What the brainstem tells the frontal cortex.
II. Role of the SC-MD-FEF pathway in corollary discharge

Marc A. Sommer and Robert H. Wurtz
Laboratory of Sensorimotor Research, National Eye Institute, National Institutes of Health, Bethesda, Maryland 20892-4435

Running head: Role of the SC-MD-FEF Pathway in Corollary Discharge

For correspondence:
Marc A. Sommer
Building 49, Room 2A50, MSC 4435
NEI, NIH
9000 Rockville Pike
Bethesda, MD 20892-4435

Phone: 301-496-1141
FAX: 301-402-0511
Email: mas@lsr.nei.nih.gov
ABSTRACT

One way we keep track of our movements is by monitoring *corollary discharges*, or internal copies of movement commands. This study tested a hypothesis that the pathway from superior colliculus (SC) to mediodorsal thalamus (MD) to frontal eye field (FEF) carries a corollary discharge about saccades made into the contralateral visual field. We inactivated the MD relay node with muscimol in monkeys and measured corollary discharge deficits using a double-step task: two sequential saccades were made to the locations of briefly flashed targets. To make second saccades correctly, monkeys had to internally monitor their first saccades; therefore, deficits in the corollary discharge representation of first saccades should disrupt second saccades. We found, first, that monkeys seemed to misjudge the amplitudes of their first saccades; this was revealed by systematic shifts in second saccade endpoints. Thus, corollary discharge accuracy was impaired. Second, monkeys were less able to detect trial-by-trial variations in their first saccades; this was revealed by reduced compensatory changes in second saccade angles. Thus, corollary discharge precision also was impaired. Both deficits occurred only when first saccades went into the contralateral visual field. Single saccade generation was unaffected. Additional deficits occurred in reaction time and overall performance, but these were bilateral. We conclude that the SC-MD-FEF pathway conveys a corollary discharge used for coordinating sequential saccades and possibly for stabilizing vision across saccades. This pathway is the first elucidated in what may be a multilevel chain of corollary discharge circuits extending from the extraocular motoneurons up into cerebral cortex.
INTRODUCTION

Generating movements is a critical part of everyday life, and it is perhaps equally important that we keep track of movements as we make them. Monitoring our actions helps us to execute complex behaviors rapidly and to ignore spurious sensory inputs caused by movements. Information about movements comes from sensory receptors, including those in muscles, and from internal records of movement known as corollary discharge.

The principle of corollary discharge (Sperry 1950) is that when a brain region sends a motor command downstream it simultaneously sends a copy upstream to be used as information about the movement (Fig. 1A). As a way to monitor movements, corollary discharge (or efference copy; von Holst and Mittelstaedt 1950) has two main advantages over sensory cues: it provides information even before movement onset and it does not rely on the integrity of sensory receptors. The concept of corollary discharge has helped to answer questions as diverse as how crickets chirp without damaging their hearing (Poulet and Hedwig 2002) and why we can tickle others but not ourselves (Blakemore et al. 2000). Impaired corollary discharge may contribute to pathologies including schizophrenia (Feinberg and Guazzelli 1999; Ford et al. 2001) and may underlie many of the sensory and motor deficits that follow brain damage (Angel 1980; Baizer et al. 1999; Duhamel et al. 1992b; Gaymard et al. 1994; Haarmeier et al. 1997; Heide et al. 1995; Rafal 1994; Versino et al. 2000). Neurons in several parts of the primate brain seem to receive corollary discharge because their visual responses change just prior to movements (Duhamel et al. 1992a; Reppas et al. 2002; Richmond and Wurtz 1980; Thiele et al. 2002; Tolias et al. 2001; Umeno and Goldberg 1997).
In the accompanying paper (Sommer and Wurtz submitted) we described a pathway from superior colliculus (SC) to frontal eye field (FEF; Fig. 1B) that transmits a variety of signals including bursts of activity just prior to contraversive saccades (i.e. saccades made into the contralateral visual field). This activity provides information about when a saccade will occur and where it will go. Because it travels away from the eye muscles and up to the FEF, a cortical region involved in visual analysis and saccadic planning (Schall 1997), we hypothesized that the activity was a corollary discharge.

The goal of the present study was to test this hypothesis by examining the consequences of inactivating the pathway. Signals sent from the SC to the FEF are relayed by neurons in the mediodorsal thalamus (MD), which from an experimental point of view is highly fortuitous; shutting off those neurons should interrupt signal flow in the pathway without directly affecting either the pathway’s source, the SC, or its target, the FEF (Fig. 1B). We injected the GABA_A agonist muscimol at the sites of previously recorded MD relay neurons (Fig. 1C; Lomber 1999). This should temporarily inactivate the neurons because GABA_A receptors are found throughout MD (Steriade et al. 1997).

We reasoned that if the pathway conveys corollary discharge signals, then during MD inactivation a monkey should be impaired at keeping track of its contraversive saccades. One task that requires the internal monitoring of saccades is the double-step task (Becker and Jürgens 1979; Hallett and Lightstone 1976; Mays and Sparks 1980), which has been used extensively in prior studies to test for corollary discharge deficits (Duhamel et al. 1992b; Gaymard et al. 1994; Heide et al. 1995). In this task, subjects make saccades sequentially to the locations of two flashed targets (Fig. 2A). To make the second saccade correctly, a subject must keep track of where its first saccade goes; thus,
deficits in monitoring first saccades should disrupt second saccades. Visual feedback is unavailable because the targets disappear before the eyes move, and information from eye muscle proprioception seems to be negligible (Bridgeman 1995; Guthrie et al. 1983; Lewis et al. 2001; Steinbach 1987). Keeping track of the first saccade should depend primarily on monitoring the corollary discharge of that saccade.

In principle, MD inactivation could impair the accuracy or the precision of corollary discharge. The concepts of accuracy and precision are classically illustrated using the example of target shooting (Fig. 2B, top row). Relative to a shooter’s normal behavior (left), he or she would be suffering an accuracy deficit if the shot cluster shifted systematically (middle) or a precision deficit if the shots became more scattered (right). Analogously, corollary discharge is an attempt to “hit the bull’s-eye” – the brain wants to create a corollary discharge signal that matches a saccade. Consider three trials of making a saccade (Fig. 2B, bottom row). The saccade is constant from trial to trial, but the corollary discharge representation of it may vary. Relative to how well the corollary discharge signals normally represent the saccade (left), they would suffer an accuracy deficit if they started to systematically misrepresent the saccade, e.g. if they became shorter on average (middle), or a precision deficit if they started to vary more (right).

These corollary discharge deficits, although not directly observable, should be detectable in the double-step task through their influence on second saccades. To illustrate this, Figure 2C depicts a monkey’s internal estimate of its behavior in the top row and its actual behavior in the bottom row. The monkey’s goal is to make a second saccade that reaches the second target location, and to do this it must monitor its corollary discharge representation of the first saccade. From trial to trial the monkey will monitor
its corollary discharge signals and make adjustments so as to keep its second saccade endpoints constant (Fig. 2C, top row), but because the first saccade does not really change, these adjustments will actually introduce errors into the second saccade endpoints (Fig. 2C, bottom row). Compared to the normal behavior (Fig. 2C, bottom left), if there is a corollary discharge accuracy deficit the second saccade endpoints will shift systematically (bottom middle) and if there is a corollary discharge precision deficit these endpoints will become more scattered (bottom right).

Finally, a critical expectation is that these changes in second saccades should be lateralized, occurring only in trials involving contraversive first saccades. This is because the putative corollary discharge signal (presaccadic activity in the SC-MD-FEF pathway) is related almost exclusively to contraversive saccades (Sommer and Wurtz submitted).

We found that our hypothesis was supported: MD inactivation caused contralateralized deficits in both the accuracy and the precision of corollary discharge. This provides direct evidence that the presaccadic signals sent from SC to FEF represent corollary discharge information about saccades. A brief report regarding the accuracy deficit was published previously (Sommer and Wurtz 2002).

**METHODS**

**Monkeys.** We used monkeys “B” and “C” from our study of MD relay neurons (Sommer and Wurtz submitted). Both monkeys had been implanted with scleral search coils for measuring eye position, a post for holding the head, and chambers for accessing the brain. All procedures were approved by the Institute Animal Care and Use
Committee and complied with Public Health Service Policy on the humane care and use of laboratory animals.

**Injection sites** We injected at a site only if it met three criteria: past recordings at the site must have yielded identified MD relay neurons (i.e. only the sites shown in Fig. 1C were considered), recordings the day before injecting at the site had to demonstrate strong multiunit activity, indicating that the site was still healthy, and electrical stimulation at the site had to evoke saccades, because we used changes in stimulation-evoked saccades to assess whether muscimol was successfully injected (see below). At each site we injected either muscimol dissolved in saline (5 µg/µL) or saline alone as a control for incidental effects (e.g. pressure or dilution) that might be caused by liquid infusion. Table 1 lists all the experiments (first column) and the agent injected in each (second column). One site in monkey C (triangle in Fig. 1C, left) was extraordinarily well suited for inactivation, as it met all three criteria and, moreover, was where we had found a particularly rich concentration of MD relay neurons (cf. Fig. 2A, left, hatched circle, in Sommer and Wurtz submitted); the surrounding sites were less attractive for injecting (less robust neuronal activity, no saccades evoked, or both). We restricted our injections in monkey C to this one site in order to minimize inactivation of MD areas that did not contain relay neurons. As shown in Table 1, we performed different tests during each inactivation at this site. In monkey B we injected at three sites that met our criteria (diamond, square, and inverted triangle in Fig. 1C, right). We terminated the study once we ran out of sites that met our criteria for inactivation. Although the number of inactivation sites was limited, it was nonetheless sufficient to demonstrate significant,
lateralized corollary discharge deficits in both the pooled data and in each monkey individually as reported in the Results.

**Injection procedure** We inserted a 30 gauge cannula through a 23 gauge guide tube into the brain until the cannula tip was at the depth of previously recorded MD relay neurons. The other end of the cannula was attached to a 10 µL Hamilton syringe, and we injected muscimol manually in boluses of 0.2 µL every 30 s. A major technical issue was ensuring that muscimol was ejected from the cannula. We aborted the experiment if resistance was felt that might indicate a plugged cannula tip or if muscimol ejection was not verified by changes in stimulation-evoked saccades. Four injections (two in each monkey) were aborted for these reasons and are not included in this report. An insulated wire threaded through the cannula, with its exposed tip extending 500 µ beyond the cannula tip, allowed us to electrically stimulate at each injection site (Crist et al. 1988). We found that stimulating at relay neuron sites (biphasic cathodal-anodal pulses, 0.25 ms/phase, 350 Hz, 150 ms trains) often evoked saccades having scattered vectors (not stereotyped as when stimulating SC or FEF) after long latencies (mean 96 ms after stimulation onset) and at moderate current thresholds (mean 36 µA); other stimulation results are beyond the scope of this report. Our indicator of successful muscimol ejection from the cannula was a marked increase in current threshold (typically >2 times the initial level) around 20-30 min. after the injection, when muscimol typically begins having strong effects (e.g. Aizawa and Wurtz 1998). This rise in threshold may have been due in part to tissue displacement; we did not systematically compare the effects of muscimol vs. saline injection to test this. Regardless of the exact mechanism(s) causing it, the increased threshold confirmed that liquid had been ejected into the brain. The increase in
current threshold marked the start of the “During” inactivation period discussed throughout this report. The current threshold increase always persisted throughout the session, paralleling the multiple hour time-course of muscimol (e.g. see Lomber 1999).

**General protocol** The day before an injection we recorded at the targeted site to ensure that neurons were active there and collected “Before” behavioral data. The day of the injection we collected baseline stimulation data, injected muscimol and collected stimulation data to verify its delivery, and collected “During” behavioral data. On a later day (usually the next day) we collected “After” behavioral data to measure recovery.

**Experimental apparatus** During each experiment a monkey faced a tangent screen onto which visual stimuli were projected. Ambient illumination was dim light or darkness. In dim light experiments we used an LCD projector that even at its darkest setting illuminated the tangent screen with a diffuse gray background (0.1 cd/m²). Visual stimuli were a blue fixation spot and red targets (0.6 cd/m²). In darkness experiments we used lasers to produce red dots for the fixation spot and targets. There was no other source of light in the room during each trial, and between trials a lamp was illuminated to prevent dark-adaptation. We sampled eye position and recorded task events every 1 ms.

**Double-step task** The purpose of this task was to test whether MD inactivation impaired corollary discharge (see Introduction). A monkey fixated a spot, the spot disappeared, and two targets briefly appeared in sequence (Fig. 2A). To receive reward (a drop of water) the monkey had to make two sequential saccades to the locations of the targets. The timings of target presentation (specifically, the first target duration, the gap between offset of the first target and onset of the second, and the second target duration) varied depending on the target pair and the monkey, because we always fine-tuned the
timings until errors were minimized. For example, if for a certain target pair a monkey often erred by making its first saccade to target 2 instead of target 1, we lengthened the target 1 duration, shortened the target 2 duration, and changed the gap between targets 1 and 2 until the errors were minimized. The only constraint was that the overall sum of the target 1 duration, the gap between targets 1 and 2, and the target 2 duration be less than ~180 ms, approximately the minimum reaction time of first saccades relative to target 1 onset. This constraint was imposed because we required all visual stimuli to disappear before the first saccade began so that there would be no visual feedback from the targets that might inform the monkey whether the first saccade was made or where it landed. In practice the typical target 1 durations were ~130 ms, the gap was ~20 ms, and the target 2 duration was ~30 ms. On-line, we used a real-time saccadic velocity detector to abort trials in which the first saccade began too early; off-line, we inspected every trial to make sure that the more precise saccade detection algorithm in our analysis program agreed with this on-line analysis, and we eliminated further trials as needed. Spatially, we randomized a variety of target pairs as will be explained in the Results.

**Single-step task** The purpose of this task was to see if inactivation affected the generation of saccades. A monkey fixated a spot, the spot disappeared, a gap of 150 ms ensued, and then a single target appeared. The monkey had to make one saccade directly to the target. In a “target-present” version of this task, once the peripheral target appeared, it stayed lit until after the monkey made a saccade to it. In contrast, a “target-absent” version involved carefully chosen parameters so that the target presentation closely matched the presentation of target 2 in the double-step task. We did this to see how monkeys responded to a flashed target when there was no intervening first saccade,
i.e. when corollary discharge was not a factor. The 150 ms gap approximated the target 1 duration plus the gap between targets 1 and 2 in the double-step task, and when the target appeared it stayed lit for the same length of time (typically ~30 ms) that target 2 would have appeared in the double-step task. Because of the brief target flash, the saccade did not begin until ~120 ms after the target disappeared (saccadic reaction times were ~150 ms), and thus the saccade went to the remembered location of the target. This memory requirement was nearly identical to that required for making saccades to target 2 in the double-step task. Spatially, we randomized a variety of target locations (see Results).

**Analysis** On-line, in the double-step task we used rather large virtual windows around the targets for judging whether saccades were correct, because we did not want monkeys to receive feedback (due to loss of reward) that their behavior had changed if their second saccades became drastically different due to corollary discharge impairment. Typically the windows were 10º horizontally by 10º vertically around target 1 and 20º x 20º deg around target 2. Initial fixation windows were typically 5º x 5º, and sometimes a bit larger; this was somewhat liberal but necessary because our monkeys seemed to find it difficult to sustain their fixation on the laser spots in total darkness, particularly when fixation was required at eccentric locations. In the single-step task we used smaller windows, typically 5º x 5º, around the target.

Off-line, we detected saccades in the data with software that used a template-matching algorithm. We manually reviewed every trial to verify the saccade detection and to remove error trials. Correct trials were those in which the first and second saccades landed in well-defined clusters of endpoints within a few degrees (exact distance depended on the target configuration) of the first or second target location,
respectively. Most error trials (see Fig. 13C) were obvious by inspection and included 
~20-35% of trials in which the first saccade went to the second target, ~5-10% of trials in 
which the first saccade was correct but the second saccade did not occur or went to the 
wrong location, ~10% of trials in which the first saccade went nowhere near the first or 
second target, and very rare saccades that were curved or otherwise atypical (e.g. the 
strongly curved upward second saccade in Fig. 3A, bottom). The only ambiguity in 
identifying error trials came from first saccades that landed between the first and second 
targets (“averaging” saccades); we decided to accept such saccades as correct if they 
landed closer to the first than the second target.

All statistical tests used a criterion of p < 0.05, Bonferroni corrected as needed if 
there were multiple comparisons on the same data set. Unless explicitly noted, 
throughout this study we compared data sets using Student’s t-test, if judged normal by 
the Kolmogorov-Smirnov test and of equal variance by the Levene Median test, or else 
the Mann-Whitney rank sum test, and we analyzed correlations using Pearson’s test.

RESULTS

Example injections

Figure 3 shows data from an example inactivation. The monkey had to make a 
rightward saccade and then an upward saccade in response to two flashed targets. Figure 
3A, top, shows all trials performed by the animal before MD was inactivated. Most 
saccades were made in the appropriate sequence, going toward the first target and then 
the second. During MD inactivation (Fig. 3A, bottom), the monkey’s behavior was 
<Insert Fig. 3 here> 
nearly the same except that the second, upward saccades seemed to land, on average, at
more contralateral locations. We selected from these raw data only trials in which the monkey made correct sequences (Fig. 3B; see Methods) and in Figure 3C we summarize these correct trials by showing the means and SDs of the initial fixations, first saccade endpoints, and second saccade endpoints before and during inactivation. The most obvious effect of the inactivation seemed to be a roughly horizontal shift in second saccade endpoints. We examined this quantitatively by testing whether the endpoints were significantly different during vs. before inactivation along the horizontal dimension and, for comparison, along the vertical dimension (criterion level p < 0.025, Bonferroni corrected from p < 0.05 due to testing in two directions). Figure 3C shows that in this example case there was indeed a significant contraversive shift in second saccade endpoints. In contrast, neither the initial fixations nor the first saccade endpoints shifted in either the horizontal or vertical direction.

We note that in Figure 3 and in subsequent examples it is obvious that the saccadic sequences often were somewhat inaccurate relative to the actual target locations. This was because, first, upward shifts sometimes occurred as a normal behavior of the monkeys. Such shifts are common when saccades are made to remembered target locations in darkness (Gnadt et al. 1991), and in our experience this happens even in dim light for some monkeys (e.g. monkey C). Second, we purposely avoided over-training the monkeys. If they were to establish and execute programmed sequences of saccades as a rote response to a particular target pair stimulus (e.g. Kowler 1990), they could then perform the task without continuously monitoring their first saccades. We therefore changed target configurations frequently and allowed monkeys to practice on them for only a few days, at most, before each injection experiment.
Figure 4A shows the three target configurations we used (left column) and example saccadic sequences generated by the monkeys in response to each (right column). Each configuration involved horizontal first saccades followed by vertical or oblique second saccades. In each injection experiment we used a single configuration with all the target pairs of that configuration randomized by trial. The first two configurations, A and B (Fig. 4A, top and middle rows), involved a central fixation point and centrifugal first saccades. The advantage of these two configurations was that the sequence was unpredictable at the start of fixation; the disadvantage, however, was that second saccades began at an eccentric location. Second saccades were the most crucial movements for us to measure, so it would be preferable if they started at the center so that they could be measured optimally (maximum linearity of the eye coil system was in the center) and so that their trajectories would be unaffected by mechanical limits at the orbital extremes. Thus in a third configuration, C (Fig. 4A, bottom row), we used centripetal first saccades and second ones starting at the center of the screen. The disadvantage of this configuration was that it introduced predictability into the paradigm (the initial fixation location provided information as to whether the sequence would be rightward or leftward), so to counter this problem we introduced extra randomness by adding many more second target locations. Each configuration, A, B, or C, resulted in a different pattern of saccadic sequences that approximately matched the arrangement of targets in the configuration (Fig. 4A, right column), and thus it appeared that the monkeys did try to perform the sequences correctly even though hampered by vertical upshifts and only limited training, as noted above. Second saccades clearly were attempts to reach the second target locations and were not just default saccades.
Figure 5 shows examples of inactivation results obtained using the various target configurations. The data in Figure 5A were collected using configuration A and demonstrate that second saccade endpoint shifts occurred for downward sequences as well as upward ones (for clarity, however, we restrict all other examples in this report to upward sequences). Figure 5B shows an example obtained using configuration B, and Figures 5C and D show examples from configuration C. In all of these cases the second saccade endpoints shifted significantly in the contraversive direction. As was illustrated in Figure 2C (middle), this implied that the underlying corollary discharge signals shrank. For comparison, changes in second saccade endpoints typically did not occur in trials involving ipsiversive first saccades (Fig. 5E) or in saline control injections (Fig. 5F).

Accuracy deficits

Our first observation as shown in the above examples was that MD inactivation often caused a systematic shift in second saccade endpoints indicative of a corollary discharge accuracy deficit. Next we will document this effect quantitatively.

Trials involving contraversive first saccades. Figure 6 summarizes the results by pooling data from all injections and both monkeys. In each experiment the data from a single target pair represented one “case” for analysis; e.g. one case was shown in Figure 3C and six more in Figure 5A-F. Combining all the inactivation experiments, there were 22 cases involving contraversive first saccades. In nearly every case (82%, 18/22) there was a contraversive shift in second saccade endpoints during MD inactivation (Fig. 6A, left). Shifts were individually significant in half of the cases (11/22) and the average shift was significantly greater than zero. The shifts were approximately the same in each
monkey (Fig. 6A, left, inset graphs) and they occurred regardless of whether the task was
performed in total darkness or in dim light (not shown; mean shifts were 1.12º in n=16
dark cases and 1.13º in n=6 dim light cases).

No other systematic shifts were seen. Along the vertical dimension (Fig. 6A,
right), shifts were rare, significant ones were equally likely to be upward as downward,
and the mean shift was not different from zero. Endpoints of first saccades (Fig. 6B)
were not shifted significantly in the horizontal direction during inactivation, except for a
single case, and similarly were not shifted vertically on average (a few individual cases
were, but they were as likely to be shifted upward as downward). Initial fixation
locations (Fig. 6C) were unchanged during inactivation in both directions.

As noted above, the contraversive direction of the shifts implied that the
underlying corollary discharge vectors shrank (Fig. 2C middle). It follows that the
maximum possible contraversive shift should equal the first saccade amplitude (10º in
target configuration A, 20º in configurations B and C). To estimate the severity of the
deficit, we compared the observed shifts to these maximal shifts. As reported previously
(Sommer and Wurtz 2002), in the 11 cases showing a significant shift (Fig. 6A, left) there
was a 19% average deficit. Considering all 22 cases, there was a 10% average deficit.

Ipsiversive saccades and saline controls. We analyzed two other types of trials for
comparison with the above results. First, because MD relay neurons represent
contraversive saccades almost exclusively (Sommer and Wurtz submitted), we expected
MD inactivation to have little or no effect on corollary discharge of *ipsiversive* saccades.
Second saccades following ipsiversive first saccades, therefore, should be unperturbed
during MD inactivation, and that is what we found. Figure 6D, left, shows the
distribution of horizontal shifts in second saccade endpoints for all 22 ipsiversive control cases; here, a corollary discharge deficit would be indicated by an ipsiversive shift. There were a few more individually significant ipsiversive shifts than contraversive ones (5 vs. 2) and the overall mean trended toward the ipsiversive direction, but this was not significant (p > 0.025). As a second point of comparison we expected that trials involving contraversive first saccades should be unaffected if only saline, sans muscimol, was injected; this too was found to be true (Fig. 6D, right).

**Angle of the shift in second saccade endpoints** The average shift during inactivation, in trials involving contraversive first saccades, was significant horizontally but not vertically (Fig. 6A, left), but that does not necessarily mean that the exact angle of the shift was horizontal. If the shift angle were appreciably different from horizontal, it would imply that the underlying corollary discharge signal not only shrank on average, but also rotated. To quantify the exact shift angle, in each case we connected the means of the second saccade endpoints before and during inactivation with a line. The angle of the line relative to horizontal (defined as $\phi$) was the shift angle while the length of the line (defined as D) was the shift distance. For the case shown in Figure 3C, for example, the line had an angle $\phi = +25.9^\circ$ and a length $D = 2.3^\circ$. We treated each line as a vector and plotted all of them in Figure 7. Vectors from inactivation experiments in which the first saccade was contraversive are shown in Figure 7A (the vector corresponding to the Figure 3C example is shown with a dashed arrow). The overall mean vector (larger, white arrow) was highly significant (p < 0.01), as zero fell outside the 99% confidence ellipse regarding its tip location. This mean vector had $\phi = +5.0^\circ$ and $D = 1.1^\circ$. Because the average shift was nearly horizontal, the underlying corollary discharge signal did
seem to be shortened but not appreciably rotated. In contrast, for the cases involving ipsiversive first saccades (Fig. 7B) and for the saline controls (Fig. 7C), the mean vectors were not significant (the 95% confidence ellipses included zero), which confirms that these cases exhibited no overall shift.

**Precision deficits**

We expected that a precision deficit in corollary discharge would increase the scatter of second saccade endpoints (Fig. 2C right), but this did not occur (Fig. 8A); in trials involving contraversive first saccades, the SD of second saccade endpoints did not change during inactivation (paired t-tests, p = 0.36 for horizontal SD, 0.62 for vertical). If there was increased scatter, it was not detectable against the background scatter. A subtle deficit was suggested, however, by the fact that in Figure 8A more data points fell above the unity line than below it (25 vs. 19). This prompted us to try a different technique for identifying a precision deficit.

Our new approach was to perform a trial-by-trial analysis. We took advantage of the fact that, like all saccades, first saccades in the double-step task vary slightly from trial to trial. If corollary discharge is precise, it will change on each trial to constantly match the first saccade. To appreciate this, consider again the sharp-shooting analogy (Fig. 2B). Now, however, the shooter must hit a target that moves in a random direction before each shot. One can maintain the same accuracy as with a stable target by just aiming at the center of the “cloud” of target locations. The average of the shots will still be at the bull’s-eye, but the scatter will increase; precision will suffer. To maintain good precision one would have to match each target movement with a corresponding change in
aim. Only this will keep the resulting shot cluster tight. Similarly, corollary discharge will be precise only if it changes on each trial to match the slightly varying saccade.

To measure how well corollary discharge matches the first saccade on a trial-by-trial basis, once again we used second saccades as our behavioral indicators. Figure 8B shows one case of saccadic sequences during and before inactivation, and Figure 8C shows each individual second saccade vector. To see if the monkey detected where each second saccade started (i.e. where each first saccade landed), we replotted all the second saccades in Figure 8D by spreading them out along the vertical dimension while maintaining their relative horizontal locations (they are arranged so that the saccade starting most to the left is at top and that starting most to the right is at bottom – not chronologically by trial number). At least before inactivation (Fig. 8D, left), the monkey did act as if it knew where each second saccade began; moving from left to right, the vectors tend to swing counterclockwise as if compensating for the different initial positions. In contrast, during inactivation (Fig. 8D, right), the monkey showed little evidence of knowing where each first saccade landed; all the angles of the second saccades were about the same regardless of where the saccades began.

To quantify this effect, we compared the observed second saccade vectors (Fig. 8C) with the ideal vectors that would have been expected from perfect compensation. Ideal vectors were modeled (Fig. 9A) by connecting the initial position of each observed second saccade to the mean endpoint location of the second saccades (we assume this mean location was where the monkey intended its saccades to land). For quantification we measured saccadic direction (θ) and amplitude (ρ; see Fig. 8D). First we evaluated how well the monkey adjusted its second saccade directions. Figure 9B plots observed
null vs. ideal null for every trial. Before inactivation (bold circles and line), the values were highly correlated with a linear regression slope near 1.0. Thus the monkey was quite adept at adjusting its second saccade directions, implying that it knew where each first saccade landed; corollary discharge was precise. During inactivation (thin triangles and line), however, precision seemed impaired because the correlation became insignificant. Next we evaluated how well the monkey adjusted its second saccade amplitudes. Figure 9C shows that the monkey was poor at this both before and during inactivation (observed null was not correlated with ideal null). The criterion level for a significant correlation was \( p < 0.025 \) because we looked for changes in both direction and amplitude of the saccades.

The results of this example were typical, and Table 2 lists all the data. In trials involving contraversive first saccades, significant decreases during inactivation occurred in the percent of cases having a significant correlation between observed and ideal null (Table 2, first row from top) and also in the average slope of the regression between observed and ideal null (Table 2, second row). Figure 9D (left) graphs this change in slope and, for comparison, the insignificant changes for ipsiversive first saccade trials (middle) and saline control trials (right). No other significant effects were found (Table 2).

The precision deficit represented by the regression slope data in Figure 9D (left) was large but not total; it was a 60% deficit measured as a percentage of baseline ([(0.97-0.39)/0.97]). Average slopes decreased a similar amount in both monkeys (by 0.55 for monkey B, from 0.81 to 0.26; by 0.60 for monkey C, from 1.16 to 0.56) and in both ambient light conditions (by 0.50 for dim light, from 1.16 to 0.66; by 0.60 for darkness, from 0.89 to 0.29). Finally, the precision deficit appeared to be more pervasive than the accuracy deficit. Precision deficits occurred both in the 11 cases that had an accuracy...
deficit (i.e. the 11 cases exhibiting an individually significant contraversive shift in second saccade endpoints – see Fig. 6A left), with average slopes decreasing by 0.54, from 0.82 to 0.28, and in the other 11 cases with no accuracy deficit (average slopes decreased by 0.61, from 1.12 to 0.51). The importance of this is questionable, however; it could just be that the precision analysis was more sensitive than the accuracy analysis.

As an aside, these results also demonstrate that the monkeys did not pre-program their saccadic sequences. The monkeys normally tailored the direction of their second saccades to compensate for changes in their first saccade endpoints, meaning that they only made a second saccade after learning about the first one. Our strategies of not over-training the monkeys and frequently changing the target configurations therefore seemed to successfully prevent pre-programming.

In sum, the precision analysis revealed both a positive and negative result. The positive finding was twofold: monkeys normally adjusted their second saccade directions from trial to trial to compensate for slight fluctuations in first saccades, and this was disrupted by inactivation. This shows that corollary discharge is normally precise and that MD inactivation impairs this precision. The negative finding was that monkeys showed little ability to adjust their second saccade amplitudes. This may explain why we found no precision deficit in our initial SD analysis (Fig. 8A). Second saccade amplitudes both before and during inactivation were non-ideal – essentially “noisy” – and this may have contributed so much scatter to the endpoints that SD increases caused by an impaired ability to adjust second saccade directions could not be detected. Only by analyzing second saccade directions in isolation could we uncover the precision deficit.
Generation of single saccades

In the above sections we considered whether corollary discharge, i.e. information about saccades, was impaired by MD inactivation; next we consider whether saccade generation itself was impaired. In brief, it was not. As shown above, inactivation had little or no effect on the generation of contraversive first saccades in the double-step task (Fig. 6B), and previously (Sommer and Wurtz 2002) we showed one example of unaffected saccades made in the single-step task, demonstrated that the dynamics of single saccades were unaffected, and reported that there were no overall accuracy or latency deficits. Here we illustrate saccades made in a different version of the single-step task and provide complete accuracy, precision, and latency results.

Figure 10A shows an example experiment that was notable because it contained the largest changes in single saccades during MD inactivation that we ever found. In contrast to the previously published example that showed saccades from the target-present version of the task (Sommer and Wurtz 2002), this example (Fig. 10A) shows saccades from the target-absent version. The target-absent version was more challenging, in that the target was flashed only briefly and its location had to be remembered during the reaction time (see Methods). In each trial the monkey made a single saccade from the center to a target appearing at one of the locations shown in Figure 4B (configuration B), and shown are the means and SDs of the saccadic endpoints before and during MD inactivation along with the radial distance (D value) of each shift. To see if the shifts were significant we tested them along the two cardinal axes, as we did in the double-step task, and superscripts following the D values indicate endpoints that were significantly shifted horizontally (h) or vertically (v). As can be seen, shifts were small in magnitude,
primarily vertical in direction, and about as likely to affect contraversive as ipsiversive saccades. Figure 10B shows the distributions of shift sizes of contraversive saccades (top) and ipsiversive saccades (bottom) from all the single-step cases. The average shift size was not significantly different between contraversive and ipsiversive saccades, and a few individually significant horizontal or vertical shifts were seen for both contraversive and ipsiversive saccades. The precision of single saccades was not affected by inactivation either (Fig. 10C; all paired t-tests of during-before changes yielded p > 0.025). Unlike in the double-step task, we saw no alternative way of testing for a precision deficit; it is possible there was a small deficit in the precision of saccade generation that was undetectable. Finally, reaction times were not affected (Fig. 10D; all paired t-tests yielded p > 0.05).

In sum, taking these single-step task results together with the lack of effect on first saccades of the double-step task, we conclude that MD inactivation has no effect on the ability to generate saccades. It should be noted that, as a point of comparison, similar injections of muscimol cause severe, lateralized impairments of saccade generation in the SC (Aizawa and Wurtz 1998; Hikosaka and Wurtz 1985) and in the FEF (Dias and Segraves 1999; Sommer and Tehovnik 1997), presumably due to silencing these structures’ descending output neurons (Everling and Munoz 2000; Munoz et al. 1991; Segraves 1992; Segraves and Goldberg 1987; Sommer and Wurtz 2000, 2001).
Alternative explanations

Returning to the double-step task results, we think that corollary discharge deficits provide the simplest explanation for the second saccade disruptions in trials involving contraversive first saccades. Nevertheless, alternative explanations should be considered.

Were second saccade endpoint shifts due to first saccade endpoint shifts? Figure 6B (left) showed that in one case there was a significant contraversive shift in first saccade endpoints during MD inactivation, and Figure 11A (left) shows the average saccades from this case. The slight (0.8°) but significant shift in first saccade endpoints may have contributed to the significant shift in second saccade endpoints of 1.8°. To see if there was an accumulation of horizontal error from first to second saccades in general, we plotted the horizontal shift in second saccade endpoints as a function of the horizontal shift in first saccade endpoints (Fig. 11A right). If the errors accumulated, then larger first saccade shifts should have tended to produce larger second saccade shifts; the data should be directly correlated. There was no correlation, however (p = 0.888). First saccade endpoint shifts did not seem to cause second saccade endpoint shifts.

Were the deficits artefacts of cumulative damage? It could also be that the behavior just kept worsening every day due to progressive neuronal damage, so that changes during vs. before inactivation were artefacts of collecting the data on sequential days. Arguing against this, we found no evidence for cumulative damage; deficits always recovered after inactivation. Figure 11B (left) illustrates one example. During inactivation the second saccade endpoints shifted contraversively, but after inactivation, i.e. the next day, the second saccade endpoints were not significantly different from those collected before the inactivation. The behavior had completely recovered. This was true
for all 11 cases in which there was a significant contraversive shift during inactivation (Fig. 11B middle); in no case was there still a significant contraversive shift after the inactivation, and the overall mean was not different from zero. Precision deficits also recovered in these 11 cases. As noted above, the regression slope between observed $\theta$ and ideal $\theta$ for these cases decreased from an average of 0.82 before inactivation to 0.28 during inactivation, but after inactivation the average slope rose to 0.81, representing almost perfect recovery (Fig. 11B right).

**Were second saccade endpoint shifts due to general rotations of all saccades?** It could also be that the second saccade endpoint shifts were an artefact of a direction deficit in saccade generation; maybe all saccades rotated contraversively. For example, we assumed that the second saccade endpoints in Figure 12A (same as in Fig. 5C) shifted rightward because of inaccurate corollary discharge. It could be, however, that any saccade made in an obliquely upward direction would have rotated to the right. To test this, in two of the single-saccade control tasks discussed above we had targets arranged (configuration $B$ in Fig. 4B) so as to match the double-step target arrangement (configuration $C$ in Fig. 4A) during the same injections, and we asked whether single, obliquely upward saccades also were rotated. They were not. Figure 12B shows the single saccade control that matched the trial type of Figure 12A. The single saccades were much more accurate than the second saccades of the double-step task, of course, as would be expected. During inactivation there was no rotation and consequently no contraversive shift (Fig. 12B top); this was always the case (bottom).

**Were the shifts due to warped visual or memory representations?** If visual perception or working memory were spatially perturbed, a monkey might think that the
second target appeared more contralaterally than it actually did. This could be why second saccades were aimed further into contralateral space during inactivation. To test this, we again looked at control saccades made in the single-saccade task (Fig. 12C). These saccades actually originated from the center of the screen (see Fig. 4B, configuration B), but for ease of comparison with the double-step task (cf. Fig. 12A) we plot the data as if the saccades started 20° to the left. For the visual system, the initial fixation location should be irrelevant, as it is the retinal location that matters (we ignore any torsional difference between fixating centrally vs. peripherally). The target timing and memory requirements in these target-absent single saccade trials were designed to match as closely as possible those of the second target in the double-step trials (see Methods). There was little evidence for any sort of warping of visual or memory space (Fig. 12C). The example (Fig. 12C, top) shows the only significant contraversive shift in single saccade endpoints during inactivation that we found. On average, there was no significant shift (Fig. 12C, bottom).

Were precision deficits due to imprecise vision or memory? An alternative explanation for the precision deficits also posits a visual or memory problem. Perhaps corollary discharge precision was normal during inactivation but the precision of detecting or remembering the target location was impaired; this also could have caused second saccade directions to deviate from the ideal during inactivation as in Figure 9B. We found no evidence for this, however. Such impairments should have increased the scatter of second saccade endpoints, but this did not occur (Fig. 8A; testing for such a visual or memory deficit was in fact the original motivation for analyzing these data in Sommer and Wurtz 2002). As a follow-up, we looked at precision in the target-absent
version of the single-step task. Detecting and remembering the target in this task should be of similar difficulty as detecting and remembering the second target in the double-step task. Precision in the single-step task, however, was unaffected by inactivation (Fig. 10C; nearly all the data are from the target-absent version). From what we can tell, therefore, the precision of detecting and remembering the second target remained normal. The best explanation for the deficit in compensation (Figs. 9B and D, left) is that the precision of corollary discharge was impaired.

**Bilateral impairments**

All the deficits in the double-step task discussed thus far affected only trials in which the first saccade was contraversive, but other, bilateral, impairments also occurred.

**Increased reaction times** Reaction times increased almost completely bilaterally during inactivation. Figure 13A (left) shows that for all double-step trials pooled together (correct + wrong), mean reaction times of first saccades increased significantly regardless of whether they were contra- or ipsiversive. Just considering correct trials, reaction times of first saccades increased slightly contraversively but not ipsiversively (Fig. 13A, second graph from left) while inter-saccadic intervals (second graph from right) and reaction times of second saccades (right) both increased bilaterally.

**Decreased percent correct** Recall that correct trials in the double-step task were those in which two saccades were made sequentially toward the target locations. The percentage of such trials relative to all trials was the percent correct. We found that percent correct decreased bilaterally during inactivation (Fig. 13B). To better understand this, we analyzed which kinds of error trials increased. A major, bilateral increase
occurred in error trials in which the first saccade went to target 2 and stayed there until the trial ended (Fig. 13C top and bottom rows, leftmost bars). We think this was related to the bilateral increase in first saccade reaction time (Fig. 13A left), since longer reaction times in double-step trials are associated with errors in which first saccades go to the second targets (Sommer and Tehovnik 1999). Two other increases in errors also occurred in trials involving ipsiversive first saccades (Fig. 13C bottom row): errors in which first saccades were correct but then no second saccades appeared (middle bars) and errors in which the first saccade headed to neither the first nor the second target (rightmost bars).

**General lethargy**  The monkeys occasionally seemed to become lethargic during inactivation. We were very familiar with the monkeys’ behaviors, so when the following effects occurred less than an hour after muscimol injection (once with monkey B, twice with monkey C) we thought they were striking: the monkeys shut their eyes, ceased to work even for greater reward, and slept. When this occurred we aborted the experiment and returned the monkeys to their cages. The next day the monkeys were completely recovered. None of the data in this report were collected during such episodes.

We do not know the underlying cause of the reaction time increases, the performance deficits, or the lethargy. Importantly, however, because all these impairments were bilateral, they could not have been related to the highly lateralized second saccade impairments that we considered markers of corollary discharge deficits.
DISCUSSION

The present results, taken together with the recording results of the accompanying paper (Sommer and Wurtz submitted), provide multiple lines of evidence supporting the hypothesis that the SC-MD-FEF pathway plays a role in corollary discharge. The accompanying paper showed that the pathway carries signals that start just prior to contraversive saccades and represent the approximate size and direction of the saccades. The presaccadic timing means that the activity is of central origin, not proprioceptive, the representation of saccadic vector means that information about specific upcoming movements is available, and the ascending route of the activity implies that it is an informative signal rather than a movement command. We hypothesized, therefore, that the pathway conveys corollary discharge of contraversive saccades. To test this hypothesis we inactivated MD relay neurons, thus interrupting signal flow in the pathway, while monkeys performed a double-step task that permitted inferences about covert corollary discharge deficits through examination of overt changes in second saccades. Mean second saccade endpoints were systematically shifted, implying a deficit in the accuracy of corollary discharge, and the ability to compensate for trial-by-trial fluctuations in first saccades was disrupted, implying a deficit in the precision of corollary discharge. These deficits occurred only in trials involving contraversive first saccades, as predicted by the contraversive representation of saccades by MD relay neurons. Although information about saccades was impaired, saccade generation itself was not, as shown by unaffected first saccades in the double-step task and single saccades in the single-step task. We think the simplest explanation for all these results, and that
which binds together the results of our recording and inactivation studies most tightly, is that the SC-MD-FEF pathway conveys corollary discharge signals.

**Nature of the corollary discharge deficit**

A single deficit disrupts both the accuracy and precision of corollary discharge. Just like a sharpshooter might experience both accuracy and precision deficits from a single injury, say to the spinal cord, so might a monkey experience both accuracy and precision deficits from one insult to the overall corollary discharge representation in the brain. We think that is what happened when we inactivated MD: we deprived cortex of a critical source of information about saccades, and this single blow compromised both the accuracy and precision of a monkey’s estimate as to where its saccades went.

To understand how the loss of input from the SC-MD-FEF pathway could cause both accuracy and precision deficits in corollary discharge, it is helpful to review the characteristics of this input. The putative corollary discharge signals, namely presaccadic activity in the pathway, are high-frequency bursts that start just before the saccade and quit just after it (Sommer and Wurtz submitted). By removing this strong, sharp activity, the brain’s overall corollary discharge representation of the saccade might be dampened and broadened. Such a compromise in the signal to noise ratio should impair both the accuracy and precision of corollary discharge. Analogously, weaker saccadic commands in the SC seem to render saccade generation both less accurate and less precise (Edelman and Goldberg 2001; Stanford et al. 1996; Stanford and Sparks 1994).

**Why were the deficits partial?** Although both accuracy and precision of corollary discharge were impaired, neither deficit was complete: accuracy was disrupted by ~10-
20% and precision by 60%. We think the apparently different sizes of these deficits were unimportant as they may be attributable to the different analyses involved. The salient point is that MD inactivation did not totally eliminate corollary discharge. We see at least four possible explanations for this. First, the pathway might not have been completely silenced; our single point injections may not have successfully inactivated all of the MD relay neurons. Second, corollary discharge signals might have continued to reach cortex through other transthalamic pathways. Many motor-related subcortical regions innervate thalamus (Steriade et al. 1997) and the dentate nucleus of the cerebellum and the substantia nigra, in particular, have been shown to contact relay neurons projecting to FEF (Lynch et al. 1994). Third, some corollary discharge signals might originate within cortex. The FEF, for example, sends saccadic instructions downstream and may simultaneously generate corollaries of those signals (Everling and Munoz 2000; Segraves and Goldberg 1987; Sommer and Wurtz 2000). Knocking out the SC-MD-FEF pathway would leave such intracortical signals unaffected. Fourth, even if corollary discharge had been totally lost, it is conceivable that monkeys relied to some extent on proprioceptive information as a “backup” way to perform the double-step task.

**Spread of inactivation from MD** Our goal was to inactivate MD relay neurons and we are convinced that we did this, because we aimed muscimol directly at them. Neighboring neurons, however, were likely inactivated as well; we did not measure the spread of inactivation. There was probably a medial bias to the spread considering that the internal medullary lamina should limit diffusion laterally (similar sheets of fibers were found to be effective boundaries in other injection studies; e.g. Weese et al. 1999). Nonetheless we recognize that our corollary discharge deficits may have been caused in
part by inactivating important lateral thalamic areas, such as the intralaminar nuclei (Schlag-Rey and Schlag 1989), that may contain relay neurons of other ascending pathways. Evaluating this possibility would require one to physiologically identify relay neurons of the other pathways, aim inactivations directly at them, and compare any corollary discharge deficits with the deficits found by inactivating MD relay neurons.

Another way that spreading inactivation might have affected our results was to cause the bilateral deficits in saccadic reaction time and percent correct that we found, as well as the occasional lethargy that we seemed to induce. We suspect that these systemic deficits were due to slightly decreased levels of arousal caused by muscimol seeping up the penetration shaft, around the cannula, to affect the overlying reticular nucleus of the thalamus that helps control sleep-wake transitions (McCormick 2002; Steriade 2003).

**Amount of muscimol needed** We injected 2.1 μL of muscimol on average (Table 1), but it is important to note that this was the volume required to cause the effect that we used for verifying successful injection: an increase in current threshold for evoking saccades (see Methods). The volume required to impair corollary discharge may well have been less. For example, the very similar deficits shown in Figure 5A, B, C, and D occurred during muscimol injections of 2.0, 1.6, 3.0, and 1.6 μL respectively. This suggests that 1.6 μL or less was needed to disrupt corollary discharge, an amount comparable to that used in other studies employing similar methods as ours (needle delivery of muscimol at 0.1-0.2 μL/30 s and at a concentration of 5 μg/μL; e.g. Shi et al. 1998 used 1-1.4 μL in the FEF and Aizawa and Wurtz 1998 used 0.3-1.5 μL in the SC).

**Other possible functions of the pathway** By concluding from these inactivation results that the SC-MD-FEF pathway plays a role in corollary discharge of saccades, we
do not mean to imply that it has no other function. Our recordings showed that a variety of signals in addition to presaccadic activity are conveyed from SC to MD to FEF (for details, see Sommer and Wurtz submitted). Most notably, the pathway is also rich with phasic visual responses, suggesting that MD inactivation may also cause visual disruptions. A systematic test of this hypothesis was beyond the goals of this study.

**Other lesion studies investigating corollary discharge in primates**

To our knowledge, the present study is the first to document the oculomotor consequences of inactivating MD in monkeys and the first to describe the effects of specifically blocking any putative corollary discharge pathway in any primate. The most similar prior study was an examination of central thalamic lesions in humans (Gaymard et al. 1994) that revealed deficits in the ability to internally monitor movements, including saccadic eye movements, using tasks very similar to the double-step paradigm used here. The lesions involved the internal medullary lamina and the ventral lateral and ventral posterolateral nuclei, while apparently sparing MD. Nevertheless it is quite possible that the lesions did disrupt the ascending pathway from SC to FEF. Damage to lateral MD abutting the internal medullary lamina cannot be ruled out, and that is precisely where MD relay neurons in monkeys are concentrated (Sommer and Wurtz submitted). Also, in humans it is not known exactly where the thalamic neurons that relay signals from SC to FEF are located; they might lie outside of MD. The FEF seems to sit more posteriorly in humans (in Brodmann’s area 6) than in other primates (area 8), implying that human SC-to-FEF relay neurons may lie more laterally, e.g. in the internal medullary lamina or the ventrolateral nucleus (reviewed by Tehovnik et al. 2000).
Many other lesion studies have shown that various parts of the brain are involved in corollary discharge (see Introduction). Surprisingly, though, corollary discharge deficits have not yet been demonstrated after permanent lesions of the FEF in either monkeys (Collin and Cowey 1980) or humans (Gaymard et al. 1999; Heide et al. 1995; Rivaud et al. 1994). This does not necessarily mean that the FEF is uninvolved in corollary discharge, however. In the monkey study (Collin and Cowey 1980), the task was to report with a lever press when one or both of a pair of lights moved; the logic was that if corollary discharge were impaired, monkeys would mistakenly report that saccade-induced displacements in the retinal images of the lights were actual movements of the lights. This did not occur after FEF (or SC) lesions, but many reasons could explain this: immediate corollary discharge deficits may have recovered in the days between surgery and testing; production of fewer saccades (Schiller et al. 1980) may have hidden a corollary discharge deficit (eye movements were not quantified); and the presentation of two lights simultaneously might have allowed the monkeys to perform the task in large part by noting when one light moved relative to the other, obviating the need to use corollary discharge so that deficits in corollary discharge went untested.

In the human FEF lesion studies, investigators have found that second saccades of the double-step task are impaired by damage to parietal cortex but not by damage to the FEF (Gaymard et al. 1999; Heide et al. 1995; Rivaud et al. 1994). Again, post-lesion recovery is an issue; subjects might recover better from FEF than parietal damage. In particular, lesions of either area might disrupt corollary discharge of saccades while parietal lesions may additionally disrupt cortical signals related to static eye position. Reversible inactivation of lateral intraparietal cortex in monkeys performing a double-
step task causes severe disruptions of eye position information (Li and Andersen 2001),
and neuronal activity modulated by eye position is common in parietal cortex (reviewed
by Andersen and Gnadt 1989) but not in the FEF (e.g. Bruce and Goldberg 1985;
Goldberg and Bruce 1990). In sum, subjects with parietal lesions may lose both corollary
discharge and eye position signals, leaving them with no hope of internally monitoring
their saccades, while those with FEF lesions might lose corollary discharge and yet
gradually adapt by making use of still-available eye position signals.

Levels of corollary discharge in the primate saccadic system

Von Holst and Mittelstaedt (1950) suggested that keeping track of one’s
movements was based on monitoring outputs to muscles, and hence their term efference
copy. The SC-MD-FEF pathway, however, is at least a couple synapses above this final
efferent level, so we have used Sperry’s term of corollary discharge that indicates the
interaction of “motor patterns” with a “sensorium” without specifying where the
interaction occurs (Sperry 1950). Corollary discharge may arise from many levels of the
nervous system, and indeed Evarts (1971) emphasized that a multilevel corollary
discharge network might be critical in coordinating movements as well as in interpreting
sensory inputs. Adapting Evarts’ ideas, we hypothesize that corollary discharge arises at
multiple levels in the saccadic system, essentially forming a chain composed of links
associated with particular circuits. From link to link up the chain, the corollary discharge
represents the actual movement less and less. Figure 14 illustrates this concept.

What the motoneurons tell the saccade generating circuit Extraocular
motoneurons may provide feedback (Fig. 14, lowest dashed arrow), in line with the
original concept of von Holst and Mittelstaedt (1950), as some have been shown to emit intra-cranial collaterals (McCrea et al. 1986). Corollary discharge from motoneurons should represent the instantaneous state of the eye, i.e. its three-dimensional position and dynamics, and it probably influences the pontine and midbrain areas collectively referred to as the saccade generating circuitry. It is doubtful, however, that this information reaches cerebral cortex (reviewed by Bridgeman 1995). When motoneurons are stimulated to evoke a saccade just prior to a visually-guided saccade, monkeys fail to compensate for the evoked saccade; they errantly make visually-guided saccades as if the eyes had not moved (Mays and Sparks 1981; Schiller and Sandell 1983). The stimulation seems to fail at creating a corollary discharge signal that can inform the monkey about the evoked saccade. In contrast, monkeys do compensate for evoked saccades if the SC or parts of the pons are stimulated (Guthrie et al. 1983; Sparks et al. 1987).

**What the saccade generating circuits tells the SC** Just above the motoneuron level is the saccade generating circuitry, and the importance of corollary discharge in this network (Fig. 14, thin solid arrow) is well known (Robinson 1975). The number of corollary discharge paths in this network, where they originate and end, and the signals they carry are still a matter of debate and modeling. It is generally agreed that the signals represent saccadic dynamics, e.g. speed, and that the feedback reaches the SC (Keller and Edelman 1994; Keller et al. 1996a; Soetedjo et al. 2002).

**What the SC tells the FEF** While it is clear that many corollary discharge paths may ascend via thalamus to cortex (Steriade et al. 1997; Tanaka 2003), the one that is best understood at this point is that running from SC to FEF (Fig. 14, bold solid arrow). The anatomy of this pathway is well established (Lynch et al. 1994), some of its signals
and functions were described in the present experiments, and a long history of research on the source of the pathway, the SC, provides valuable insight as to the nature of the corollary discharge signal sent to the FEF. This latter point is discussed in detail below.

**What the FEF tells other cortical areas** The highest level of the chain in Figure 14 depicts a hypothesis that corollary discharge may course from FEF to other areas of cortex. The FEF is well situated to be a gateway of corollary discharge, as it receives corollary discharge from the SC, it may create its own corollary discharge of saccadic instructions that it sends downstream, and it sends efferents to wide areas of the prefrontal, dorsomedial frontal, parietal, and temporal lobes (Leichnetz and Goldberg 1988; Schall 1997). An apparent conundrum, however, is why the FEF – itself an apparent generator of saccadic commands – would even need to receive corollary discharge from the SC. This may be explained by the fact that presaccadic activity in the SC is more tightly linked to saccade generation than that in the FEF (reviewed by Sommer and Wurtz in press; Wurtz et al. 2001). The FEF gains more detailed and credible information as to when and where a saccade will go by listening to the SC than by relying only on its own internal signals.

That the FEF may distribute corollary discharge to the rest of cortex is consistent with the classic view of Teuber (1966) that frontal cortex in general plays such a role. We do not presume that the FEF is the only such gateway of corollary discharge to the rest of cortex, but it seems well suited to be one such gateway.
The role of the SC-MD-FEF pathway in corollary discharge

There are two key questions one must ask when analyzing any corollary discharge signal: what is the signal a corollary of, and how does the recipient structure use it? First, because we know that the neurons projecting from SC to MD are similar to those in the overall population of neurons in the SC intermediate layers (Sommer and Wurtz submitted), we can infer what is represented by the signals sent into the SC-MD-FEF pathway based on what is known about SC neurons in general. In this paper and the accompanying one (Sommer and Wurtz submitted) we have used the shorthand terminology of saying that presaccadic activity in the SC-MD-FEF pathway encodes where a saccade will go. This is true when saccades are made to stationary visual targets, but if the actual saccade differs from that specified by the target it becomes clear that the SC saccadic command is in target, not motor, coordinates (Frens and Van Opstal 1997; Goossens and Van Opstal 2000; Keller et al. 1996b; Stanford and Sparks 1994). The SC activity still represents a saccadic command, as it is intimately tied with executing the saccade (e.g. Everling et al. 1998; Sparks 1978) and is present with spontaneous saccades in darkness, sans visual targets (Wurtz and Goldberg 1971); it is just that, spatially, the command encodes the retinotopic location to achieve, not the exact saccadic trajectory that will be made. This is probably adequate for the cortex since the discrepancy between the SC representation of the saccade and the actual saccade would be negligible during the most typical natural behavior of inspecting a visual scene.

Another important aspect of the SC saccadic signal is its two-dimensional nature: it encodes direction and amplitude but not torsion (Hepp et al. 1993). The brain, however, seems to use corollary discharge of all three dimensions of eye movement
Corollary discharge of torsion therefore must arise from outside of the SC.

Finally, we must consider how the FEF uses the corollary discharge signals that it gets from the SC. Our recording and inactivation results indicate that these signals represent the vector of a planned saccade. Under the hypothesis that the FEF can perform vector subtraction (Goldberg and Bruce 1990), from this vector and one representing the visual target location relative to the fovea (carried by visually responsive FEF neurons) the second saccade in a double-step task could be calculated. Similar calculations could contribute to more complex behaviors as well (e.g. triple-step sequences, Tian et al. 2000). The FEF may also use SC-derived corollary discharge for purely visual purposes. The visual receptive fields of many FEF neurons shift prior to a saccade to the locations they would be expected to occupy after the saccade (Sommer and Wurtz 2003; Umeno and Goldberg 1997), and such presaccadically remapped receptive fields may mediate the perception of space constancy across saccades (Ross et al. 2001). Recent psychophysical studies suggest that SC-derived corollary discharge contributes unequally to coordination of saccadic sequences as opposed to maintenance of visual stability, being more important for the latter than the former (Bahcall and Kowler 1999; Tanaka 2003). Future inactivation studies of the SC-MD-FEF pathway are needed to directly test this hypothesis.
Acknowledgements

We thank our colleagues in the Laboratory of Sensorimotor Research for helpful comments and Mitchell K. Smith for technical help with the inactivations.
References


**Schiller PH and Sandell JH.** Interactions between visually and electrically elicited saccades before and after superior colliculus and frontal eye field ablations in the rhesus monkey. *Exp Brain Res* 49: 381-392, 1983.


Sommer MA and Wurtz RH. What the brainstem tells the frontal cortex. I. Oculomotor signals sent from superior colliculus to frontal eye field via mediodorsal thalamus. Submitted.


Figure Legends

**Figure 1:** Hypothesis and methods. (A) We hypothesized that the superior colliculus (SC) sends a corollary discharge upstream at the same time it sends a motor command downstream. (B) To test our hypothesis we interrupted the signals (X) flowing upstream through the pathway from SC to mediodorsal thalamus (MD) to the frontal eye field (FEF) and studied the monkey’s behavior. The interruption was achieved by injecting muscimol at the sites of previously recorded MD relay neurons. (C) Injection sites relative to recording sites. Previously (Sommer and Wurtz submitted) we found MD relay neurons at sites marked with a dot or polygon. Here we performed injections at the sites marked with polygons as follows: ▲, injections 1, 2, and 3 (all muscimol); ♦, injection 4 (muscimol) and 7 (saline); ■, injection 5 (muscimol); ▼, injection 6 (saline). Table 1 provides details of each injection. Note that the injection sites in the two monkeys were in opposite hemispheres, but for consistency throughout this paper we will depict all *contraversive* saccades (relative to the injection site) as *rightward*.

**Figure 2:** Detecting corollary discharge deficits using the double-step task. (A) Spatial (*left*) and temporal (*right*) aspects of the task. Monkeys initially foveated a fixation spot (Fix) and then two targets (T1 and T2) appeared sequentially in the periphery. The task was to make two saccades (Sac1 and Sac2) to the locations of the extinguished targets. Contra, contraversive; Eye$_h$ and Eye$_v$, horizontal and vertical components of the eye position. (B) Accuracy and precision deficits. Normal behavior (*left column*) is compared with deficits in accuracy (*middle column*) or precision (*right column*). *Top*
row: Normal and impaired sharp-shooting. In multiple trials, shots (blue dots) are made in attempt to hit the bull’s-eye (orange ring). Bottom row: Normal and impaired internal monitoring of saccades. In multiple trials, the brain creates corollary discharge signals (CD, blue arrows) in attempt to represent a saccade (orange arrow). (C) Normal and impaired double-step behavior. The monkey’s internal estimate of its behavior (top row) is contrasted with its actual behavior (bottom row). Relative to the normal behavior (left), second saccades should change considerably during a corollary discharge accuracy deficit (middle) or precision deficit (right). Second saccades from two of the three hypothetical trials are labeled (trial 1 and 3) to help illustrate how the monkey’s reliance on its CD signals (top row) causes the various patterns of second saccades (bottom row). See Introduction for details.

Figure 3: Example data from the double-step task before (blue) and during (orange) MD inactivation. Superimposed are saccades from (A) all trials and (B) correct trials only. The dots represent the fixation spot (Fix) and target locations (T1 and T2). (C) Summary of the correct trials before and during inactivation, showing the means and SDs of initial fixation locations, first saccade endpoints, and second saccade endpoints. The only significant change during inactivation was a contraversive shift in second saccade endpoints. n.s.d., not significantly different. The label “2MDLA1c” in panel A identifies the data according to the following code: the first five characters correspond to the five columns of Table 1 (Injection 2, Muscimol, Double-step task, Light, configuration A) and the subscript identifies the specific target pair used (target pair 1, contralateral).
Diagrams of target configurations and specific target pairs are shown in Figure 4A. This labeling system is used throughout the paper.

**Figure 4:** The target configurations used in this study. (A) In the left column are shown double-step configurations A (top), B (middle), and C (bottom). Each configuration comprised several target pairs that shared a common first target in the contra- or ipsilateral hemifield but differently located second targets; each target pair is labeled with an italicized number and letter by its second target. In the right column are shown examples of saccadic sequences generated in response to each configuration. The sequences are from before inactivation only, so as to illustrate the normal baseline behavior. Mean first and second saccade vectors are shown (as in Fig. 3C), although the first saccade vectors on each side mostly overlap. Horizontal and vertical SDs of all second saccade endpoints are also shown. Dashed lines shows vertical meridians. (B) Single-step task configurations. In each trial, monkeys made a single saccade from a central fixation spot (black circle) to a target (white circle).

**Figure 5:** Examples of impairments using various target configurations (A-D) and of lack of impairments in ipsiversive (E) and saline control (F) trials. Note that the examples in panels A-D are from four different inactivation experiments and that the data in panels E and F are the ipsiversive and saline control complements of the data shown in panel C. Occasionally, as in panels A,B, and D, contraversive shifts in second saccade endpoints were accompanied by vertical shifts, but these always seemed to be carried over from vertical shifts in first saccade endpoints.
Figure 6: Summary of data that revealed an accuracy deficit in corollary discharge. (A) Horizontal (left) and vertical (right) shifts of second saccade endpoints during inactivation relative to before. In the inset graphs at left, the data from the main graph are split into the component data from each monkey (the mean shift for each monkey was significantly greater than zero, p < 0.025). Also shown are horizontal and vertical shifts in the (B) first saccade endpoints and (C) in initial fixations, as well as the horizontal shifts of second saccade endpoints from (D) trials involving ipsiversive first saccades (left) and saline control trials (right). Some of these data were published previously (Sommer and Wurtz 2002).

Figure 7: Exact directions of second saccade endpoint shifts. Plotted are the vectors representing the shift in each individual case, the mean vectors, and confidence ellipses regarding the mean vector tips, for (A) trials involving contraversive first saccades, (B) trials involving ipsiversive first saccades, and (C) saline control trials.

Figure 8: Analysis of corollary discharge precision. (A) The SDs of second saccade endpoints during vs. before MD inactivation. Filled symbols show cases in which the SD changed significantly (p < 0.025) during inactivation. (B) Summary data from an example injection. (C) The individual second saccades from this example before (top) and during (bottom) inactivation. We depicted each saccade as a vector by connecting its initial and final position with a line. (D) Same saccades as in panel C, but spread along the vertical dimension so that each can be seen distinctly. Each x-axis is expanded as compared to that in panel C. At the lower right are illustrated our two quantifications of
each saccade: the saccadic direction (θ) and amplitude (ρ). Panel A was modified from Sommer and Wurtz (2002).

**Figure 9:** Comparison of *observed* second saccade vectors with *ideal* ones expected if corollary discharge had been perfectly precise. (A) Ideally compensating second saccades for the Figure 8 example case (cf. Figure 8C). Circle and triangle show means of the second saccade endpoints before and during inactivation, respectively (from Fig. 8B). (B) Analysis of how well the monkey adjusted its second saccade *directions* to account for trial-by-trial fluctuations in its first saccades. The observed θ for each second saccade (from the vectors in Figure 8C or D) is plotted against the ideal θ (from panel A of this figure). Before inactivation there was a direct correlation between observed θ and ideal θ with a linear regression slope near unity (1.24), but during inactivation the correlation was not significant and the slope was only 0.32. (C) Same as in panel B, except now the ability to adjust second saccade *amplitude* trial-by-trial is evaluated; observed ρ is plotted vs. ideal ρ. Neither correlation is significant, either before or during inactivation. (D) Overall results showing how the ability to adjust the direction of the second saccade trial-by-trial was impaired by MD inactivation. For trials involving contraversive first saccades (left), the average slope of the linear regression describing the observed θ vs. ideal θ relationship dropped by 0.58, which was highly significant as shown. In contrast, for trials involving ipsiversive first saccades (middle) and for saline control trials (right) there was no significant change in slope.
**Figure 10:** Lack of impairments to saccades made in the single-step task. See Results for details. (A) Summary of single saccades made before and during one example inactivation. (B) Histograms showing how accuracy was affected by inactivation. (C) Scatter plots of the SDs of saccadic endpoint clusters before vs. during inactivation as a measure of how precision was affected by inactivation. (D) Scatter plots of reaction times of the saccades before vs. during inactivation. The data in panels B-D represent 14 pairs of before-during saccadic endpoints in each direction (contraversive and ipsiversive), 12 of which were from the target-absent version of the task and 2 from the target-present version; we collected some endpoint pairs that we later omitted from analysis due to low number of saccades to analyze (we required a minimum of five in each before or during endpoint cluster) or because they were vertically directed (see Fig. 4B, configuration A) rather than ipsi- or contraversive.

**Figure 11:** First two possible alternative explanations for the double-step accuracy deficit. (A) Maybe the shifts in second saccades were due to horizontal errors of first saccades. *Left:* The single case in which there was a significant contraversive shift in first saccade endpoints. *Right:* Plot of the horizontal shift in first second saccade endpoints for all cases (ordinate) as a function of the horizontal shift in first saccade endpoints. There was no relation; larger first saccade shifts were not associated with larger second saccade shifts. Horizontal errors did not accumulate. (B) Maybe the shifts in second saccades were due to accumulating neuronal damage. *Left:* An example showing “after” data compared with before data. For reference, the during data are shown too, using lines but no symbols. After data were not significantly different from before data; recovery
was complete. Middle: For the 11 cases in which there was a significant accuracy deficit, the behavior recovered completely after inactivation. Right: Also, for these 11 cases here was no lingering precision deficit. The after data were collected one day following inactivation in 8 of the 11 cases and one to three weeks later in the 3 other cases.

**Figure 12:** Third and fourth possible alternative explanations: maybe all saccades were rotated or visual/memory space was warped. (A) Example case showing a contraversive shift in second saccade endpoints (from Figure 5C). (B) Single-step control case for this particular example showing that saccades did not just rotate clockwise to cause a contraversive shift (top) and that this was true in general (bottom). (C) Another single-step control case for this example, showing the only possible evidence for a contraversive warping of visual perception or memory (top). This case was the exception to the rule; in general (bottom) there were no shifts in these vision- and memory-matched control trials.

**Figure 13:** Bilateral effects of MD inactivation. (A) Increased reaction times. Bars show means and SEs of the average reaction times (or inter-saccadic intervals) of individual cases; each bar thus represents n = 22 cases. Asterisks label significant changes (at p < 0.05) during inactivation vs. before. From *left to right* are graphed the reaction times of first saccades from all trials and, from correct trials only, the reaction times of first saccades, the inter-saccadic intervals (ISIs), and the reaction times of second saccades. All reaction times were measured relative to the appearance of the first target. (B) Impaired overall performance. The bars show means and SEs of the average percent corrects from each case (n = 22 cases per bar). A schematic depicting correct
performance is shown below the bar graph. (C) Distribution of the various types of error trials before and during inactivation from trials involving (top) contraversive first saccades and (bottom) ipsiversive first saccades. Underneath the top distribution, each class of error trial is diagrammed below its respective spot on the abscissa.

**Figure 14:** Multiple levels of corollary discharge in the visuosaccadic system.

Downward arrows depict gradual progression of the saccadic command, and upward arrows depict corollary discharge signals. The MD relay node is omitted from the SC-to-FEF feedback pathway for clarity. This is a highly simplified diagram that certainly will have to be revised as more ascending pathways are studied physiologically. In particular, anatomical evidence hints that many more corollary discharge pathways from subcortical regions up to cortex may be found. See Discussion for details. At bottom are depicted the eye and an extraocular muscle.
Table 1. Summary of Experiments

<table>
<thead>
<tr>
<th>Injection Number</th>
<th>Agent (Amount)</th>
<th>Experiments Performed</th>
<th>Ambient Illumination</th>
<th>Target Configuration*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (C)</td>
<td>Muscimol (2.4 μL)</td>
<td>Double-step</td>
<td>Light</td>
<td>A</td>
</tr>
<tr>
<td>2 (C)</td>
<td>Muscimol (2.0 μL)</td>
<td>Double-step</td>
<td>Light</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Double-step</td>
<td>Dark</td>
<td>A</td>
</tr>
<tr>
<td>3 (C)</td>
<td>Muscimol (1.6 μL)</td>
<td>Double-step</td>
<td>Light</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Double-step</td>
<td>Dark</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single-step</td>
<td>Light</td>
<td>A</td>
</tr>
<tr>
<td>4 (B)</td>
<td>Muscimol (3.0 μL)</td>
<td>Double-step</td>
<td>Dark</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single-step</td>
<td>Dark</td>
<td>B</td>
</tr>
<tr>
<td>5 (B)</td>
<td>Muscimol (1.6 μL)</td>
<td>Double-step</td>
<td>Dark</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Single-step</td>
<td>Dark</td>
<td>B</td>
</tr>
<tr>
<td>6 (B)</td>
<td>Saline (4.4 μL)</td>
<td>Double-step</td>
<td>Dark</td>
<td>C</td>
</tr>
<tr>
<td>7 (B)</td>
<td>Saline (4.4 μL)</td>
<td>Double-step</td>
<td>Dark</td>
<td>C</td>
</tr>
</tbody>
</table>

*Target configurations represented by the letters A, B, and C are shown in Figure 4.
Table 2. Results of Precision Analysis

<table>
<thead>
<tr>
<th>Change During vs.</th>
<th>Contraversive Sac1 Cases</th>
<th>Ipsiversive Sac1 Cases</th>
<th>Saline Control Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Inactivation</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Second Saccade Direction: Actual $\theta$ vs. Ideal $\theta$

- Percent Correlated*:
  - Contraversive: $-36\%$ (50%; 14%; 0.022)
  - Ipsiversive: $-14\%$ (59%; 45%; 0.55)
  - Saline Control: $8\%$ (17%; 25%; 1.0)

- Regression Slope†:
  - Contraversive: $-0.58$ (0.97; 0.39; 0.0013)
  - Ipsiversive: $-0.12$ (0.75; 0.63; 0.43)
  - Saline Control: $0.06$ (0.57; 0.62; 0.65)

- Regression Intercept:
  - Contraversive: $-3.6$ (-1.7; -5.2; 0.49)
  - Ipsiversive: $-0.04$ (-7.0; -7.0; 0.99)
  - Saline Control: $-0.31$ (-2.4; -2.7; 0.83)

Second Saccade Amplitude: Actual $\rho$ vs. Ideal $\rho$

- Percent Correlated:
  - Contraversive: $-18\%$ (36%; 18%; 0.31)
  - Ipsiversive: $-9\%$ (50%; 41%; 0.76)
  - Saline Control: $0\%$ (18%; 18%; 1.0)

- Regression Slope:
  - Contraversive: $-0.46$ (0.74; 0.28; 0.028)
  - Ipsiversive: $-0.14$ (0.69; 0.54; 0.38)
  - Saline Control: $0.19$ (0.59; 0.79; 0.47)

- Regression Intercept:
  - Contraversive: $5.1$ (3.4; 8.5; 0.079)
  - Ipsiversive: $2.2$ (4.7; 7.0; 0.32)
  - Saline Control: $-4.6$ (8.2; 3.6; 0.22)

* Percent Correlated cell contents show difference in the percent of cases having a significant correlation during vs. before inactivation (percent with significant correlations before inactivation; percent during inactivation; p value of Fisher Exact test).

Significance levels were p < 0.025 because two correlation tests were performed on each data set. † Regression Slope and Intercept cell contents show difference in mean values...
during vs. before inactivation (means before inactivation; means during inactivation; p value of paired t-test). Significance levels were p < 0.0125 because changes in four parameters were evaluated for each data set. Significant data are shown in bold. Due to round-off error, some differences do not match those that would be calculated from the parenthesized means.
Figure 1
Sommer & Wurtz (paper II)

A

Corollary Discharge
(information about saccades)

Motor Command
(generation of saccades)

B

muscimol

FEF

MD

C

Monkey C

Monkey B

Anterior (mm)

Lateral (mm)

Midline
A Double-Step Task

B Shots relative to bull's-eye:

C Monkey's internal estimate of behavior:

Actual behavior:

Figure 2 Sommer & Wurtz (paper II)
Figure 3
Sommer & Wurtz
(paper II)

During
Before
Contra
All Trials

A

B

Correct Trials Only

C

Before vs. During Summary

-5 20
5
10
15
20

2MDLA_{lc}

-5

Before

During

p < 0.001

2.1°

n.s.d.

n.s.d.

n.s.d.
**A** Double-Step Task Configurations

- **Fix**
- ○ **T1** → Sac1
- ○ **T2** → Sac2

**Configurations**

**Ipsilateral**

- 1i
- 2i

**Contralateral**

- 1c
- 2c

**Example Sequences**

**B** Single-Step Task Configurations

**Configuration A**

**Configuration B**
A  Second Saccade Endpoints

B  First Saccade Endpoints

C  Initial Fixations

D  Second Saccade Endpoints in Comparison Cases

- Monkey B: Mean 0.98° (n.s. from zero)
- Monkey C: Mean 1.29° (greater than zero, p < 0.001)
- Contra-Ipsi: Mean 1.12° (greater than zero, p < 0.001)
- Saline Control Trials: Mean 0.08° (n.s. from zero)
- Ipsiversive Sac1 Trials: Mean -0.41° (n.s. from zero)
- Up-Down: Mean 0.06° (n.s. from zero)

- Mean -0.03° (n.s. from zero)
- Mean 0.03° (n.s. from zero)
- Mean 0.08° (n.s. from zero)
- Mean -0.41° (n.s. from zero)
- Mean 1.29° (greater than zero, p < 0.001)
- Mean 1.12° (greater than zero, p < 0.001)
- Mean 0.08° (n.s. from zero)
- Mean -0.41° (n.s. from zero)
Figure 8
Sommer & Wurtz
(paper II)

A

B

C

Second Saccades

D

Before

During

Horizontal Position (deg.)
Figure 9
Sommer & Wurtz
(paper II)

A. Ideal Second Saccades

Before

\[ y = 1.24x - 2.2 \]
\[ R = 0.71, \, p = 0.00064 \]

During

\[ y = 0.35x + 6.1 \]
\[ R = 0.34, \, p = 0.16 \]

B. Observed \( \theta \) (deg.) vs. Ideal \( \theta \) (deg.)

Before

\[ y = 0.32x + 14.1 \]
\[ R = 0.25, \, p = 0.27 \]

During

\[ y = 0.35x + 7.2 \]
\[ R = 0.41, \, p = 0.068 \]

C. Observed \( \rho \) (deg.) vs. Ideal \( \rho \) (deg.)

Before

\[ y = 0.35x + 6.1 \]
\[ R = 0.34, \, p = 0.16 \]

During

\[ y = 0.35x + 7.2 \]
\[ R = 0.41, \, p = 0.068 \]

D. Overall Results, All Injections

Before

\[ \text{Contraversive Sac}1 \]
\[ \text{Ipsiversive Sac}1 \]
\[ \text{Saline Controls} \]

Difference:

\[ -0.58 \] \( (p = 0.0013) \]
\[ -0.12 \] \( (\text{n.s.d.)} \]
\[ +0.05 \] \( (\text{n.s.d.)} \]
**A** Single Saccades: Example

- **Before**
- **During**

D = 1.29°, 1.90°, 1.38°, 0.68°, 0.67°, 0.96°, 0.01°

**B** Accuracy

- Significant shift either horizontally or vertically (p < 0.025)

- **Contra** Mean 0.85 (n.s.d. from ipsi)
- **Ipsi** Mean 0.80

**C** Precision

- ○ Horizontal SD
- △ Vertical SD

**D** Reaction Times

- **Contra**
- **Ipsi**
A Were Sac2 shifts due to Sac1 shifts?

Lack of Correlation Between Sac1 and Sac2 Shifts

B Were Sac2 shifts due to cumulative tissue damage?

Recovery of Accuracy Deficits

Recovery of Precision Deficits

Significant (p < 0.025)

Difference: -0.01 (n.s.d.)

Mean 0.28° (n.s.d. from zero)
Other possible reasons for Sac2 shift

Due to a rotation of all saccades?

Due to a shift in visual or memory representation?

Due to a rotation of all saccades?

Due to a shift in visual or memory representation?
A Reaction Times

- **All Trials: First Saccades**
  - Reaction Time (ms)
  - Contra: 200, 300, 400, 500
  - Ipsi: 200, 300, 400, 500

- **Correct Trials: First Saccades**
  - Reaction Time (ms)
  - Contra: 200, 300, 400, 500
  - Ipsi: 200, 300, 400, 500

- **Correct Trials: ISIs**
  - Inter-Saccadic Interval (ms)
  - Contra: 100, 200, 300, 400, 500
  - Ipsi: 100, 200, 300, 400, 500

- **Correct Trials: Second Saccades**
  - Reaction Time (ms)
  - Contra: *500, 400, 300, 200, 100, 0
  - Ipsi: *500, 400, 300, 200, 100, 0

B Performance

- **Percent Correct**
  - Contra: 80, 60, 40, 20, 0
  - Ipsi: 80, 60, 40, 20, 0

C Types of Errors

- **Contraversive Sac1 Cases**
  - Sac1 to T2, then no Sac2
  - Sac1 to T2, then Sac2 made
  - Sac1 to T1, but no Sac2
  - Sac1 to T1, but Sac2 wrong
  - Sac1 to neither T1 nor T2

- **Ipsiversive Sac1 Cases**
  - Sac1 to T2, then no Sac2
  - Sac1 to T2, then Sac2 made
  - Sac1 to T1, but no Sac2
  - Sac1 to T1, but Sac2 wrong
  - Sac1 to neither T1 nor T2
Figure 14
Sommer & Wurtz
(paper II)