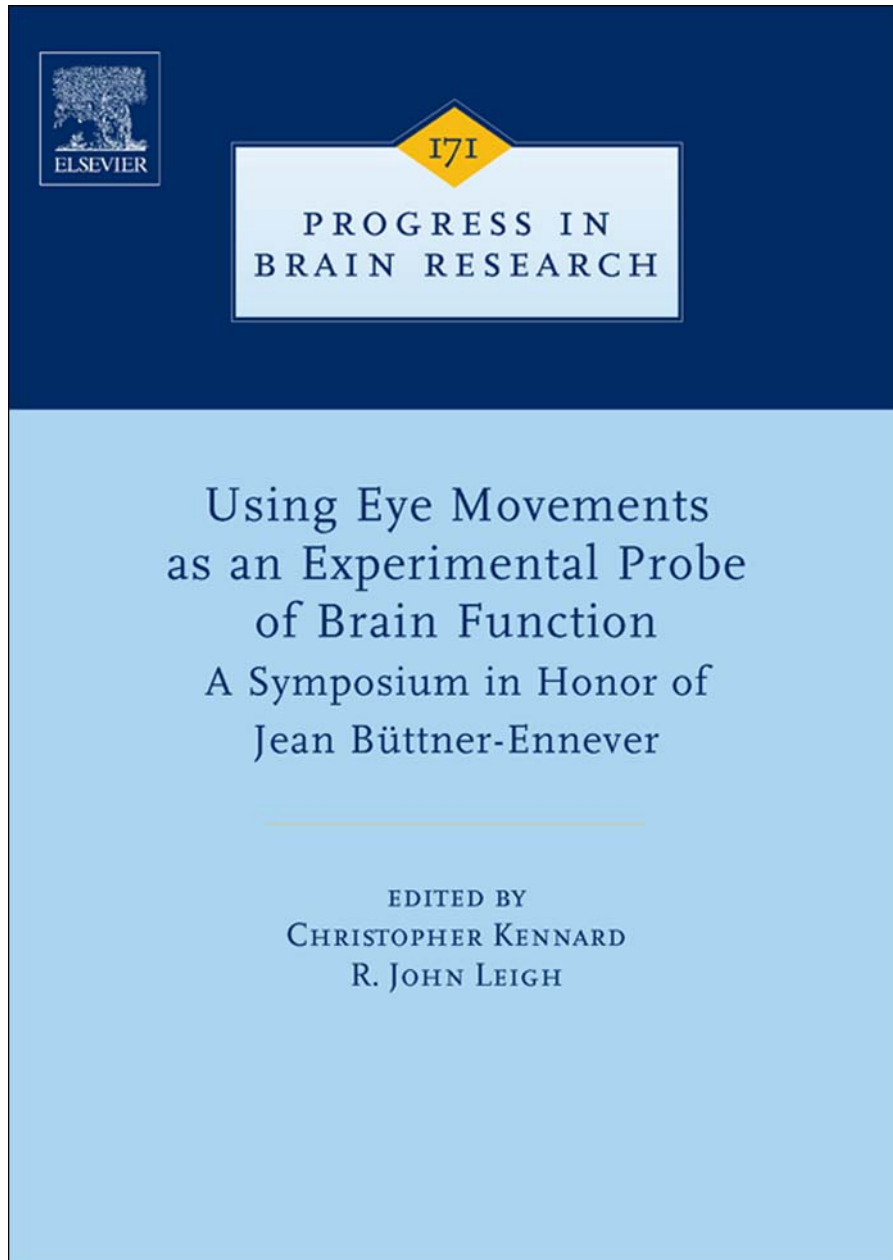


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CHAPTER 4.21

Private lines of cortical visual information to the nucleus of the optic tract and dorsolateral pontine nucleus

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Abstract: The subcortical nucleus of the optic tract and dorsal terminal nucleus of the accessory optic system (NOT-DTN), along with the dorsolateral pontine nucleus (DLPN), has been shown to play a pivotal role in controlling slow eye movements. Both nuclei are known to receive cortical input from striate and extrastriate cortex. To determine to what degree this cortical input arises from the same areas, and potentially from the same individual neurons, in one set of experiments we placed different retrograde tracers into the NOT-DTN and the DLPN. In the ipsilateral cortical hemisphere the two projections mainly overlapped in the middle temporal (MT) area, the middle superior temporal (MST) area, and the visual area in the fundus of the STS (FST) and the surrounding cortex. In these areas, neurons projecting to the NOT-DTN or the DLPN were closely intermingled. Nevertheless, only 3–11% of the labelled neurons in MT and MST were double-labelled in our various cases. In a second set of experiments, we identified neurons in areas MT and MST projecting to the DLPN and/or to the NOT-DTN by antidromic electrical stimulation. Again, neurons projecting to either target were located in close proximity to each other and in all subregions of MT and MST sampled. Only a small percentage of the antidromically identified projection neurons (4.4%) sent branches to both the NOT-DTN and the DLPN. On the population level, only neurons activated from the NOT-DTN had a clear preference for ipsiversive stimulus movement whereas the neurons activated from the DLPN, and neurons not antidromically activated from either target, had no common directional preference. These results indicate that the cortical input to the NOT-DTN and DLPN arises from largely separate neuronal subpopulations in the motion sensitive areas in the posterior STS. Only a small percentage of the projection neurons bifurcate to supply both targets. These findings are discussed in relation to the effects of cortical lesions on the optokinetic and smooth pursuit system.

Keywords: optokinetic; smooth pursuit; slow eye movements; monkey; MT/MST

Neuronal substrate of eye movement control

Eye movement control is widely distributed over cortical and subcortical structures. There is a wealth of literature correlating neuronal response properties in certain cortical, pretectal, tectal, and brainstem areas with different kinds of eye

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movements or phases thereof. Assuming that such a widespread network exists, a crucial question is how information is exchanged between related areas and how specificity is generated and maintained.

Here we want to discuss the connectivity between cortical areas: middle temporal (MT) and middle superior temporal (MST) with the pretectal nucleus of the optic tract and the dorsolateral pontine nucleus (DLPN) subserving slow eye-movements during optokinetic reactions, ocular following, and smooth pursuit. Slow eye movements are crucial for stabilizing the image of the world on the retina and thus for compensation of self-motion or externally generated movement of the visual world. For many years, the nucleus of the optic tract and the dorsal terminal nucleus of the accessory optic system (NOT-DTN) were regarded as the key visuomotor interface for the optokinetic reflex that stabilizes large field retinal image motion or slip on the retina. The DLPN has been largely implicated in slow eye movements during smooth pursuit of small stimuli and in the ocular following response (OFR).

Probably the most significant and directly eye-movement-related cell type, both in the NOT and the DTN, is retinal slip neurons that are directionally selective for ipsiversive image motion and project to the dorsal cap of the inferior olive and nucleus praepositus hypoglossi (NPP) in all mammals investigated so far. In monkeys, in addition to the retinal slip neurons (Hoffmann et al., 1988; Mustari and Fuchs, 1990), omnidirectional pause neurons, anatomically clearly offset with respect to the retinal slip neurons, have been described in the NOT (Mustari et al., 1997) but not the DTN (Mustari and Fuchs, 1990). Based on the homogeneous response properties, the orthodromic and antidromic latencies from their input and output structures, and morphological distribution of retrogradely labelled retinal slip cells after injection of the inferior olive, we consider the NOT and DTN as a functional unit (Hoffmann et al., 1988; Hoffmann and Fischer, 2001; for further discussion see Distler et al., 2002).

Retinal slip neurons in the monkey NOT-DTN prefer large field ipsiversive visual motion (Hoffmann et al., 1988; Mustari and Fuchs, 1990). Some NOT-DTN neurons also respond

to small spots of light moving ipsiversively (Hoffmann and Distler, 1989; Mustari and Fuchs, 1990; Ilg and Hoffmann, 1991), a stimulus that elicits smooth eye movements in awake animals. Electrical stimulation in the NOT-DTN provokes optokinetic eye movements with the slow phase towards the stimulated side (Schiff et al., 1988; Mustari and Fuchs, 1990; Taylor et al., 2000; Hoffmann and Fischer, 2001). Similarly, lesion or inactivation of the NOT-DTN leads to deficits of optokinetic eye movements during visual stimulation towards the lesion (Kato et al., 1988; Schiff et al., 1990; Ilg et al., 1993; Inoue et al., 2000; Hoffmann and Fischer, 2001). Interestingly, lesions of the NOT-DTN also impair smooth pursuit and ocular following (Ilg et al., 1993; Inoue et al., 2000; Yakushin et al., 2000b). Thus, the NOT-DTN in the monkey not only plays an important role for optokinetic nystagmus (OKN), but for all slow eye movements.

In DLPN, the visual and visual-pursuit neurons respond direction-selectively to moving large area random dot patterns, and, in part, to moving single spots of light. In contrast to NOT-DTN, these neurons as a population do not code for a common direction of movement (Suzuki and Keller, 1984; Mustari et al., 1988; Thier et al., 1988; Suzuki et al., 1990). Especially the eye movement-related and visual-pursuit neurons of the DLPN are supposedly part of the smooth pursuit pathway. Lesion of the DLPN causes impairment of smooth pursuit and of the initial phase of optokinetic eye movements whereas the steady-state optokinetic response is unaffected (May et al., 1988; Thier et al., 1991). In addition, DLPN contains neurons that fire before eye movements, and whose response properties implicate them in the OFR (Kawano et al., 1992, 1996).

Within the cerebral cortex pursuit-related neurons have been identified in several cortical areas including the frontal eye fields, the lateral intraparietal area, and the superior temporal areas MT and MST. In MT and MST, these direction selective neurons include the representation of the fovea in their receptive fields but differ in their preferred stimulus and receptive field size, with MT neurons having smaller receptive fields and preferring small instead of large area visual stimuli

(Komatsu and Wurtz, 1988). Lesions in MT produce a retinotopic deficit in smooth pursuit whereas MST lesions lead to retinotopic as well as directional deficits in smooth pursuit and the slow build up of OKN (Newsome et al., 1985; Duersteler and Wurtz, 1988). Area MST also contains neurons related to ocular following (Kawano et al., 1994). Both MT and MST project to the DLPN (Maunsell and Van Essen, 1983; Ungerleider et al., 1984; Boussaoud et al., 1992). The main cortical input to the NOT-DTN comes from MT (Distler and Hoffmann, 2001).

Anatomical overlap but cellular specificity of cortical input to NOT-DTN and DLPN

To examine the relative strength of cortical projections to the NOT-DTN and DLPN, respectively, we performed dual retrograde tracer injections into these nuclei and analysed which cortical areas and to what extent these areas contained retrogradely labelled cells (Distler et al., 2002). The cortical input to the NOT-DTN turned out to originate mainly from motion sensitive areas MT, MST, fundus of the STS (FST), and visual areas in the anterior part of the STS, followed by V1, V2, and V3. By contrast, injections into the DLPN yielded retrogradely labelled cells mainly in MST, followed by MT and FST with some sparse labelling in intraparietal and frontal cortex. Significantly, the only region of substantial overlap of neurons labelled from the NOT-DTN and the DLPN was the posterior part of the STS with the motion sensitive areas MT, MST, and FST. In these areas, neurons labelled from both targets were closely intermingled, i.e., they were lying very close to each other. However, double-labelled cells were rather rare indicating that only few cortical neurons simultaneously project both to the NOT-DTN and the DLPN. Depending on the size of the injection, 0–3.4% of the NOT-DTN projecting cells in MT also projected to the DLPN, 0–10.4% of the DLPN-projecting cells in MT also projected to the NOT-DTN. For area MST, 0–9.6% of the NOT-DTN projecting neurons and 0–11.1% of the DLPN projecting population simultaneously also projected to the other target. Thus, the

quantitatively strongest input to the NOT-DTN originates from area MT, and to the DLPN from area MST. The specificity within each projection is very high. Even though in both cortical areas neuronal discharges related to optokinetic responses and smooth pursuit have been reported, and lesions of these areas affect eye movements in both behavioural contexts, only about 4% of the subcortically projecting cortical neurons (averaged over all cases and over both MT and MST) project both to the NOT-DTN and the DLPN thus distributing their information to both targets (Distler et al., 2002).

Cortical information transmitted to the NOT-DTN and the DLPN

In order to specify the kind of information that is transmitted from motion sensitive areas in the STS to the NOT-DTN and DLPN, respectively, we employed electrical stimulation in these subcortical nuclei while simultaneously analysing the response properties of antidromically activated cortical neurons in anaesthetized and paralysed monkeys. Similarly to our anatomical results, neurons in MT and MST that could be activated from the NOT-DTN, or the DLPN, and neurons that could not be activated from either target were found next to each other and were distributed over the whole extent of MT and MST sampled in our experiments. Only about 4% of the cortical projection neurons could be antidromically activated from both the NOT-DTN and the DLPN thus confirming our anatomical results. Antidromic latencies did not differ after stimulation of the NOT-DTN or the DLPN suggesting that the conduction velocity and therefore axon calibre of the cortical neurons projecting to either target were in the same range.

There was one response parameter that clearly differed between cortical neurons projecting to the NOT-DTN and to the DLPN: the preferred direction of stimulus motion. As expected, the vast majority of cortical neurons recorded in MT and MST were direction selective, regardless whether they projected to the NOT-DTN, the DLPN, or to none of these targets. As reported earlier (Ilg and

Hoffmann, 1993; Hoffmann et al., 2002), cortical neurons projecting to the NOT-DTN as a population strongly prefer ipsiversive stimulus movement thus matching the direction preference of their target neurons, the retinal slip cells in the NOT-DTN. By contrast, neither cortical neurons projecting to the DLPN nor neurons not projecting to either target showed a common directional preference. Again, in the case of the DLPN this matches the directional properties of the target neurons in this nucleus because direction selective neurons in the DLPN do not exhibit a common preferred direction.

Private lines?

Our data on the cortical projections to subcortical centres involved in eye movement control, i.e., the NOT-DTN and the DLPN, clearly indicate that indeed there are private lines between cortical areas MT and MST and their target nuclei NOT-DTN and DLPN.

These results seem surprising. Although information from almost completely separate populations of neurons in MT and MST reaches the NOT-DTN and DLPN, lesions especially of the NOT-DTN lead to a deterioration of slow eye movements, not only in OKN but also in ocular following and smooth pursuit. Lesions in the DLPN spare most of the slow phases of OKN. Nevertheless the different subcortical routes for slow eye movements, despite their private lines of cortical input seem to be highly interdependent. Lesions in NOT-DTN could create a tonus asymmetry almost like a lesion in the vestibular nuclei. Such a lesion leads to spontaneous nystagmus that would interfere with other slow eye movements. Even after spontaneous nystagmus ceases this asymmetry in the signal from the left and right NOT-DTN which is transformed into eye velocity at later stages would be a handicap for normal gain in smooth pursuit and ocular following. The ipsiversive deficits after lesions of MT and MST in OKN, ocular following, and smooth pursuit might all be attributed to the altered cortical input to the NOT-DTN with its projection

to the NPP and from here directly to the vestibular nuclei. The projection to the DLPN can reach the brainstem oculomotor circuitry only via the cerebellum and may be much more important for the predictive properties, like keeping a selected object within the fovea, of smooth pursuit. A comparison of the cortical neurons projecting to NOT-DTN and DLPN in awake, trained monkeys will have to give us the answer to these questions.

In many cases, projections from a given cortical area to different cortical or subcortical areas are not identical. Interestingly, most studies showing evidence for functionally distinct projections concern brain regions that have been very well characterized, e.g., V1, MT, LIP, FEF (Finlay et al., 1976; Segraves, 1992; Movshon and Newsome, 1996; Paré and Wurtz, 1997; Everling and Munoz, 2000; Sommer and Wurtz, 2000, 2001; Hoffmann et al., 2002; Ferraina et al., 2002). It may be a prerequisite for recognizing functionally distinct subpopulations that the diversity of response properties in a brain area be fully understood. This hypothesis, however, does not make room for exceptions like the findings of Churchland and Lisberger (2005) in MST. Nevertheless, more importantly strong similarities in the response properties of the projection neurons and the target area can always be found. This raises an important issue for developmental neurobiology. How are these distinct projections established? Clearly, in addition to molecular guidance cues, activity-dependent matching mechanisms (Hebb, 1948) have to play an important role to set up these parallel cortical and corticofugal processing streams.

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