reaction time and intersaccadic time intervals

The mean saccade reaction time of the first saccade (S1.1) in S1 across all trial types for each of the control and exogenous double-step experiments had a considerable range, 200–800 ms, depending on the subject and trial type (Fig. 3A). Across ipsiL-ipsiL and contral-contral trials, the pattern of inter-subject saccade reaction time variability was different, but within a class (e.g. ipsiL-ipsiL, ipsiL-contral) the pattern was similar.

We used a combination of saccade direction and the time interval between saccades to define the end of S1 and start of S2. Figure 3B compares, for all trials in which
there were two saccades in ΣS1—there were too few (or no) trials with three (four) saccades in ΣS1—the time intervals between S1.1 and S1.2 start (lightly shaded bars) and the time intervals between the S1.2 end and S2.1 start (dark bars). The overall long time between ΣS1 start and ΣS2 end emphasizes that it was critically important to give the patients more than the 1000 ms used by Heide et al. (1995) to complete a trial (Part 3). Our subjects were given 2500 ms.

Exogenously-driven saccades to T1: FEP1 accuracy

For each subject, the regression equations between mean FEP1 (that included up to four saccades) and T1 were determined for each of the visually-guided (v-g) and exogenous double-step flashed (f) trial types; ipsiL-ipsiL, contraL-contraL, ipsiL-contraL and contraL-ipsiL (FEP1 vs T1 in Supplementary Tables 16 and 17; example subjects Patients PL1 and PR1 in Supplementary Fig. 3A and B). For every subject on each task (except Patient PL4 who did not complete enough accepted trials to analyse the contraL-ipsiL condition), we found a significant regression coefficient—similar to the control data considered in the previous section—thereby proving that each subject was able to tailor the amplitude of ΣS1 (FEP1) based on T1 for both ipsilesional and contralesional directions in the exogenous flashed double-step task. Importantly, this again supports our multiple-saccade analysis.

Exogenous task: corollary discharge evaluation

To analyse the data for accepted trials we plotted, separately for each trial type, the actual ΣS2 amplitude versus the expected ΣS2 amplitude (= T2–FEP1) that was required to successfully foveate the T2 location for each trial. The data of example Patients PL1 and PR1 are presented in Fig. 3C and D, respectively. One can appreciate visually that the actual ΣS2 varied convincingly with the expected ΣS2. To quantify this, we performed linear regression analyses on these data [see ΣS2 vs (T2–FEP1) in Supplementary Tables 16 and 17]. A significant slope in the expected direction indicated that the participant was performing ΣS2 in the correct direction and of appropriate amplitude. We found, for each subject and for each trial type—except for Patient PL2 in the contraL-contraL condition—that regression coefficients were significant and in the expected direction. (Patient PL4 did not complete enough trials in the contraL-ipsiL condition to adequately evaluate performance.)

Importantly, these data show, across all patients and trial types, that in 20 of 21 trial types we could test, both the left and right parietal patients made ΣS2s of appropriate amplitude and in the correct direction that compensated for variations in ΣS1 across tasks. Equivalent figures for our control subjects are in Fig. 6 of Rath-Wilson and Guitton (2015), and their control regression equations (comparable to our parietal group) are in Supplementary Tables 16 and 17.

Though compelling, the preceding results do not specify unambiguously whether subjects were actually using a motor corollary discharge about the vector of ΣS1 or whether they were making visual vector manipulations to calculate ΣS2 using the retinotopic vectors from fovea to T1 and T2, respectively, as in: ΣS2 = T2 − T1. To resolve this issue, we performed an additional analysis. For each subject and for each trial type, we analysed independently, saccades to two example target combinations for which we had the greatest number of accepted trials and an inter-target distance greater than 5°. We plotted for each trial the ΣS2 amplitude against its respective ΣS1 amplitude and performed a linear regression analysis to evaluate the relationship between variations in ΣS2 and those in ΣS1 (Fig. 4 and Table 1). A linear relationship between the amplitudes of ΣS2 and ΣS1 for a given target combination can only be explained by a subject using corollary discharge information about motor performance in ΣS1 for use in generating ΣS2 (Rath-Wilson and Guitton, 2015). If calculations had been done in visual space there would be no compensation for variations in ΣS1.

Exogenous task: ipsilesional corollary discharge (first saccade is ipsilesional)

Figure 4A, third quadrant, shows results of two example ipsiL-ipsiL tasks for Patient PL1. For each data set, ΣS2 amplitude varied significantly and inversely with ΣS1 amplitude (ΣS2 vs ΣS1 in Table 1). Thus, despite small variation in the distributions of ΣS1 in the ipsiL-ipsiL conditions (due to the patient’s fairly accurate FEP1) and the data points lying well off the single blue dashed line (which indicates perfect performance) Patient PL1’s regression coefficients were significant (Table 1). In the two ipsiL-contraL conditions (Fig. 4C) the regression equations for Patient PL1 were also significant (Table 1). These data together with those in Fig. 3C show that Patient PL1 was using a corollary discharge of ipsilesional ΣS1 in generating either ipsilesional or contralesional ΣS2.

The data for Patient PR1 (ΣS2 vs ΣS1 in Table 1) were not as consistent as for Patient PL1. Indeed, in the ipsiL-ipsiL trial types (Fig. 4B), Patient PR1 did not compensate for the small variations in ΣS1; regression coefficients were not significant. We cannot ascertain whether these results indicate: (i) a lack of corollary discharge; (ii) whether the corollary discharge signal was not precise enough to distinguish small variations in FEP1; or (iii) whether the ‘noise’ in the generation of ΣS2 masked the use of corollary discharge. Despite the uncertainty about Patient PR1’s use of an ipsilesional corollary discharge in ipsiL-ipsiL trials, this patient clearly used an ipsilesional corollary discharge in both examples of the ipsiL-contraL trial type (Fig. 4D), as evidenced by significant regression coefficients.

In summary, every patient who completed the exogenous double-step task (Patients PL1, PL2, PL3, PL4 and PR1) showed evidence of a corollary discharge for ipsilesional ΣS1 in at least one experimental trial type (Table 1).
Exogenous task: contralesional corollary discharge (first saccade contralesional)

The regression coefficients for Patient PL1 (Fig. 4A and C; $\Sigma S_2 vs \Sigma S_1$ in Table 1) were significant for each of the two examples of the contraL-contraL and contraL-ipsiL tasks, indicating functional corollary discharge for contralesional saccades when $\Sigma S_2$ was either contralesional or ipsilesional.

By comparison, the regression coefficient for Patient PR1 was significant in only one of the two contraL-contraL examples (Fig. 4B, third quadrant, ex2; Table 1). Patient PR1 did, however, succeed in using a contralesional corollary discharge in both examples of the contraL-ipsiL trial type (Fig. 4D and Table 1).

In summary (Table 1) of contralesional corollary discharge: (i) every subject, except Patient PR2, showed a contralesional corollary discharge in the contraL-contraL trial type, with a significant regression coefficient for at least one example data set; (ii) every subject showed evidence of contralesional corollary discharge in both examples of the contraL-ipsiL trial types; (iii) Patient PL4 did not provide enough accepted trials in the contraL tasks; and (iv) even Patients PL2 and PL3—whose pattern of rejected trials could have been interpreted as due to a lack of corollary discharge for contralesional saccades because they frequently did not generate $\Sigma S_2$ after a contralesional $\Sigma S_1$—had significant regression coefficients for all accepted trials of the contraL-ipsiL trial type, and most of the contraL-contraL trial types.

These results concerning contralesional corollary discharge differ significantly from those in the literature. Importantly, this was not due to a difference in the size...
or location of our patients’ lesions. Rather, our tests of the same patients in the classic double-step task (Part 3), revealed that the above results differed from those of Duhamel et al. (1992) and Heide et al. (1995) because of: (i) paradigm differences; (ii) our acceptance of multiple-step saccades to reach each target; and (iii) the amount of time allowed to complete each trial.

Control subjects

The control population was very accurate on our exogenous double-step task to both T1 and T2 resulting in an almost perfect correlation between actual and expected ΣS2 amplitudes Rath-Wilson and Guitton (2015). However, within patients, the small variability in their ΣS1 and ΣS2 amplitudes, relative to T1 and T2, respectively, prevented us from evaluating their corollary discharge via regression analyses of the type in Fig. 4 and Table 1.

### Part 2: Endogenous double-step task

**Accepted versus rejected trials**

Of 5348 endogenous double-step trials in six patients, we accepted 2904 (54%) trials. Most rejected trials had false starts (Supplementary Tables 4 and 5) in which the patient, before fixation point was extinguished, made a saccade to the target location, or initiated an endogenously-driven saccade. We accepted 60% (43%) of trials when the first saccade was to be directed ipsilesionally (contralesionally), similar to the results of the exogenous task, further suggesting a deficit in suppressing contralesional saccades (Supplementary Tables 4 and 5).

**S1 start and intersaccadic time intervals**

In the endogenous double-step task, patients often made more than one saccade, both for ΣS1 (endogenously-driven) and ΣS2 (towards the previously seen target). When ΣS1 was directed ipsilesionally, there were fewer multiple-step saccades (mean = 1.4) than when ΣS1 was directed contralesionally (mean = 1.6, Supplementary Tables 12 and 13). This is important because, in studies in which corrective saccades were not evaluated (Duhamel et al., 1992), the second step in ΣS1, for say contraL-ipsiL trials, would be falsely categorized as an erroneous second saccade in the contralesional direction. This would falsely suggest a more frequent lack of corollary discharge for contralesional first saccades.

<table>
<thead>
<tr>
<th>Patient</th>
<th>ipsiL–ipsiL</th>
<th>ipsiL–contral</th>
<th>contral–contral</th>
<th>contral–ipsiL</th>
</tr>
</thead>
<tbody>
<tr>
<td>ΣS2vΣS1</td>
<td>r²(n)</td>
<td>Reg. eq.</td>
<td>r²(n)</td>
<td>Reg. eq.</td>
</tr>
<tr>
<td>PL1(6)</td>
<td>0.34(36)</td>
<td>−0.6x − 11.1</td>
<td>0.74(20)</td>
<td>−0.9x − 6.5</td>
</tr>
<tr>
<td>(ex1)</td>
<td></td>
<td></td>
<td>0.42(30)</td>
<td>−1.5x + 21.0</td>
</tr>
<tr>
<td>(ex2)</td>
<td>0.31(20)</td>
<td>−0.6x − 12.6</td>
<td>0.86(23)</td>
<td>−0.8x + 4.2</td>
</tr>
<tr>
<td>PL2(6)</td>
<td>0.88(21)</td>
<td>−2.3x − 28.2</td>
<td>0.58(23)</td>
<td>−1.3x − 9.8</td>
</tr>
<tr>
<td>(ex1)</td>
<td></td>
<td></td>
<td>0.64(11)</td>
<td>−1.5x + 35.2</td>
</tr>
<tr>
<td>(ex2)</td>
<td>0.68(13)</td>
<td>−0.9x − 22.0</td>
<td>0.26(21)</td>
<td>−0.8x − 2.7</td>
</tr>
<tr>
<td>PL3(6)</td>
<td>0.17(19)</td>
<td>−0.4x − 11.7</td>
<td>0.56(14)</td>
<td>−0.8x − 8.1</td>
</tr>
<tr>
<td>(ex1)</td>
<td></td>
<td></td>
<td>0.12(25)</td>
<td>−0.6x + 16.6</td>
</tr>
<tr>
<td>(ex2)</td>
<td>0.52(12)</td>
<td>−1.2x − 24.7</td>
<td>0.60(10)</td>
<td>−1.6x − 20.9</td>
</tr>
<tr>
<td>PL4(6)</td>
<td>0.88(7)</td>
<td>−1.5x − 19.7</td>
<td>0.36(10)</td>
<td>−0.9x − 6.5</td>
</tr>
<tr>
<td>(ex1)</td>
<td>(5)</td>
<td></td>
<td>(4)</td>
<td></td>
</tr>
<tr>
<td>(ex2)</td>
<td></td>
<td></td>
<td>(3)</td>
<td></td>
</tr>
<tr>
<td>PR1(6)</td>
<td>0.01(21)</td>
<td>−0.3x + 24.0</td>
<td>0.77(15)</td>
<td>−0.8x + 1.0</td>
</tr>
<tr>
<td>(ex1)</td>
<td></td>
<td></td>
<td>0.01(13)</td>
<td>0.1x − 10.7</td>
</tr>
<tr>
<td>(ex2)</td>
<td>0.14(14)</td>
<td>−0.7x + 20.9</td>
<td>0.80(7)</td>
<td>−1.0x + 2.8</td>
</tr>
<tr>
<td>PR2(6)</td>
<td>0.03(10)</td>
<td>−0.3x − 21.3</td>
<td>0.43(10)</td>
<td>−1.5x − 22.9</td>
</tr>
<tr>
<td>(ex1)</td>
<td></td>
<td></td>
<td>0.74(13)</td>
<td>−0.8x − 1.4</td>
</tr>
<tr>
<td>(ex2)</td>
<td>0.16(8)</td>
<td>−0.5x − 23.5</td>
<td>0.81(9)</td>
<td>−1.1x − 6.0</td>
</tr>
</tbody>
</table>

For each patient and for each trial type, the r² value, the number of accepted values in each condition (n), and the regression equation (Reg. eq.) are given above for two example target combinations (ex1 and ex2) in each of the trial types indicated. Reg. eq. and r² values indicate relationship between ΣS2vΣS1: ΣS2 amplitude (y = ) and ΣS1 amplitude (x). Bold type indicates significance, with Bonferroni correction, (<=0.025) within regression equation.

aPatient did not complete enough trials to determine reliable value (n < 7).

bPatient was not available to participate in the task.

Indicates patient whose data is depicted in Fig. 4.

**Endogenously-driven FEP1 range**

We did not want subjects to always generate their endogenous saccades to the same spatial location after fixation point offset because this could create motor memory or practice effects. Therefore, we encouraged our subjects to generate endogenous saccades of various amplitudes. The colour-coded insets in Fig. 5A–F show the FEP1 for each of the accepted trials of each trial type for Patients PL1 (Fig. 5A–C) and PR1 (Fig. 5D–F). Patients PL1, PR1 and all other subjects varied their FEP1 within each trial type within a range of at least 10°.

**Endogenous trials: corollary discharge evaluation**

For the endogenous double-step task, we plotted the actual ΣS2 amplitude in each trial against the expected ΣS2...
amplitude (=T–FEP1) that was required to successfully fixate T’s location. All saccades took place in total darkness and the first saccade was self-determined (endogenously-driven), without any external cue as to FEP1 ([C6S1’s end-point). Therefore, any variations in [C6S2 amplitude that correlated with T–FEP1 could only be explained by the subject’s ability to monitor [C6S1 amplitude internally via corollary discharges and use this information (along with the visual vector between the original fixation point and T) to generate [C6S2. A significant slope in the expected direction indicated that the subject was performing [C6S2 in the correct direction and of appropriate amplitude, indicating an effective use of corollary discharge. The data of example Patients PL1 and PR1 are presented in Fig. 5A–C and 5D–F, respectively. Overall, when the first endogenous [Sigma]S1 was directed ipsilesionally, every patient showed evidence of compensating for its amplitude, as determined by a significant regression coefficient in at least two of the ipsiL-ipsiL, ipsiL-contraL and ipsiL-contraL–X trial types (Fig. 5 and Table 2). This indicates a corollary discharge signal for ipsilesional saccades, because the only information available to the oculomotor system about [Sigma]S1 was the motor command itself. Similarly, and even more surprisingly, for every trial type involving a first contralesional endogenous [Sigma]S1, every parietal patient had a significant regression coefficient, indicating a corollary discharge for [Sigma]S1 under all experimental conditions (Fig. 5 and Table 2; more details available in Supplementary Tables 18 and 19). Equivalent data for control subjects are in Fig. 8 of Rath-Wilson and Guitton (2015). They had very significant regression coefficient across all endogenous tasks (Table 2), indicating accurate corollary discharges for saccades to the left and right and slightly better performance than parietal patients on this task.
Table 2: Endogenous double-step results summary for all accepted trials for each patient

<table>
<thead>
<tr>
<th>Patient</th>
<th>Ipsil-ipsL</th>
<th>Ipsil-contraL</th>
<th>Ipsil-contraL-X</th>
</tr>
</thead>
<tbody>
<tr>
<td>PL1b</td>
<td>0.65(145)</td>
<td>0.5x – 1.3</td>
<td>0.76(100)</td>
</tr>
<tr>
<td>PL2</td>
<td>0.71(139)</td>
<td>0.7x – 2.8</td>
<td>0.23(79)</td>
</tr>
<tr>
<td>PL3</td>
<td>0.40(155)</td>
<td>0.4x – 2.3</td>
<td>0.38(143)</td>
</tr>
<tr>
<td>PL4</td>
<td>0.24(71)</td>
<td>0.2x – 3.4</td>
<td>0.01(22)</td>
</tr>
<tr>
<td>PR1b</td>
<td>0.73(59)</td>
<td>0.9x + 1.5</td>
<td>0.38(121)</td>
</tr>
<tr>
<td>PR2</td>
<td>a</td>
<td>a</td>
<td>a</td>
</tr>
<tr>
<td>Control pop.</td>
<td>0.87(142)</td>
<td>0.9x – 0.7</td>
<td>0.8(132)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>PL1b</td>
<td>0.56(108)</td>
<td>0.8x + 2.6</td>
<td>0.65(138)</td>
</tr>
<tr>
<td>PL2</td>
<td>0.17(70)</td>
<td>0.3x + 12.3</td>
<td>0.46(33)</td>
</tr>
<tr>
<td>PL3</td>
<td>0.55(100)</td>
<td>0.7x + 5.1</td>
<td>0.58(174)</td>
</tr>
<tr>
<td>PL4</td>
<td>0.32(35)</td>
<td>0.4x + 3.2</td>
<td>0.27(32)</td>
</tr>
<tr>
<td>PR1b</td>
<td>0.35(102)</td>
<td>0.3x – 6.1</td>
<td>0.12(87)</td>
</tr>
<tr>
<td>PR2</td>
<td>0.29(43)</td>
<td>0.5x – 5.3</td>
<td>0.67(37)</td>
</tr>
<tr>
<td>Control pop.</td>
<td>0.79(81)</td>
<td>0.9x – 0.9</td>
<td>0.83(165)</td>
</tr>
</tbody>
</table>

For each patient and for each trial type, the $r^2$ value, the number of accepted values in each condition (n), and the regression equation (Reg. eq.) are given above. $r^2$ values indicate relationship between $S_2$ (ipsil) amplitude ($T – FEP_1$). Bold type indicates significance, with Bonferroni correction, ($< 0.017$) within regression equation.

Part 3: Classic double-step task

We have shown that our patients are almost normal in their use of the corollary discharge when: (i) they are tested in our exogenous modified double-step saccade task in which T2 is shown first, T1 second; and (ii) their data are analysed with a method that, notably, allows for multiple-step saccades and a 2500 ms execution time. Given that our conclusions go against accepted ideas that originated in the classic studies of Duhamel et al. (1992) and Heide et al. (1995), it is critically important to show that our patients are similar to theirs when tested in the classic double-step task. We now show that analysing our data as in Duhamel et al. (1992) replicated their conclusions. Further analysis of our results for the visually-guided version of the classic double-step task, as well as more details concerning the classic task itself are provided in Supplementary Box 2 and Supplementary Fig. 4.

Our data analysed as in Duhamel et al. (1992)

Here, as in Duhamel et al. (1992), we evaluated only the first two saccades, S1 and S2, of each trial in the classic double-step task. Then, as described in their study, we evaluated, for each patient, the mean S2 amplitude (S2amp) for each trial type and compared it with the expected S2amp, defined as $T – T_1$. We standardized the data such that a positive (negative) amplitude indicated the contralesional (ipsilesional) direction. Duhamel et al. (1992) tested only one patient, lesioned on the right. The circled values in each column of Supplementary Table 20, reproduced in Fig. 6C (hashed purple bars), are the mean S2amp values on the identified trial types for their patient. Clearly, our right patient, Patient PR1, (Fig. 6C solid purple bars), behaved very similarly to Duhamel et al. (1992)'s patient. We also tested our four left-lesioned patients; we calculated a weighted average of their S2amps for each trial type. Supplementary Table 20 shows that this average was also similar to that of Duhamel et al. (1992)'s right patient.

Our data analysed as in Heide et al. (1995)

Unlike Duhamel et al. (1992), Heide et al. (1995) did account for multiple-step saccades. However, and most importantly, their double-step paradigm allowed only 1000 ms for a patient to complete the task, which our results indicate is inadequate (Fig. 6B) because S2.1 (the first saccade in S2) often started after 1000 ms following the GO signal.

Heide et al. (1995) measured the final eye position (FEP) of S2, at 1000 ms after the GO signal and, by comparing this value to the T2 position, calculated a position error and used it to indicate whether a corollary discharge had compensated for S1. We also measured the position error at 1000 ms on each trial. Our left patients performed very similar to Heide et al.’s left patients (their Fig. 5) as shown...
in Fig. 6D, green solid and hashed bars, respectively. The position error at trial-end for left patients was highest in the across hemifield conditions. Our results for Patient PR1 are similar to the right patient population tested in Heide et al. (1995) in all tasks except the ipsiL-contraL task wherein Patient PR1’s severe contralesional hypermetria resulted in large errors (Fig. 6D, solid purple bars). A by-patient breakdown of the data is in Supplementary Table 21. We conclude that analysing our patients as did Heide et al. (1995) shows the two populations were similar.

Heide et al. (1995) argued that their error measurements (Fig. 6D), coupled with their measure of the relative percentage of rejected trials—which we could not replicate with an analysis of our own data because they did not adequately describe their ‘rejection’ methods—showed that patients with parietal lesions lack a corollary discharge for contralesional saccades, especially in patients with right parietal lesions. We have argued in Part 1 that a more objective approach to evaluate corollary discharges is a $C_6S_2$ vs versus $C_6S_1$ plot (Fig. 4). We performed a $C_6S_2$ versus $C_6S_1$ regression analysis on our data processed as in Heide et al. (1995) (including, as they did, multiple-step saccades and analysing the first 1000 ms of a trial), and found no evidence of corollary discharge for any patients in any trial type in the classic double-step task, whether the first saccade was directed ipsilesionally or contralesionally (Supplementary Table 22). Put another way, a Heide et al. (1995) type analysis would have led us to conclude, erroneously, that no unilateral parietal patient had a corollary discharge in any direction. However...
when we used our complete analysis approach—accepting multiple steps and 2500 ms trial duration—we found that all patients (except Patient PL1) had a corollary discharge for contralesional first saccades, and half the patients had a corollary discharge for ipsilesional first saccades (Supplementary Box 2 and Supplementary Fig. 3E). This is still an underestimate of their true corollary discharge encoding shown in Parts 1 and 2 but shows that the classic task can reveal a corollary discharge in some parietal patients.

The above analyses have shown that our patient population is representative and behaves similarly to those tested by others, implying that conclusions regarding the integrity of corollary discharge are dependent on task and analysis method.

Discussion

We tested six patients with lesions—some extensive—of the parietal lobe (Fig. 1) on two modified and one classic version of the double-step saccade task. Our ‘exogenous’ task involved presenting targets for a long time, and presenting T2 prior to T1. In our ‘endogenous’ task (Rath-Wilson and Guitton, 2015), subjects were shown one target (T) and asked to first make a self-generated saccade, in the dark either contralesionally or ipsilesionally, before making a second saccade to the remembered location of T. We found, surprisingly, that all patients generated and used corollary discharge for exogenously- or endogenously-driven saccades directed either contralesionally or ipsilesionally. When tested using the classic double-step saccade task and analysis methods, our patients had impaired corollary discharges, as described in the literature.

Previous double-step studies implicating the parietal lobe

The classic double-step task has been the primary tool for investigating the corollary discharge of saccadic eye movements. In this task, patients with parietal lobe lesions, like those in the present study, are believed impaired at generating an accurate ipsilesional saccade if it follows a contralesional saccade (Duhamel et al., 1992; Heide et al., 1995). However, in our study of hemidecorticate patients, we found that the paradigms and analyses used in previous studies are suboptimal for evaluating patients’ performance (Rath-Wilson and Guitton, 2015). In tasks used previously, targets were presented very briefly and in close proximity to each other. Patients with parietal lesions have trouble distinguishing the temporal presentation of targets in opposite hemifields unless they are separated by more than 200 ms (Rorden et al., 1997; Ro et al., 2001; Baylis et al., 2002). In Duhamel et al. (1992) and Heide et al. (1995), T1 and T2 were presented for only 80–140 ms and there was no time between target presentations. Furthermore, when two targets are presented together in the contralesional hemifield, only one may be detected by parietal patients (Vuilleumier and Rafal, 2000; Baylis et al., 2002). This poses a clear problem for interpreting the results of the classic double-step task. Indeed, failure to complete the double-step task cannot unambiguously be ascribed to a lack of contralesional corollary discharge. Additionally, Duhamel et al. (1992) did not evaluate multiple-step saccades, which would lead to a bias in rejecting trials with contralesional first saccades since, as shown here, these are more likely to involve multiple steps. Moreover, Heide et al. (1995) provided subjects with only 1000 ms to complete a trial which, we also show, is too brief (Fig. 6B). (Note that the performance of our control subjects was not, contrary to our parietal patients, significantly altered by evaluating corrective saccades and allowing more than 1000 ms to complete the task; parietal lesioned patients clearly had abnormal saccade generating mechanisms unrelated to corollary discharge.) We also found that each study used a potentially ambiguous method of evaluating saccade corollary discharge. Duhamel et al. (1992) considered the mean S2 amplitude in relation to the expected S2 amplitude of T2–T1 in order to determine the presence or absence of corollary discharge (as we did in Fig. 6C). Heide et al. (1995) considered the mean absolute error after S2 in relation to T2 in a given trial type (as we did in Fig. 6D). These methods do not show whether S2 compensates for variations in S1 since many oculomotor impairments can influence the accuracy of S2. We believe that a more appropriate method for investigating corollary discharge specifically is to evaluate the relationship between the S1 and S2 amplitudes in each trial within a given task type; i.e. if S2 compensates for variations in S1 when both are generated in the dark, the planning areas of S2 must have access to corollary discharge about S1.

As we showed, patients with lesions of the parietal lobe have a corollary discharge for bilateral saccades, when multiple-step saccades are evaluated and subjects are given enough time to complete a task, even using the classic double-step task (Supplementary Fig. 4). Using the methods of previous studies, our patients would have been classified as impaired. We propose that the difficulties that patients demonstrate in completing the classic double-step saccade task are the result of visual-processing and attentional deficits that commonly result from lesions of the parietal lobe that are unrelated to the corollary discharge system and suggest that the exogenous modified double-step task, or our endogenous task, serve as a better evaluator of corollary discharge in patients with parietal lesions.

Pisella et al. (2011) investigated a patient with both a callosal and a right parietal lesion in the classic double-step task and argued for right-hemisphere dominance for corollary discharge generation in humans. Moreover, a lack of corollary discharge has been considered a possible cause of the common attentional deficit ‘hemi-neglect’, often suffered by patients with parietal lesions, most often of the
right hemisphere (Pisella and Mattingley, 2004). The present study, together with Rath-Wilson and Guitton (2015), questions these conclusions: both hemidecorticate and the present parietal patients (five of whom showed evidence of hemi-neglect through their Posner scores, Fig. 1F) generated and used a corollary discharge for saccades in both directions.

**Previous spatiotopic updating studies implicating the parietal lobe**

Other studies investigating, without the double-step task, corollary discharge generation in the right parietal lobe, do not suggest a specific impairment in monitoring contralesional saccades. One study reported that transcranial magnetic stimulation over the right parietal lobe of normal subjects disrupts trans-saccadic memory for multiple objects for both right and left saccades (Prime et al., 2008). By contrast, another study found that remembering a target location in space is more impaired in patients with lesions of the right parietal lobe after a saccade directed ipsilesionally, not contralesionally (Vuilleumier et al., 2007; Russell et al., 2010). Studies of inhibition of return found that patients with long-term lesions of the right parietal lobe (Sapir et al., 2004) and normal control subjects who underwent transcranial magnetic stimulation of the right parietal lobe (van Koningsbruggen et al., 2010) do not remap inhibition of return after a saccade in either direction. These studies indicate that there are perceptual impairments after lesions of the right parietal lobe, but they are unable to specify whether they are due to a lack of corollary discharge for contralesional or ipsilesional saccades, or even whether there is any impairment in the corollary discharge system at all.

**Neurophysiological mechanisms**

One interpretation of our results is that a parietal-encoded corollary discharge has indeed been abolished in our patients but that the vector subtraction, \( \Sigma S2 = T2 - \Sigma S1 \), was implemented in head coordinates with eye position at the end of \( \Sigma S1 \) given by eye muscle proprioception. This signal is thought to be slower acting than a corollary discharge—it follows the eye movement instead of being sent predictively or in tandem with the motor command as in the case of corollary discharge (Karn et al., 1997; Umeno and Goldberg, 1997, 2001). To provide insight into this we analysed the accuracy of Patient PR1 in the contraL-ipsiL-X task as a function of the time interval between the end of \( \Sigma S1 \) and beginning of \( \Sigma S2 \) and found no correlation (not shown).

We have previously shown a conserved corollary discharge for endogenous saccades in hemidecorticate patients missing an entire cortical hemisphere (Rath-Wilson and Guitton, 2015). These findings argue that mechanisms for endogenously driving bilateral saccades and encoding their corollary discharges are present even in a single hemisphere, thereby rendering the quest to precisely localize the site of corollary discharge generation quite daunting as it could be a labile circuit distributed bilaterally according to the available territory and time following a lesion (Heiser and Colby, 2006).

Are corollary discharges for endogenous and exogenous saccades co-localized to a single region and mechanism? Pathways for an ascending corollary discharge signal have been proposed to originate in the superior colliculus (Sommer and Wurtz, 2004a, b), a structure closely linked to brainstem motor circuits for saccades and therefore quite agnostic as to the encoding of exogenously- or endogenously-driven saccades (Kopecz, 1995; Trappenberg et al., 2001). Corollary discharge information is sent unilaterally from each superior colliculus via the thalamus to the frontal eye fields of the same hemisphere, each side carrying information about contralateral saccades. However, this view of a single ascending corollary discharge signal seems oversimplified: monkeys and humans with isolated unilateral lesions in the thalamus have impaired—but not absent—corollary discharge for contralateral saccades in a double-step paradigm (Gaymard et al., 1994; Sommer and Wurtz, 2004b; Bellebaum et al., 2005). Furthermore, evidence for the wide distribution of corollary discharge for bilateral eye movements to each cortical hemisphere is substantial in monkeys (Colby et al., 2005; Heiser and Colby, 2006) and humans (Medendorp et al., 2003, 2006). Importantly, a variety of patients with different unilateral lesion sites, such as hemispherectomy (Rath-Wilson and Guitton, 2015), frontal lobe (Rivaud et al., 1994; Heide et al., 1995; Gaymard et al., 1999), and here parietal lobe, have access to corollary discharge for bilateral saccadic eye movements. Our results support the hypothesis that corollary discharge for visually- and self-triggered saccades in both directions is available to each hemisphere.

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**Supplementary material**

Supplementary material is available at Brain online.
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