The pontine nuclei (PN) are the major intermediary elements in the corticopontocerebellar pathway. Here we asked if the PN may help to adapt the spatial reference frames used by cerebrocortical neurons involved in the sensory guidance of movement to a format potentially more appropriate for the cerebellum. To this end, we studied movement-related neurons in the dorsal PN (DPN) of monkeys, most probably projecting to the cerebellum, executing fixed vector saccades or, alternatively, fixed vector hand reaches from different starting positions. The 83 task-related neurons considered fired movement-related bursts before saccades (saccade-related) or before hand movements (hand movement-related). About 40% of the SR neurons were "oculocentric," whereas the others were modulated by eye starting position. A third of the HMR neurons encoded hand reaches in hand-centered coordinates, whereas the remainder exhibited different types of dependencies on starting positions, reminiscent in general of cortical responses. All in all, pontine reference frames for the sensory guidance of movement seem to be very similar to those in cortex. Specifically, the frequency of orbital position gain fields of SR neurons is identical in the DPN and in one of their major cortical inputs, lateral intraparietal area (LIP).

Keywords: electrophysiology, frame of reference, PN, rhesus monkey

Introduction

The corticopontine projection taps any cortical area known to contribute to spatial perception and the control of movement (Glickstein et al. 1985, 1990). Projection neurons in the pontine nuclei (PN), the targets of corticopontine afferents, in turn project to the cerebellar cortex (Brodal 1979; Brodal and Bjøljo 1992, 1997), and are also involved in the control of movement (Thier et al. 2002; Ito 2005; Bastian 2006; Nowak et al. 2007; Tseng et al. 2007). Hence, the conclusion suggests itself that the corticopontocerebellar projection linking the 2 cortices conveys information relevant to the sensory guidance of movements. Indeed this notion has received ample support from studies of patients and animals (Fisher 1967; May et al. 1988; Thier et al. 1991; Kim et al. 1995, Suzuki et al. 1999; Schmahmann et al. 2004a; 2004b).

In order to generate a successful sensory-guided movement, information on the location of the target has to be integrated into a motor plan. A large body of work suggests that several cerebrocortical areas play a key role in forming and updating such movement plans (e.g., Batista and Andersen 2001; Kakei et al. 2003; Pesaran et al. 2006). Typically, neurons in these areas are tuned to specific types of sensory-guided movement represented in a distinct sensorimotor frame of reference (Lacquaniti et al. 1995; Rizzolatti et al. 1997; Andersen et al. 1998; Crawford et al. 2004). For instance, the parietal reach area (PRR) encodes visually-guided hand reaches in eye-centered coordinates (Batista et al. 1999; Cohen and Andersen 2000) or neurons in parietal area 5 represent reaches in body-centered coordinates (Kalaska et al. 1990; Lacquaniti et al. 1995). Representing such movements in distinct frames of reference requires the integration of information from different sensory channels and from different parts of the body. For instance, parietal areas like area 7a and 7m combine retinal, eye, and hand information, giving rise to complex interactions between gaze angle and hand position (Ferraina et al. 1997; Battaglia-Mayer et al. 2007). A comparable diversity of preferences characterizes motor and premotor cortical areas contributing to hand movements (Weinrich et al. 1984; Scott et al. 1997, Kakei et al. 1999, 2003; Fuji et al. 2002, Pesaran et al. 2006). Irrespective of the profound differences, most of the hand movement-related cerebrocortical areas share the coding of object location relative to hand and arm and the changes this relationship experiences in the course of the movement. By way of the corticopontocerebellar pathway, all these cerebrocortical areas have the same privileged access to the cerebellar cortex, a structure devoted to movement kinematics rather than spatial relationships. This notion is based on the observation that cerebellar Purkinje cells encode kinematic parameters such as position, velocity, and acceleration of limb and eye movements (Noda and Fujikado 1987; Shidara et al. 1993; Thier et al. 2000, 2002; Townsend et al. 2006; Ebner et al. 2011). On this account, the information it receives has to be brought into an appropriate frame of reference.

How is the transformation brought about between representations that differ so profoundly? We hypothesized that the PN might provide the key.

Methods

Subjects and Surgery

We recorded from single units of 2 male rhesus monkeys (Macaca mulatta) B and N. The surgical procedure was as described earlier (Thier and Erickson 1992; Tziridis et al. 2009). In short, both monkeys were implanted with individually adapted titanium head posts and recording chambers (tilted 15° toward posterior, inner diameter of 28 mm) centered on the sagittal midline above the occipital cortex as well as with scleral search coils for the recording of eye position (Judge et al. 1980). All animal preparations and procedures fully complied with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were approved by the local animal care committee (RP Tübingen, FG Tierschutz).

Setup, Timing, and Spatial Configuration of the Stimuli

All data were recorded in complete darkness. Eye movements of the monkeys were monitored and recorded using a search coil system at 1-kHz sampling rate (spatial resolution <0.1° visual angle), and hand movements were recorded with an ultrasonic 3D tracker using a sampling rate of 100 Hz.
and providing a spatial resolution <1 mm (CMS10, Zebris Medical GmbH, Isny, Germany). A CRT-monitor (CM20MKR, Tatung, Taipei, Taiwan, 20” diagonal, 1024 × 768 resolution, 72-Hz refresh rate) was located in reaching distance (33-cm naseon-screen distance) in front of the monkeys. This distance was used to calculate the displacement of eyes and hand in degree visual angle. The monkeys were trained to tolerate the loose restraining of one arm to the monkey chair and the placement of the ultrasound emitter on the other hand. The emitter was attached by an elastic band yoking the 3 middle fingers at the level of the proximal interphalangeal joint such as to lie above the middle finger. The emitter signal was associated with hand position by asking the monkey to move his hand to predefined locations on the screen cued by small dots of light (diameter 20 min of arc). A corresponding procedure was used to calibrate the search coil signal. During experiments, the eyes and the hand had to stay inside quadratic position windows whose size was typically 3 × 3 for the hand and 2 × 2” for the eyes if the desired location was central and 5 × 5” and 4 × 4”, respectively, if it was peripheral.

Monkeys learned to execute memory-guided saccades and memory-guided reaching movements of the hand to one of 8 possible target locations at eccentricities of 12” of visual angle relative to the starting position on a radial that were separated by 45° (0°, 45°, 90°, etc.). Movements started from 3 distinct starting positions on the horizontal meridian (7° left, center, 7° right) with the second, nonmoving effector keeping fixation of one of these 3 positions throughout. The 5 possible combinations of eye and hand starting/fixed positions were tested in blocks, whose order was pseudorandomized except for the first (“baseline”) block, in which both effectors were centered at the start of the trial. Each block required at least 6 correctly executed sets of movements of each effector in all 4 directions, yielding a minimum number of 96 trials per block and a minimum of 480 correct trials for a complete test of a given neuron. Note that for a given trial, the effector to be moved was chosen at random by providing appropriate cues as described next (Fig. 1A).

To start a trial, the monkeys had to place one hand onto the blue hand fixation dot (diameter 20 min of arc visual angle) and at the same time start fixating the green eye fixation dot (diameter 20 min of arc visual angle), both located at the starting positions determined by the current condition. After 800-1200 ms, a colored spatial cue—either blue for hand movements or green for eye movements—was flashed for 200 ms in one of the 8 possible target positions. The monkeys had to memorize the location of the spatial cue as well as the type of movement required for 300-500 ms after the disappearance of the cue, whereupon the 2 fixation dots were extinguished, telling the monkey to start the movement to the memorized location. The monkeys had 500 ms to perform the requested movement. They had to keep fixation of the acquired target location with the effector that had carried out the movement for another 400 ms, while keeping the second, nonmoving effector at its original fixation position throughout the whole trial.

Monkeys were rewarded for successful trials by the delivery of a drop of juice or water, depending on their individual preference. Monkeys were motivated to work for these liquid rewards as free access to liquid outside the experiments was restricted according to standard procedures (Laule et al. 2003) (see also technical bulletin and guidelines of the German Primate Center on fluid restriction in the shaping of behavior of rhesus monkeys in neurophysiological experiments, Kaup F-J and Treue S, 16 April 2007). After a successful trial, monkeys had 1 s to reach the fixation dot in order to start the next trial. If the monkey exceeded this limit, a time-out of 1 s followed. A trial was aborted, the data discarded and no reward delivered if the monkey violated one of the control windows or failed to use the effector required. An overview of all conditions with the different starting positions of hand and eyes is given in Figure 1B, which also introduces the icons used in later figures to identify specific conditions. To the right of the icons, all possible target positions for hand and eyes are sketched.

**Offline Analysis of Behavioral Data**

Saccade and hand movement onsets were defined as the time when the acceleration of the eyes or hand exceeded a threshold (2000 /s² for the eyes and 500 /s² for the hand, respectively). To this end, we analyzed the acceleration in a time window after the go signal (for the eyes 50–300 ms and for the hand 50–500 ms after the go signal) in which we expected the onset of the movement. The termination of the movement was determined as the time when the acceleration fell below the threshold. All analyses were performed offline with custom-made programs written in commercial software (Matlab, MathWorks Inc., Natick, MA, USA; StatSoft Inc., Tulsa, OK, USA). The electrophysiological data (see below) were aligned to movement onset.

**Electrophysiological Recording**

The localization of the PN in the 2 monkeys used in the present study is described in detail in an earlier publication that was based on the same 2 monkeys (Tziridis et al. 2009). The neurons presented in this study were recorded in the same region as described in the histological reconstruction there. Compared with the earlier study, we did not record from the whole dorsal and dorsolateral PN but concentrated on the region where we found an overlap between the 2 classes of movement-related neurons that corresponds to a volume from 1.5 to 3.5 mm lateral from midline, 2.0 mm anterior-posterior range, and approximately 2.0 mm in depth. Recordings were performed in the contralateral PN relative to the arm used.

Extracellular action potentials were recorded with self-made glass-coated platinum-tungsten electrodes (fiber diameter 80 μm, impedance 1–2.5 MΩhm) using a 5-probe multielectrode system (Thomas Recording, Gießen, Germany) and separated on-line by a template matching algorithm (Wörgötter et al. 1986) using a commercial detector (Multi Spike Detector, Alpha Omega Engineering, Nazareth, Israel). We recorded up to 2 isolated neurons per electrode simultaneously with up to 5 independently movable electrodes. The electrodes were arranged in a cross-like shape with a distance of 150 μm between neighboring electrodes. Only units recorded long enough to have at least 6 trials per direction and condition were considered. We only considered neurons with movement-related bursts and without any accompanying visual responses for further analysis. Out of 248 neurons recorded, 120 (48.39%) were task related and 12 were discarded because of visual response components. In accordance with previous work (Dicie et al. 2004; Tziridis et al. 2009), we estimate that both groups may amount to about 50% of all neurons in the region explored. Neurons discharging during saccadic eye movements but not during hand movements were defined as saccade-related (SR) neurons. Conversely, neurons that discharged during hand movements but not during saccades were identified as hand movement-related (HMR) neurons. We know from our earlier work (Tziridis et al. 2009) that the percentage of neurons responding to eye as well as to hand movements is very low (less than 2%). In this study, none of them were found.

**Data Analysis**

For the generation of raster plots and perievent time histograms (PETH), trials were aligned with respect to the onset of the movement. Bursts were quantified in individual trials by applying a Poisson spike train analysis that allowed us to determine the onset and the offset of a burst and the characterization of the burst amplitude (Hanes et al. 1995). To characterize the directional preference of a unit, a cosine function was fitted to the polar plots of mean burst discharge rates (illustrated in Figure 2A) for the 8 directions for each combination of eye and hand starting positions (=condition). Directionality was assumed if a Rayleigh test indicated that the data differed from randomness. In this case, the preferred direction was estimated by the location of the circular mean, and the selectivity of the preference was given by the circular dispersion. The dependence of the preferred direction on the condition was tested by comparing the discharge rates as a function of direction for the baseline condition (both eyes and hand centered) with all the other conditions, by adopting pairwise Watson-Williams tests with Bonferroni corrections for multiple comparisons. A summary of the preferred direction and mean spike rate in the baseline condition of all movement-related neurons considered is given in Figure 2B.

For further analysis of possible interactions between the variables "preferred direction" and "discharge strength," we normalized the preferred direction of the baseline condition (eyes and hand centered)
Figure 1. Experimental paradigms. (A) Sequence of events. Each panel refers to a specific period of the monkey’s task; the durations are given below the panels. The arm is shown in gray (gray fixation dot), gaze direction in white (white fixation dot), and the white rectangle symbolizes the computer CRT screen. After a variable time of fixation, a peripheral target appeared, whose color matched the one of the effector the monkey was supposed to use upon the presentation of a later “go signal.” The monkey had to maintain fixation until the fixation dots disappeared and execute the requested movement with the requested effector only. (B) Overview of the $2 \times 5$ combinations considered, distinguished by the choice of the effector and the varying combinations of the starting position of the eyes and the hand, respectively. In the center panel, the HC/EC (= hand centered/eyes centered) condition is shown. The eccentric panels describe the conditions in which one of the effectors was positioned left and right, respectively (upper left: HL/EC: hand left/eyes centered; lower left: HC/EL: hand centered/eyes left; upper right: HR/EC: hand right/eyes centered; lower right: HC/ER: hand centered/eyes right). The plots to the right of the icons, which describe the combinations of hand and eye starting positions, represent the end points for the resulting hand-only movements (gray symbols) and the resulting eye-only movements (black symbols).
to zero degrees and calculated the changes relative to the zero degree baseline. Positive values indicate a rotation of the preferred direction in a counterclockwise manner, while conversely negative values express rotations in a clockwise direction. Data were statistically analyzed using an analysis of variance (ANOVA).

We categorized the recorded bursting neurons by the change of preferred direction and/or change of discharge strength in preferred and nonpreferred effector movement conditions. If one of both variables showed significant changes for the preferred effector movement, we classified the neuron as being starting position dependent for that effector. Otherwise, we counted it as vector coding for that effector. In nearly all cases, the response of the bursting neurons was independent of the nonpreferred effector. In the case of bursting SR (SRburst) neurons, we compared our population of pontine neurons with the population of cortical neurons of areas LIP and 7a described by Andersen et al. (1990) by a chi-square test. For this comparison, the data taken were those that were closest to our sample of neurons, namely the SR neurons in LIP and area 7a without subtraction of the background activity (Table 1 in the mentioned paper), in other words 71 SR neurons with “gain fields” and 20 vector coding neurons. For a second chi-square test of the linearity of peak response changes, we used the 35 LIP/7a neurons with planar gain fields and 36 cortical neurons with different gain fields to compare with our pontine neuron population with eye position-dependent firing rates, categorized by Spearman rank tests.

Figure 2. Effector specificity of responses of movement-related neurons recorded from the DPN. Neurons tested for responses to isolated hand and eye movements. (A) Distribution of preferred directions of all recorded HMR (black lines) and SR (gray lines) units for the hand centered/eyes centered (HC/EC) conditions. Note that recordings were from the PN located on different sides in the 2 monkeys. Preferred directions for recordings from the right PN in monkey N were mirrored to the left PN in order to make them comparable to data from monkey B. (B) Exemplary cosine fits (right polar plot) of plots of discharge rate as a function of direction (peak discharge rate ± standard deviation [left polar plot]) of a HMR neuron tested in the HC/EC condition during preferred effector (black lines) and nonpreferred effector movements (gray lines). (C) Plot of responses evoked by movements with the preferred effector as a function of movements with the nonpreferred one in the HC/EC condition. SR neurons are depicted by open circles, hand movement-related (HMR) units by filled squares. The histograms above and to the right side of the scatter plot give the number of SR (open bars) and HMR (filled bars) neurons responding with particular mean movement-related burst rates, binned in 10 spikes/s and 5 spikes/s for movements with the preferred and the nonpreferred effector, respectively.
The population responses of the 2 subgroups of bursting HMR (HMRburst) neurons were calculated adopting the approach described by Georgopoulos and colleagues in their analysis of motor cortex neurons (Georgopoulos et al. 1988; Schwartz et al. 1988). In short, for a particular reaching movement, we calculated the vector sum of the preferred directions of all neurons in the subgroup. Each directional vote was weighted according to the individual direction-tuning curve of a neuron. The resulting movement directions predicted by the population response were compared with the true movement directions in each of the 5 conditions by multiple linear regressions. The regressions obtained for the 2 subgroups of HMRburst neurons were tested against each other by t-tests. In all tests, differences were considered to be significant if \( P < 0.05 \). In the case of multiple comparisons, this level was Bonferroni corrected.

**Results**

We reasoned that the PN might contribute to the coordinate transformations needed for the sensory guidance of movements. In order to test this hypothesis, we tried to identify the frames of reference of 2 classes of PN neurons in the dorsal PN (DPN), known to be involved in target-directed movements, SR (Dicke et al. 2004), and reaching-related neurons (Tziridis et al. 2004), respectively. To this end, 2 monkeys learned to perform memory-guided saccades and hand reaches to locations in the frontoparallel plane in complete darkness. All movements had one and the same fixed movement amplitude and direction but started from different positions (Fig. 1B).

We recorded 108 movement-related units from the DPN of 2 monkeys, activated by either saccadic eye movements (SR, \( n = 45 \) [41.6%]; e.g., see Figs 3 and 4) or hand reaches (HMR, \( n = 63 \) [58.4%]; e.g., see Figs 7 and 8), selected for their lack of additional visual responses. This was assured by \( t \)-tests comparing the time of peripheral stimulus presentation with the baseline time during fixation. Of these neurons, 83 (83/108, 76.8%) responded with a burst before and/or during the movement, 27 (27/108, 25%) with saccade-related bursts (SRburst), and 56 (56/108, 51.8%) with reach-related bursts (HMRburst). As described in a previous study of movement-related neurons in the DPN (Tziridis et al. 2009), movement-related bursts were in any case at least broadly direction selective (compare Figs 2A and 5B) as well as effector specific, that is, neurons preferring saccades were not or at most marginally activated by hand reaches, and vice versa hand movement neurons were not responsive to saccades (Fig. 2C). The latencies of the burst responses in the preferred directions were also comparable to those reported earlier (Tziridis et al. 2009), with SRburst neurons showing a mean burst onset of 29.8 ms before saccade onset and HMRburst neurons bursting earlier at 71.1 ms before hand movement onset. The remaining 25 neurons responded to eye (18/108, 16.6%) or hand position (7/108, 6.5%) with modulations already prominent during fixation in different starting positions and were not considered for further analysis (for further information on the composition of the sample, refer to Table 1).

**Effects of Varying the Starting Position of the Eye on SR Neurons**

Figure 3 shows the example of a SRburst neuron broadly tuned for saccades to the right (Fig. 3A, right panel), completely ignoring hand reaches (Fig. 3A, left panel). The responses of the neuron to movements in 8 directions in the frontoparallel plane are documented by raster plots and filtered PETH (second-order low-pass filtered at 100-Hz corner frequency), aligned with respect to movement onset. The eyes started from a central position and the hand held the same central position throughout the trial. As explained in the methods, the directional dependence of a neuron’s discharge was assessed by Rayleigh tests, the preferred direction was estimated by the location of the circular mean, and the strength of the response in this direction read out from the cosine fit. Figure 3B compares the resulting fits for the exemplary SRburst neuron shown in Figure 3A for the 5 combinations of hand and eye starting position explored. As documented by this figure, varying the starting positions of the 2 effectors had no significant effect on the orientation or the maximal deflection of the tuning functions (directions: Bonferroni-corrected Watson–Williams tests, \( P > 0.05 \) corrected for all 4 cases; firing rates: one-way ANOVA, \( p > 0.05 \)). An SRburst that is independent of the starting position of the eyes and the starting position of the hand is in accordance with the representation of a saccade-related signal in an oculocentric frame of reference.

Figure 4A illustrates another SRburst neuron in the same format as the previous example. This neuron also preferred saccades to the right (Fig. 4A, right panel) without significant responses to hand movements (Fig. 4A, left panel). As suggested by Figure 4B, the preferred direction as well as the response amplitude remained unaffected by changes of the starting position of the hand (directions: Watson–Williams tests, \( p > 0.05 \) corrected; firing rates: one-way ANOVA, \( p > 0.05 \)). However, unlike the previous example, this neuron exhibited a significant influence of the starting position of the eyes, which is also depicted in Figure 4C where the SR response of the neuron is given for the 2 peripherally shifted starting positions of the eyes. Its preferred direction rotated in a clockwise manner when the starting position of the eyes was

<table>
<thead>
<tr>
<th>Group</th>
<th>Subgroup</th>
<th>Number of units</th>
<th>No. (%) of significant angle differences (Watson-Williams test)</th>
<th>No. (%) of significant peak discharge changes (one-way ANOVA)</th>
<th>No. (%) of monotonic changes of significant ANOVAs (Spearman rank test)</th>
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</thead>
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<td>SR</td>
<td>Vector response</td>
<td>11</td>
<td>0</td>
<td>1 (9.1) in “hand eccentric”</td>
<td>1 (100) in “hand eccentric”**</td>
</tr>
<tr>
<td></td>
<td>Eye position</td>
<td>16</td>
<td>2 (12.5) in 1 condition</td>
<td>16 (100) in “eyes eccentric”</td>
<td>6 (37.5) in “eyes eccentric”</td>
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<tr>
<td></td>
<td>dependency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMR</td>
<td>Vector response</td>
<td>19</td>
<td>2 (10.5) in 2 conditions in “eyes eccentric”</td>
<td>2 (10.5) in “eyes eccentric”</td>
<td>2 (100) in “eyes eccentric”</td>
</tr>
<tr>
<td></td>
<td>Hand position</td>
<td>37</td>
<td>14 (37.8) in 1 condition</td>
<td>1 (2.7) in “eyes eccentric”</td>
<td>1 (2.9) in “eyes eccentric”</td>
</tr>
<tr>
<td></td>
<td>dependency</td>
<td></td>
<td>22 (55.4) in 2 conditions</td>
<td>33 (89.2) in “hand eccentric”</td>
<td>17 (50) in “hand eccentric”</td>
</tr>
</tbody>
</table>

**Note:**

*Hand eccentric* refers to the 2 conditions hand left/eyes centered and hand right/eyes centered.

*Eyes eccentric* refers to the 2 conditions hand centered/eyes left and hand centered/eyes right.

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Table 1

Number of neurons with and without significant changes of preferred direction (Watson–Williams test) and linearity of response changes (Spearman rank test for monotonic changes within the significant one-way ANOVAs at normalized peak discharge rate)
shifted to the right hand side (Watson-Williams test, \( P < 0.05 \) corrected). Its peak discharge rate exhibited larger responses for eye excursions to the left, that is in a direction opposite to the preferred saccade direction (one-way ANOVA, \( P < 0.05 \)).

Out of the 27 SR burst neurons studied, 11 were characterized by a complete independence of their response amplitude and/or the direction of the starting position of the eyes. In one of these 11 neurons, however, we found the peak firing rate depended on the starting position of the hand (one-way ANOVA, \( P < 0.05 \)). In other words, these neurons showed oculocentric coding as with the first example. The other 16 neurons exhibited a significant modulation of their responses by changing the starting position of the eyes—but never by changing the starting position of the hands. We compared this pontine population of SRburst neurons with a neuronal population from the cerebral cortex taken from the literature. Andersen et al. (1990) described a population of 91 SR neurons in cerebral areas LIP and 7a. Twenty of them lacked a modulation of their SR responses by orbital position, whereas the other 71 units exhibited a significant dependency on the orbital starting position. Actually, a percentage of 59.3% (16/27) of PN SRburst neurons showing position-dependent modulation of SR bursts is not significantly different (chi-square test, \( P > 0.05 \)) from the corresponding percentage 78% (71/91) of the parietal population. Unlike the study mentioned, we not only compared the strength of neuronal responses in the preferred direction but also considered the changes in preferred direction when making saccades with either the eyes

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**Figure 3.** Exemplary SR burst neuron, exhibiting bursts independent of the eye starting position. (A) Absence of response during hand-only movements (left panel) and direction-selective burst during eye-only movements (right panel) for 8 directions in the frontoparallel plane tested in the hand centered/eyes centered (HC/EC) condition. Movements are aligned with movement onset. For each direction, the \( x \)- (gray lines) and \( y \) position (black lines) of the 2 effectors are shown. The black dots with horizontal whiskers indicate the mean time ± standard deviation (STD) of the go signal. The neuronal discharge is represented by raster dots and filtered PETHs (bin width 5 ms, histogram second-order low-pass filtered with 100-Hz corner frequency) in spike/s plotted below the behavioral data. The light gray area indicates the time used for extracting the mean burst activity around movement onset (black vertical line). The analysis window for hand movements was based on the time window during which SR bursts were observed. This neuron preferred saccades to the right. (B) Direction tuning curves for the 5 combinations of starting positions. The curves shown are cosine fits of mean discharge rate (small black circles) during SR bursts for the 8 directions (black) with the vector (black line) indicating the preferred direction. The gray curve shows the corresponding curve for hand movements (in this particular case completely collapsed to a dot). The preferred saccade direction of this particular neuron was independent of the starting position of the eyes and the hand.
in different starting positions, or the hand in different positions relative to the body. Figure 5 compares the relative changes in preferred directions of SR responses compared with the direction obtained in the central position (“normalized preferred direction”) as well as the discharge rate at these directions for the 3 starting positions of the eyes (Fig. 5A)

Figure 4. Exemplary SR burst neuron, exhibiting the dependence of its response on the starting position of the eyes. (A) No response of the neuron to isolated hand movements (left panel) but clear SR bursts evoked by isolated eye movements (right panel) in the baseline hand centered/eyes centered (HC/EC) condition. Movements are aligned with movement onset. (B) Direction tuning curves for the eye (black) and the hand (gray) for the 5 combinations of starting positions. The preferred saccade direction obtained for the hand centered/eyes right (HC/ER) condition was significantly different from the baseline condition, while the other eccentric conditions did not yield different preferred saccade directions. Moreover, changing the starting position of the eyes modulated the peak discharge rate, with larger responses for eye excursions to the left. SR responses were independent of hand position. (C) SR burst responses of the neuron in the hand centered/eyes left (HC/EL) (left panel) and the hand centered/eyes right (HC/ER) (right panel) condition, respectively.
and the hand, respectively (Fig. 5B), separately for these 2 groups of SRburst neurons. Those exhibiting independence of the initial orbital position are shown on the left hand side in each panel, those showing dependence on the right. Significant changes in normalized preferred direction were found in 15/16 (93.7%) eye position-dependent SRburst neurons (one-way repeated ANOVAs, \( P < 0.05 \)), while all 16 neurons in addition exhibited significant changes in their discharge rates, as demonstrated by the example neuron shown in Figure 4. Spearman rank tests indicated 6/16 (37.5%) eye position-dependent neurons sporting a linear rate change over the 3 different eye starting positions. We also compared this subpopulation of pontine neurons with the subgroup of eye position-related neurons from areas LIP and 7a, showing a linear dependency of their SR responses on the starting position of the eyes by a chi-square test. Again we found no significant differences (\( P > 0.05 \)) between the 2 populations.

We divided the SRburst neurons with significant dependence on the orbital starting position into 2 subgroups according to their preferred direction when the eyes started from straight ahead. The first subgroup comprised the 9 out of the 16 neurons, whose preferred direction lay within ±45° around the horizontal, that is they emphasized the horizontal, whereas the second, the complementary group of 7 neurons, preferred vertical saccades. In subgroup 1, the change of angle of the preferred direction showed a significant change to smaller angles for saccades starting from the position in the preferred direction, compared with saccades starting from the position away from the preferred direction (one-way repeated ANOVA, \( P = 0.04 \)). The discharge strength of these 8 neurons increased by 15.4% on average, if the starting position of the eyes was shifted from the central starting position to the starting position in the preferred direction and, conversely, decreased by 23.2% if shifted to the opposite direction, a difference that was statistically significant (one-way repeated ANOVA, \( P = 0.02 \)). The second subgroup of eye position-dependent SRburst neurons (7/16) preferring vertical saccade directions did not show any of the above-mentioned changes (one-way repeated ANOVAs, angle change: \( P = 0.27 \); discharge strength: \( P = 0.32 \)). In summary, this comparison suggests that at least in neurons preferring horizontal saccades (along the tested axis of position change), eye position modulates discharge strength along the preferred-antipreferred axis.

**Effects of Varying the Starting Position of the Hand on Hand Movement-Related Neurons**

Like bursting SR neurons, the overwhelming majority of bursting hand movement–related (HMRburst) neurons did not change their response depending on the position of the nonpreferred effector, that is the eyes. Actually, only 2 neurons showed a significant modulation of their hand movement-related bursts by eye position (one-way repeated ANOVA with the factor eye position, \( P < 0.05 \)), which was monotonic in both cases, while the firing of these neurons was not dependent on the starting position of the hand (one-way repeated ANOVA with the factor eye position, \( P > 0.05 \)). One of these 2 neurons is exemplarily depicted in Figure 6A, with its response in the baseline condition and its preferred direction and response amplitudes in all starting conditions in Figure 6B. The remaining 54 effector-specific HMRburst neurons can be divided into 2 groups, a first one comprising neurons that encoded hand movement vectors independent of the starting

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**Figure 5.** Population means of \( n = 27 \) SR burst neurons. (A) Compares the preferred directions and peak discharge rates for the 3 starting positions of the eyes. Upper panel: changes of the preferred directions of SR responses relative to the preferred direction obtained for the baseline condition (“normalized preferred direction”). Lower panel: mean peak discharge rates at these directions. (B) Compares the preferred directions and peak discharge rates for the 3 starting positions of the hand panels as in (A). The subgroups of neurons exhibiting independence of the initial orbital position (\( n = 12 \)) are shown on the left in each panel, those showing dependence on the right (\( n = 15 \)). The plots for the discharge rate show the 95% confidence intervals for the discharge rate. In order to ensure visual separability, we do not show the confidence intervals for the change of direction plots. The gray box includes the subgroup of neurons showing significant orbital position effects on either the preferred direction or on their peak discharge rate. The thicker black lines mark neurons with preferred directions coinciding with the horizontal axis. Abbreviations: HL/EC: hand left/eyes centered; HC/EL: hand centered/eyes left; HR/EC: hand right/eyes centered; HC/ER: hand centered/eyes right.
position of the hand ("hand-vector neurons"); one-way repeated ANOVA: no significant influence of hand starting position, \( n = 17 \), and a second group of neurons that exhibited various effects of the starting position on the HMR burst ("non-vector HMRburst neurons," \( n = 37 \)). Figure 7 and Figure 8 show typical examples of either group. The hand-vector neuron shown in Figure 7 preferred hand movements to the upper right (Fig. 7A, left panel) and did not respond to saccades (right panel). As shown in Figure 7B, the hand movement-related response was independent of the starting position of the hand and, moreover, independent of the starting position of the eyes, as is to be expected for a neuron encoding a hand movement vector. The lack of influence of the starting position of the hand and the eyes respectively was reflected by nonsignificant one-way repeated ANOVAs, with the factors starting position of the hand and of the eyes, respectively (Fig. 9A). Moreover, it was documented by plotting the response for one starting position of the hand as a function of the response for each of the other 2 starting positions. Two aspects of the response were considered, first the preferred hand movement direction (left panel in Fig. 10A), and second the mean discharge rate (right panel in Fig. 10A). The terms "ipsiversive position" and "contraversive position" in Figure 10A refer to starting positions that are ipsiversive and contraversive respectively relative to the hand used. Open circles give the data of the hand-vector neurons without any eye position influence; open squares indicate the 2 neurons with eye position influence in the case of the hands starting peripherally. Finally, the same neurons tested in the "eyes peripheral condition" are given by filled squares. As shown in Figure 10A, the data points in the 6 regression plots shown (2 response measures \( \times 3 \) combinations of starting positions; i.e., ipsiversive vs. central, contraversive vs. central,
ipsiversive vs. contraversive) were always in perfect register with the bisector, as is to be expected for neurons not dependent on the starting position. All 3 possible linear regressions for the interaction in angle changes as well as the 3 linear regressions for the change of spike rate showed very high regression coefficients independently of looking at ipsiversive versus central position (I), contraversive versus central position (II), or ipsiversive versus contraversive position (III). Note that only the data of the “hand peripheral condition” (open symbols) were taken into account for the calculation of the linear regressions. We did not apply the same kind of analysis used for the SR bursting neurons because of the huge variability especially in the nonvector HMR neurons indicated in Figure 9B.

The responses of the hand-vector HMRburst neurons described up to here were clearly different from the nonvector HMRburst neurons, of which a representative example is shown in Figure 8. This neuron discharged hand movement-related bursts whenever the movement contained a rightward component, preferring strictly horizontal reaches (Fig. 8A). Starting the reaches from noncentral starting positions influenced the response strength as well as the preferred direction. As shown in Figure 8B, its preferred direction exhibited a strong downward component, when the hand started from the right position (Watson-Williams-test, $P < 0.05$ corrected), which is also illustrated in the right panel of Figure 8C. Furthermore, it exhibited changes in its peak discharge rate when starting from the left position compared with the central starting position (one-way repeated ANOVA, $P < 0.05$; Scheffé test left vs. central, $P < 0.05$) while the overall movement-related response was reduced (Fig. 8C, left panel). On the other hand, leaving the hand in the central starting position and shifting the starting position of the eyes did not influence the hand movement-related responses (both peripheral vs. central vector angle: Watson-Williams tests, $P > 0.05$, corrected; peak response: one-way repeated ANOVA, $P > 0.05$). Four of the 37 neurons in this group

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Figure 7. Typical hand movement–related neuron, exhibiting hand movement–related bursts, which were independent of the starting position of the hand and the eye. (A) Responses of the neuron to hand movements in the frontoparallel plane (left panel) and absence of SR responses to saccades in the hand centered/eyes centered (HC/EC) condition. Responses aligned with movement onset. (B) Direction tuning curves for hand movements (gray) and eye movements (black) for the 5 combinations of starting positions of the effectors. The direction tuning curves are independent of the starting positions of the eyes and the hand.
exhibited statistically significant effects of the hand starting position on their preferred direction only, one neuron showed only effects on the peak discharge rate and 32 on both preferred direction and peak discharge rate (one-way repeated ANOVAs, $P < 0.05$). None of them exhibited any modulation by the starting position of the eyes on the hand movement–related bursts.

While response latencies were usually stable in both groups of HMBburst neurons as well as in SRburst neurons, we identified 3
nonvector HMR burst neurons, deviating from this rule. An example of a neuron firing hand movement-related bursts with little directional preference but a clear dependence of the burst timing on the hand starting position is shown in Figure 11.

The effects of the hand starting position on the preferred direction and the peak discharge rate of nonvector HMR burst neurons did not follow a consistent rule. This is expressed by Figure 10, which plots preferred direction and peak discharge rate for one starting position of the hand as a function of one of the other 2. Shades of gray are used to distinguish 3 subgroups of nonvector HMR burst neurons, namely one whose preferred direction had a strong vertical component (dark gray symbols), a second subgroup emphasizing ipsiversive movements (light gray symbols), and a third one favoring contraversive movements (black symbols). The reason for considering these subgroups was the assumption that the biomechanical requirements would be more similar for neurons within subgroups. For instance, neurons preferring upward movements might be related to the elevation of the shoulder joint, and therefore might be comparatively insensitive to changes of the hand starting point along the horizontal, primarily requiring changes in shoulder rotation. On the other hand, neurons involved in shoulder rotation would be expected to show stable horizontal preferences, with a strong dependence of their discharge rate on the horizontal starting position. Finally, neurons preferring oblique directions in the frontoparallel plane should show both changes to their preferred direction as well as their peak discharge rate with shifting of the starting position. As can be seen, none of these expectations were met, and out of the 18 regressions, actually only 8 were significant (Bonferroni corrected F-tests, significant P values between 0.05 and 0.001), 4 of them for the vertically tuned neurons. Note that the majority of significant results were found in the multiple linear regression calculations for ipsiversive versus central position (I) and contraversive versus central position (II). But the lack of a consistent pattern of starting position dependence is hardly compatible with the direct encoding of shoulder rotation or rotations of other arm joints contributing to the reaching movement.

Bewildering as these individual patterns may seem, they add up to a simple population response that is able to accurately capture the direction of the reach, independent of the starting position of the hand. The population response for a particular reaching movement was calculated as the vector sum of the preferred directions of individual neurons, weighted according to their individual direction tuning curves (see Methods for details). Figure 12 plots the direction predicted by the population response as a function of the actual direction of the reach for all nonvector neurons (closed symbols) and all hand-vector neurons (open symbols). The data points for both groups lie on or close to the bisector, independent of the starting position and without any significant difference.
between the 2 groups of neurons ($F$-tests, $P$ values between 0.13 and 0.91). In other words, not only the hand-vector neurons but also the nonvector HMRburst neurons dispose of all the information needed in order to encode the reach direction, albeit in a format that is distributed across neurons, which individually seem to prefer highly idiosyncratic frames of reference.

**Discussion**

We studied 2 classes of movement-related neurons in the DPN, SR neurons, and HMR neurons. In our experiments, in which the monkeys had to execute movements to remembered locations, either moving their hand or their eyes. In accordance with our previous work (Tziridis et al. 2009), we found that these neurons were effector selective, that is they responded to the movement of their preferred effector in a direction-selective manner while ignoring the movement of the respective other effector. The effector-selective discharge response was usually not influenced by bringing the other respective effector into different positions. Both groups of movement-related neurons fell into 2 subgroups each. The first one was characterized by independence of the movement-related discharge from the starting position of the preferred effector ($n = 30$, 36.1% of our sample of movement-related burst neurons). The second one showed an influence of the starting position ($n = 53$, 63.9%). SR bursts of DPN neurons that are constant for a given saccade vector, independent of the starting position of the eyes, reflect oculocentric coding of saccades. Correspondingly, HMR bursts that are independent of the hand starting position are consistent with hand-centered coding of reaches. In other words, these 2 groups of neurons represent movement vectors in an effector-congruent egocentric frame of reference. Neurons with very similar properties have been found in the cerebral cortex. For instance, hand-vector neurons are found in the primary motor cortex, in area 5 and other parts of parietal cortex, and in the ventral premotor cortex (Kalaska et al. 1983; Georgopoulos et al. 1986; Kakei et al. 2003). Indeed, the hand-vector neurons we found in the DPN resemble those described in the cortex. However, it seems unlikely that primary motor or ventral premotor cortex might determine the responses of hand-vector neurons in the DPN as the first project to the ventral parts of the PN (Brodal and Bjaalie 1992) and the latter to the medial PN (Wiesendanger et al. 1979). A more likely candidate source is therefore PPC, known to project to the DPN (Schmahmann and Pandya 1989).

**Figure 10.** Plots of preferred direction (left in each panel) and peak discharge rate (right) for one starting position of the hand as a function of one of the other 2 starting positions. (A) Data points for the subgroup of $n = 20$ of “vector coding” neurons. “Ipsiversive” refers to an eccentric starting position on the side of the moving hand and “contraversive” to an eccentric starting position opposite to the side of the hand. Panel (I) compares the data of ipsiversive and central positions, (II) compares contraversive and central positions, and (III) compares the data of the 2 extreme positions. The 2 neurons in this sample that exhibited the influence of eye position are distinguished by gray square symbols (open squares: different hand starting positions; filled squares: different eye starting positions; the corresponding values are connected by a gray line). (B) Data points for the subgroups of $n = 36$ neurons that had been demonstrated to be “nonvector” neurons. Neurons in this subgroup are further differentiated according to the orientation of their preferred direction of hand movement (vertical, contraversive, or ipsiversive to the side of the hand; for details, see Methods) by different shades of gray. The significant linear regression lines ($P < 0.05$, corrected for multiple comparisons; solid lines) for the vector-coding neurons (open circles) in (A) lie exactly on the bisector (broken lines). Also, the neurons influenced by eye position lie close to the bisector. Of the 8 (8/18, 44%) significant regressions only 2 coincided with the bisector, namely the 2 regressions for the neurons preferring vertical movements for “central position” as a function of “contraversive position” (that is for these subset of neurons set to leftward position) for both variables investigated.
Neurons discharging SR bursts lacking orbital position dependency have been observed in the frontal and the parietal saccade representations (Andersen and Zipser 1988; Mitz and Godschalk 1989; Thier and Andersen 1998). However, quantitative information on their respective shares is only available for parietal areas 7a and LIP (Andersen et al. 1990), known to project heavily to the DPN (May and Andersen 1986; Brodal and Bjaalie 1992). In these parietal areas, SR neurons lacking a significant influence of the orbital starting position form a minority (22% vs. 78% with orbital position dependency), having a share that is not significantly different from that of saccade vector neurons in the DPN. With the qualification that we lack information on the relative weights of input from frontal versus parietal SR areas to the DPN and, moreover, quantitative information on the shares of SR neurons with and without orbital position dependency in the frontal “eye fields,” the tentative conclusion is that the number of DPN neurons encoding saccade vectors may not be different from cerebral cortex.

The other, larger part of our sample of DPN neurons consisted of movement-related burst neurons that exhibited effector-specific position dependencies. Those involved in saccades closely resembled position-dependent SR neurons in parietal area LIP and other parts of the cerebral cortex, which typically show a monotonic modulation of their burst amplitudes associated with constant saccade vectors by the starting position of the eyes (Zipser and Andersen 1988; Andersen et al. 1990; Salinas and Thier 2000). These “gain-fields” of SR neurons in the cortex are understood to be the basis of a distributed representation of saccade goals in head-centered coordinates and the same spatial interpretation may be pertinent for saccade gain fields in the DPN.

On the other hand, the position dependencies of DPN “nonvector” HMRburst neurons turned out to be too heterogeneous to allow for simple comparisons with their putative input in the cerebral cortex. The DPN receive input from a variety of hand-motor areas in the cerebral cortex, among them parietal areas 5, 7a, the PRR/medial intraparietal (MIP) (Glickstein et al. 1985; May and Andersen 1986; Schmahmann and Pandya 1989; Giolli et al. 2001), as well as frontal lobe areas (Legg et al. 1989; Fries 1990; Shook et al. 1990; Leichnetz 2001). In general, these cortical areas sport representations that facilitate the integration of multimodal information for the description of target attributes and spatial context in very different frames of reference. Examples are the representation of desired locations in world-centered coordinates in area 7a (Snyder et al. 1998; Andersen and Buneo, 2002), target velocity in world-centered coordinates in area MST (Dicke and Thier 1999; Ilg et al. 2004; Ilg and Schumann 2007), the encoding of reaching movements in...
eye-centered coordinates in MIP (Colby and Duhamel 1996; Johnson et al. 1996), in body-centered (Lacquaniti et al. 1995; Batista et al. 1999) or shoulder-centered coordinates in area 5 (Ferraina and Bianchi 1994), or in shoulder coordinates in the premotor cortex (Caminiti et al. 1991). The profound heterogeneity of nonvector HMR_{burst} neurons precluded the identification of distinct categories unambiguously associable with one of the coding schemes prevailing in the cerebral cortex. What is clear, though, is that we could not obtain any evidence that pontine HMR_{burst} neurons would encode reaches relative to the shoulder or in eye-centered coordinates, similar to area 5 or to the PPR. We think that we may easily have missed such neurons in the DPN, given the fact that our sample of HMR_{burst} neurons is small relative to the size of the DPN and the size of hand movement–related corticopontine projections to the PN. At first glance, it may seem implausible that neurons sampled from a circumscribed region of the DPN, having an extension of only about $3 \times 2 \times 2$ mm, should be that different. A possible explanation may be provided by the highly fractured architecture of the PN, characterized by small clusters of pontocerebellar projection neurons, with each cluster receiving selective input from a different part of cortex (Schwarz and Thier 1999; Schwarz et al. 2005; Thier and Möck 2005) or one of the subcortical centers that—like the superior colliculus—project to the PN (Harting 1977). The fact that the SR neurons appeared to be much more homogeneous is not necessarily at odds with this interpretation. The anatomical data available suggests that SR input to the DPN is dominated by a comparatively small set of parietal and frontal areas (LIP, MP, FEF, and SEF) (Leichnetz et al. 1984; May and Andersen 1986; Legg et al. 1989; Shook et al. 1990; Brodal and Bjaalie 1992), containing neurons whose functional properties bear a much higher degree of resemblance than those of neurons in hand movement–related areas. This is probably a consequence of the smaller degrees of freedom and in general

Figure 12. Direction predicted by the population response as a function of hand movement direction. The 5 individual plots (I–V) reflect the varying starting positions of the hands and the eyes. Vector and nonvector coding neurons are distinguished by specific symbols. The plots were subjected to linear regressions, independently for the 2 subgroups of neurons. The linear regressions were all significant ($P < 0.05$, corrected for multiple comparisons) and, moreover, in no case did they differ significantly from the bisector (dotted line; 2-tailed $t$-tests, $P < 0.05$).
the simpler biomechanics of saccades compared with hand movements.

Unlike the heterogeneous responses of individual members in the sample of nonvector HMRburst neurons, their population response was surprisingly unambiguous, describing the direction of the hand reach, similar to individual vector HMRburst neurons. Given the fact that there is good reason to assume that these neurons in the DPN are not only functionally heterogeneous but also dependent on different input areas, this result was unexpected. Bewildering as this result may be, it should not be taken as indication that the cerebellum would also receive hand-vector signals from the nonvector HMRburst neurons. This would require the convergence of groups of DPN neurons like the one underlying the population response to individual micro-modules in the cerebellar cortex, a requirement that is at odds with the considerable degree of divergence of the pontocerebellar projection (Brodal 1979; Bower et al. 1981; Brodal and Bjaalie 1997).

In summary, our observations on the influence of the starting position on movement-related response of saccade and HMR neurons in the dorsal parts of the PN demonstrate a stunning resemblance to the situation in the cerebral cortex. Obviously, one might not expect that this first study of the position dependency of movement-related responses in the DPN, out of necessity based on a limited sample of neurons, would have retrieved any pattern of position dependency described in a large body of studies of numerous movement-related areas in cerebral cortex. Yet the congruence already revealed seems large enough to suggest that the types of position dependencies in the DPN, reflecting specific formats for the encoding of spatial relationships of desired locations and effector positions, are surprisingly similar to those in cerebral cortex. The complementary conclusion is that the signals found at the level of the DPN and probably the PN at large are very different from those characterizing their targets in the cerebellar cortex, which emphasize precisely timed kinematic parameters (Thier et al. 2000, 2002; Townsend et al. 2006; Ebner et al. 2011). In other words, the corticopontine projection does not seem to contribute to a major functional transition between the cerebral cortex and the cerebellum, which may be loosely understood as a spatiotemporal transformation of movement relation information.

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References


