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Initiation of a Goal-directed Movement in the Monkey

Role of the Cerebellar Dentate Nucleus

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Summary. The participation of the dentate nucleus (DN) in the initiation of a voluntary movement was investigated in five baboons (Papio papio). In these experiments, we have analyzed the effects of excluding the DN on the latency (reaction time, RT) of a learned goal-directed movement.

Two techniques were used for excluding the DN. In three animals, the structure was cooled with a probe, stereotaxically implanted on the side ipsilateral to the active hand. In two others, a partial electrolytic destruction of the DN ipsilateral to the operant hand was undertaken. In one further animal, both DNs were destroyed electrolytically.

A comparison was made of the effect of DN inactivation on the latency of stereotyped goal-directed movements of constant amplitude and direction, and of goal-directed movements whose amplitude and/or direction were varied in random fashion.

The exclusion of DN brought about a prolongation of RTs in all animals. This prolongation was not accentuated by variation of different characteristics (amplitude and/or direction) of the impending goal-directed movement.

A recovery of the RTs to their prelesion values was observed after irreversible unilateral DN lesion, but not so easily after bilateral destruction.

These results show that in the monkey DN is concerned with the initiation of a goal-directed movement, but is not critically implicated in the encoding of direction and amplitude parameters. These findings are discussed in view of the role that is usually attributed to the neocerebellum in programming voluntary movements.

Key words: Dentate nucleus – Reaction time – Goal-directed movement initiation – Cooling – Lesion – Monkey

The delay in initiation of muscular contraction is one of the fundamental symptoms of neocerebellar lesions (Holmes 1917, 1939; Fulton and Dow 1937), since it appears to be an underlying cause of many other subsequent disturbances (Sasaki 1979). These clinical results, along with anatomical and physiological findings on the existence of cerebello-cortical interrelations (Allen and Tsukahara 1974), have led some workers to attribute a critical role to the cerebellum in the initiation of voluntary movements (Evarts and Thach 1969; Brooks 1979b), and particularly ballistic movements (Kornhüber 1971).

The cerebellar dentate nucleus exhibits a prominent development in phylogeny (Verdie 1976; Chan-Palay 1977; Sasaki 1979). In humans it accounts for 90% of the intracerebellar neurones (Heidary and Tomasch 1969) and constitutes the principal output of the cerebellar hemispheres. Its development parallels that of the primate motor cortical hand area and coincides with the appearance of manipulatory ability (Sasaki 1979). Electrophysiological (Grimm and Rushmer 1974; Robertson and Grimm 1975; Allen et al. 1978; Thach 1978) and anatomical (Chan-Palay 1977; Thach and Jones 1979) studies have demonstrated the complexity of its organization. Experimental data suggests that this nucleus participates in movement generation, with units altering their firing rate slightly before those in the motor cortex, prior to the onset of movement (Thach 1975). In addition, Meyer-Lohmann et al. (1977) have shown that cooling the interpositus and dentate nuclei of the cerebellum causes a prolongation of the latency of flexion-

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extension movements of the elbow. While these observations suggest that the dentate nucleus is concerned in the initiation of voluntary movement, it is more difficult to pinpoint the precise manner in which this may occur. The existence of a repertory of motor programs within the central nervous system is at present not questioned (Keele 1968; Paillard and Beaubaton 1978; Brooks 1979a); such central program may intervene in goal-directed limb movements, as shown by the persistence of these movements in deafferented monkeys (Taub et al. 1975; Polit and Bizzi 1979). Within this context, important questions are whether the dentate nucleus merely releases motor programs elaborated in other structures, or whether it intervenes more directly in motor preparation, that is to say, in the elaboration of such programs (Massion and Sasaki 1979).

The observations of Thach (1978) and Strick (1979) suggest that the dentate nucleus is concerned with specifying the directional parameters of movements and therefore plays a critical role in programming these parameters; such programming appears necessary for the execution of goal-directed movements (Paillard 1980). In the experiments reported here, the role of the dentate nucleus in the initiation of goal-directed movements in the monkey was analyzed by using a task that involved pointing a finger at a luminous target. More precisely, the effect of suppressing dentate control on the latency of movements (with variable amplitude and/or direction) was studied.

Recovery phenomena have frequently been reported after various lesions of the dentate nucleus (Carrea and Mettler 1947; Growdon et al. 1967; Zervas et al. 1967; Goldberger and Growdon 1973; Poirier et al. 1974), but they mainly concerned disorders of movement execution, such as dyskinesias and intention tremor. No quantitative studies of the recovery of movement initiation following destruction of the dentate nucleus have been carried out. Yet one purpose of the present study was to determine the occurrence and rate of any functional recovery from impairment of initiation observed after unilateral or bilateral dentate lesion.

Preliminary accounts of these results have been published (Beaubaton et al. 1978; Trouche et al. 1979).

Methods

Material

The experiments were carried out on five adult baboons (Papio papio) weighing between 8 and 10 kg. Three of the animals (LIL, PEN, BER) had cryoprobes chronically implanted in DN. The other two (NEF, BAS) underwent unilaterally on electrolytic lesions, followed in one case (BAS) by a lesion in the contralateral DN.

Techniques for Exclusion of the Dentate Nucleus

Implantation of thermodes and electrocoagulation were carried out under nembutal (35 mg/kg I.V.) and under aseptic surgical conditions. DN was located stereotaxically using the atlas of Riche et al. (1971) and electrophysiologically by recording its spontaneous activity. The latter is characterized by fast, high-amplitude activity, contrasting with the scarce, low-amplitude activity of the white matter.

The cryoprobe was implanted ipsilateral to the operant hand. The probes and the cooling device were of the type developed and described by Dondey et al. (1962) and Benita (1972). The external diameter of the probe did not exceed 1.1 mm. The tip was insulated by a deposit of gold to avoid too fast a destruction of the nervous tissue (Schmied et al. 1979). A copper-constantan thermocouple fixed to the tip of the probe allowed continuous temperature control. The probe was introduced in the lateral part of the nucleus, thus avoiding a possible spread of cooling to nucleus interpositus. The probe was held by a special support (Massarino et al. 1979a) fixed to the skull by a series of screws cemented into the bone.

The cooling temperature was chosen using previous observations by Benita (1972) on the effects of local cooling upon nervous transmission. In our experiments, two cooling temperatures were used: one tip temperature at 0° C, and another at 25° C; the latter has no effect on nervous transmission any longer but still elicits the mechanical disturbances due to the cooling device itself, to freon circulation and to vibration of the system.

Electrolytic DN lesions were performed by passing a DC current (1.5 mA for 15 s), using against a broad reference electrode. Twenty partially overlapping coagulation points were made.

The recording sessions began 5 days after probe implantation or electrolytic lesion.

Experimental Apparatus

In each session, the baboon was placed in a work cage (Fig. 1) situated in a dimly lighted and soundproof room. A cage of the type designed and described by Trevarthen (1972) was adapted to the requirements of the present experiment. An apparatus for partial head restraint consisted of a series of grooved horizontal and vertical plates. The incompletely immobilized head was fixed in a mask placed in the front part of the cage, facing the pointing board. This ensemble made it possible to standardize the animal posture, and easy to connect the thermode with the tubes of the cooling apparatus.

For successful trials, reinforcement consisted of apple juice (2 ml), delivered directly to the mask in which the animal's muzzle was placed.

Facing the cage, a vertical, 60 cm × 45 cm panel was placed about 20 cm away from the animal. On its lower part there was a lever, 4 cm × 1.5 cm, that opened a microswitch when pressed with a minimal force of 30 g. On the upper part of the board was a square screen on which visual stimuli were presented. These stimuli consisted of LEDs (5 mm in diameter) with a luminosity of 500 μcd and were used as pointing targets. The screen consisted of a printed circuit in a 5 mm grid, which registered the spatial coordinates of the first contact of the finger with the board.

The programmed sequences and reinforcement were controlled on-line by a microprocessor system (MOTOROLA) which

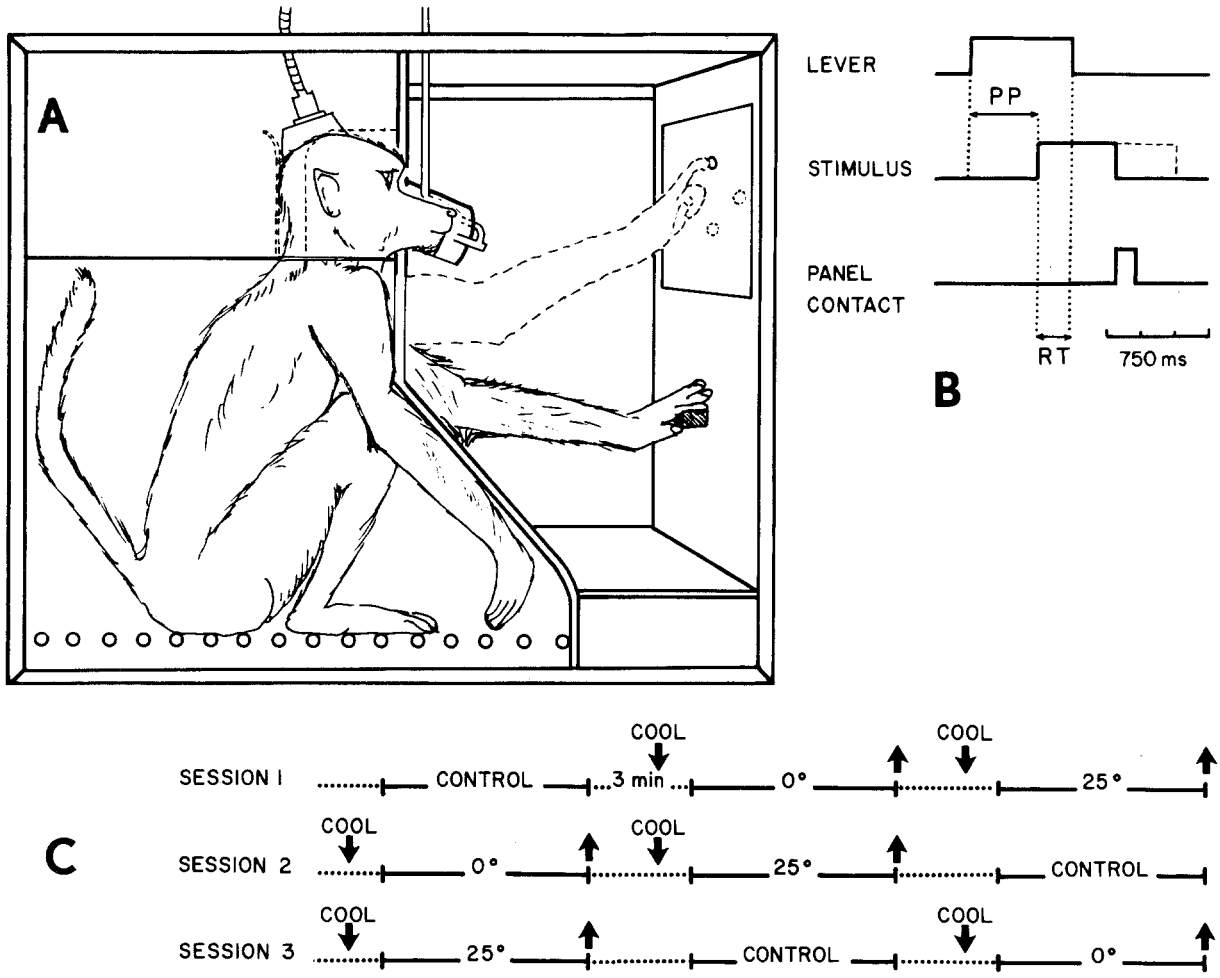

Fig. 1. **A** Experimental cage and monkey performing the goal-directed movement. The animal places its left hand (continuous line) on a lever which lights up a target on the work panel. After releasing the lever, the animal should point at the luminous target with the left index finger (dotted lines). For the exact distances between targets see Methods. **B** Experimental procedure. By pressing on the lever, the monkey causes the stimulus to light up after a variable delay. In the example the duration of this preparatory period (PP) is 500 ms. The reaction time (RT) is the interval separating the appearance of the luminous stimulus and the release of the lever. Although the maximum duration of the stimulus is 1 s, it disappears when the finger makes contact with the panel as a result of pointing. **C** Description of cooling sessions. Three successive sessions are represented. Continuous lines: periods of RT recordings with the corresponding probe tip temperatures. Dotted lines: 3 min rest periods separating the recording series. Downward and upward arrows correspond respectively to initiation and cessation of cooling. Note that cooling is applied 1 min prior to RT recording

also recorded data and carried out statistical analysis for the session: mean, standard deviation, confidence limits. For each subject, the average RT were computed afterwards and submitted to Student's *t*-test or variance analysis.

Procedure

The visuomotor task, of which different spatial characteristics could be analyzed (Paillard and Beaubaton 1978), consisted of pointing with the finger at the luminous target. In the present work, only the latency of the movement towards the target will be considered.

Description of a Trial

The animals were trained to press a lever and keep it down until the visual signal appeared. The foreperiod, defined as the interval between lever pressing and signal occurrence, could have any one of four durations (0.5, 1.0, 1.5 or 2.0 s), distributed in a rectangular frequency and with a balanced pseudo-random order of presentation. On appearance of the luminous signal, the subject had to release the lever and point at the target with its index finger (Fig. 1). The reaction time (RT) was defined as the time interval between appearance of the signal and release of the lever. The maximum duration of signal presentation was 1 s; however, it disappeared as soon as the finger made contact with the panel. The criteria of reinforcement which were adopted took account of the pointing response and the speed of execution of the whole sequence.

Description of a Session

In the animals implanted with probes, the effects of different temperature levels (see Methods) on the performance were

studied in each session (Fig. 1). Each session consisted of 96 trials, each temperature being applied for a series of 32 trials. The series were separated by 3 min rest periods, allowing the structure to reach the chosen temperature. The adoption of random presentation of the temperatures, in a latin square, minimized any possible effects due to the order of presentation. Furthermore, the random use of a non-blocking temperature (25° C) made it possible to avoid conditioning effects, such as those described by Benita et al. (1979).

In DN-lesioned animals, 64 trials were carried out in the same experimental conditions at each session.

Description of the Different Conditions

The animals were submitted to different experimental conditions in which the position of the target was or was not changed between trials.

Condition 1 – Single target position: The target was presented in the center of the screen at each trial. The single position of the target imposed stereotyped pointing movements having essentially the same amplitude and direction. This condition could therefore approximate a simple RT situation in which the only uncertainty was the moment of signal occurrence.

Conditions 2 and 3 – Multiple target positions: In these two conditions, the position of the target was varied from trial to trial in a pseudo-random fashion of rectangular frequency. The pointing response in these cases required different spatial trajectories and therefore resembled RT situations involving choice. In condition 2, the signal could appear, depending on the trial, in either of two places situated on the same vertical meridian, 16 and 20 cm, respectively, from the lever and 2 cm to each side of the center. The position of the target on the vertical axis and therefore the amplitude of movement required were unpredictable. In condition 3, the signal could be distributed between four different places; two more points, 4 cm to either side of the center of the screen on the horizontal axis, were added to those described above. In this case, the animal had to perform movements in different directions as well as of different amplitudes.

The animals with implanted probes were confronted with each of three experimental modes in sequence, while the animals with permanent lesions were studied in modes 1 and 2 on alternate days. In this latter group, ten sessions preceding coagulation were taken as controls (Pre-op). A series of ten experimental sessions were carried out on the coagulated animals as soon as they had recovered from the operative shock (Post-op 1). Ten further sessions, corresponding to Post-op 2, were carried out about 20 days after operation. Finally, a last series (Post-op 3) of ten sessions was performed 100 days postoperatively.

Histological Control

At the end of the series of experiments, the animals were sacrificed with an overdose of nembutal. Intracarotid perfusion of 10% formol was performed. The cerebellum was removed and subsequently cut in transverse or horizontal frozen sections at 50 μ; the sections were alternately stained by the Nissl and Klüver and Barrera methods.

Cryoprobe Placement. Histological examination (Fig. 2) showed that in subject LIL the probe was situated in an anteroposterior plane corresponding to P5 in the atlas of Riche et al. (1971); lateroventrally it penetrated slightly into the cerebellar white matter. In PEN, the probe was in essentially the same anteroposterior plane (P5). In BER, the tip of the probe was located more anteriorly (P4) and more laterally in the nucleus.

Location and Size of Electrolytic Lesions. The unilateral lesion in subject NEF (Fig. 2) extended anteroposteriorly from P2 to P7. In BAS, the first lesion extended from P3 to P8. At its greatest extent, it encroached slightly laterally on cerebellar fibers; the second lesion in this animal had essentially the same rostrocaudal extent, but seemed to be a bit less extensive medially and ventrally in the nucleus.

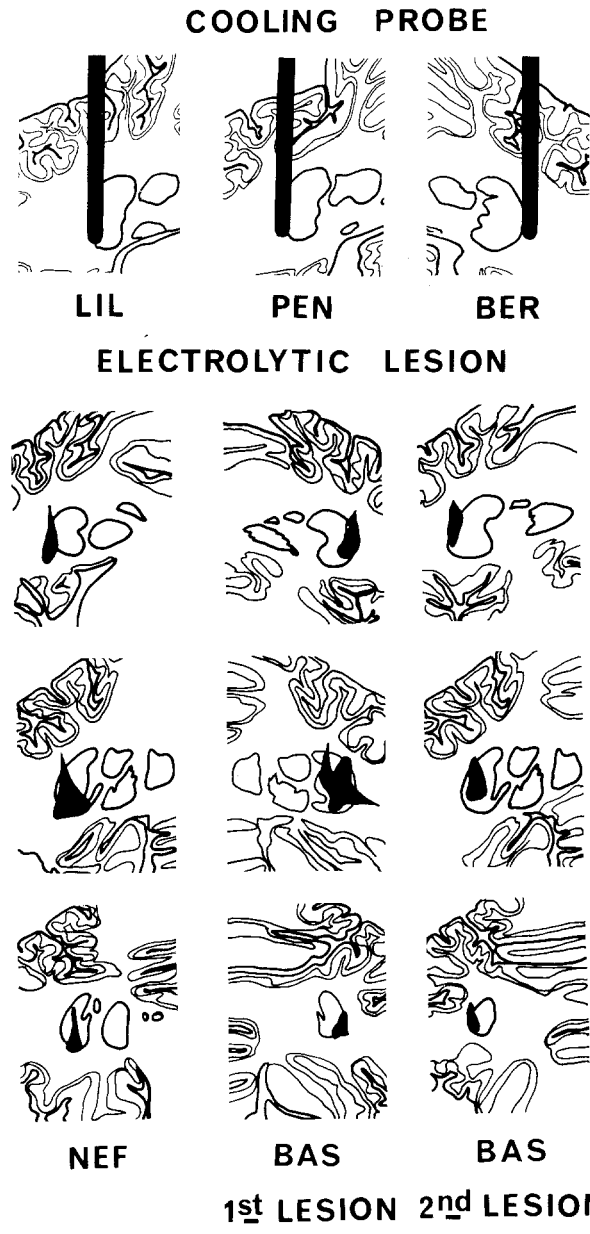

Fig. 2. Histological controls: frontal sections of the cerebellum. On top probe placement in subjects LIL, PEN and BER. Below size and extent of the electrolytic lesion in subjects NEF and BAS. Rostro-caudal diagrams are represented from top to bottom

Results

General Observations

Behavioral observations were regularly made on lesioned animals put back into the colony after

recovery from surgery. These observations particularly concerned posture and locomotion, the latter consisting of walking, jumping, exploration and grasping food. In addition, simple visuomotor tests were applied on lesioned and probe implanted animals in the experimental cage. These consisted of presentation of food in cylinders of different diameter and opening of a latch-box after training (Massarino et al. 1979b). No notable deficit in the initiation of spontaneous movements or of movements required by the tests was observed. It was noted, however, that the animals had a tendency to use the limb contralateral to the lesion. The principal symptoms observed – misreaching and intention tremor – resulted from defective control in the performance of movement. In the pointing task we noted a lower frequency of lever pressing after dentate exclusion.

Control Experiments

These were carried out systematically throughout the experimental period on the three animals with implanted probes. It was noted that implantation in itself did not cause any change in performance, and it was also verified that the observed changes during cooling could not be attributed to mechanical disturbances associated with the functioning of the probe.

Comparison of Reaction Times Before and After Thermode Implantation. The comparison of mean RTs recorded before implantation and those observed afterwards at normal temperature (Fig. 3) did not show any significant differences (LIL: $t = 0.47$, PEN: $t = 0.29$, BER: $t = 0.01$). The observed changes during cooling were therefore not due to mechanical damage brought about by implantation of the probe.

Comparison of Reaction Times at Normal Cerebral Temperature and at 25° C. Cooling to 25° C does not produce blocking of the affected structures (Benita 1972), but brings about mechanical disturbances due to the cooling system. Comparison of mean RTs recorded at normal cerebral temperature and at 25° C (Fig. 3) showed no significant difference (LIL: $t = 0.23$, PEN: $t = 0.44$, BER: $t = 0.38$). These results showed that the mechanical disturbances had a negligible effect on the test performance.

Exclusion Effects on Reaction Times

The mean RT values observed in the control trials varied from 220 ms (LIL) to 290 ms (BER), and appeared to depend on the individual strategies

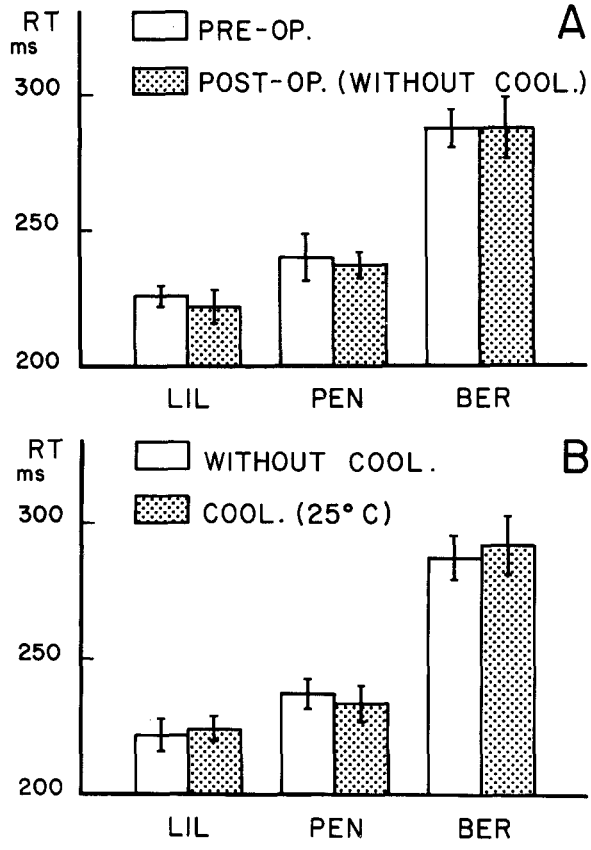

Fig. 3A, B. Control experiments. **A** RTs before (pre-op) and after (post-op) probe implantation, at normal cerebral temperature. Mean values corresponding to about 250 trials. RT values on ordinates. Averaged RTs are indicated with their confidence limits at $p = 0.05$ probability threshold. **B** Comparison of RTs at normal cerebral temperature and at probe tip temperature of 25° C

employed by each animal. The mean values observed, as well as the inter-individual variations, corresponded to those generally recorded in monkeys of the same species for a manual RT task (Beaubaton and Requin 1972). In animals with electrolytic DN destruction, the mean RTs corresponding to the pre- and postoperative periods were compared. For each period the mean RT was calculated from 300 trials. With animals carrying implanted probes, statistical analysis was carried out on 250 trials executed at normal cerebral temperature and 250 with DN blocked by cooling. The overall data were analyzed by means of a two-way (DN exclusion X target position) variance analysis, in which the error-term for each factor was formed by the interaction of the factor with the subjects.

The first important point to note is that DN exclusion, either by destruction or by cooling, never caused suppression of movement; the animals continued to execute the pointing movement with the

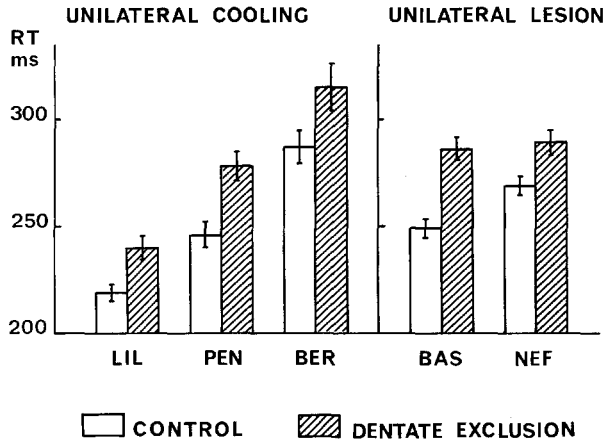

Fig. 4. Exclusion effects on RTs. Effects of eliminating DN ipsilateral to the active hand, in the five subjects. For animals LIL, PEN and BER, the cooling period is compared to the control period without cooling. Each column corresponds to the mean of 250 trials. For animals NEF and BAS, the preoperative period is compared to the postoperative period after destruction of DN; each column corresponds to the mean of 300 trials. RTs values on ordinates. Averaged RTs are shown with confidence limits at $p = 0.05$ probability threshold

required sequence without any necessity for retraining.

The results collected together in Fig. 4 and Table 1 clearly show that in all animals and in both types of experimental conditions (single target position, condition 1; multiple target position, conditions 2 and 3), exclusion of DN brought about an increase in RT. This increase was statistically significant ($F_{1,4} = 37.64$, $p < 0.01$).

The increase in RT appeared to correlate directly with the volume of DN inactivated. Thus BAS, with the largest lesion, exhibited the greatest increase in RT. Conversely, the least effect on RT occurred in BER, with a probe position such that only a limited volume of the nuclear tissue was cooled (Fig. 2).

Effects of Varying the Target Position

The animals were confronted with different experimental conditions in which the target was either fixed (condition 1; single position target) or variable (conditions 2 and 3; multiple position target).

The results (Table 1) show that in all animals, the mean RTs in condition 3 were higher than those recorded in condition 1 ($F_{1,4} = 8.81$, $p < 0.05$). Moreover, RTs in conditions 1 and 2 did not differ significantly from one another ($F_{1,4} = 4.28$). These results demonstrate that RTs were not affected by the choice between two different amplitudes (condition 2), whereas they were significantly prolonged by the choice between four trajectories with different amplitudes and/or directions (condition 3).

When comparing the effects of DN inactivation on mean RTs in different conditions, no significant interaction between the exclusion effect and the target position effect could ever be observed, neither between conditions 1 and 2 ($F_{1,4} = 0.02$) nor 1 and 3 ($F_{1,4} = 0.03$). Therefore, the increase in RT following DN inactivation seems independent of the amplitude and direction of the subsequent response.

Table 1

Dentate exclusion	Subjects	Single target position Condition 1		Multiple target positions Condition 2		Multiple target positions Condition 3	
		Control	Exclusion	Control	Exclusion	Control	Exclusion
Unilateral Cooling	LIL	218.95[a] (28.84)[b]	240.11 (50.43)	222.31 (46.28)	241.06 (50.91)	250.69 (27.06)	274.71 (47.64)
	PEN	246.95 (55.32)	278.66 (59.38)	237.29 (42.36)	252.23 (48.82)	262.88 (95.13)	292.66 (73.81)
	BER	287.01 (55.91)	315.40 (81.59)	303.85 (71.61)	337.89 (89.63)	370.46 (95.69)	385.68 (93.20)
Unilateral Lesion	BAS	249.04 (82.19)	286.38 (57.08)			252.73 (76.37)	285.16 (79.62)
	NEF	269.14 (69.22)	289.39 (55.05)			300.03 (92.27)	313.86 (81.54)
Bilateral Lesion	BAS	222.23 (56.47)	288.92 (71.93)			230.05 (42.43)	288.13 (55.26)

[a] RTs
[b] standard deviations

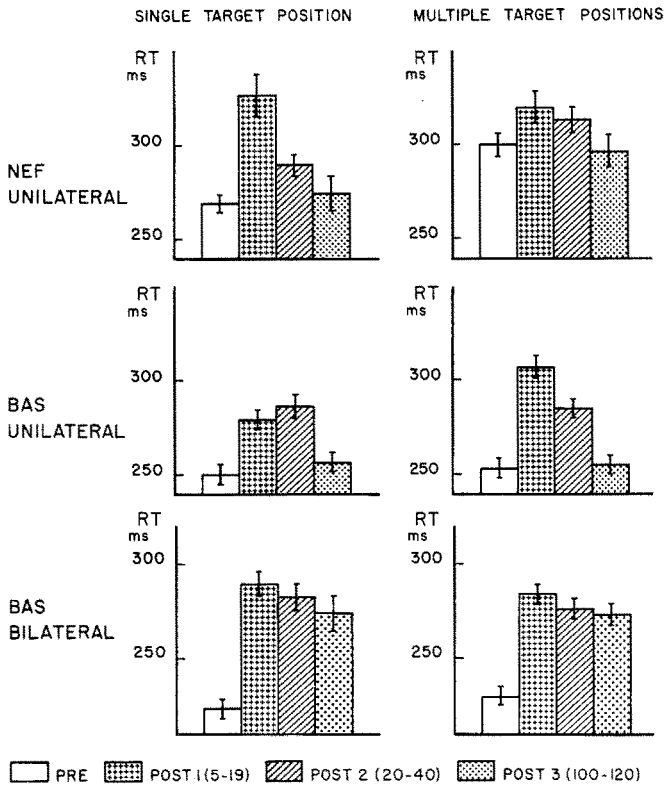

Fig. 5. Recovery of RTs after unilateral and bilateral DN destruction. In NEF and BAS, after unilateral lesion ipsilateral to the active hand, the preoperative period (unshaded column) is compared with three postoperative periods. The same comparison is made in BAS (lower part of the figure) after a second lesion on the other side. This was carried out after total recovery of RTs from the first lesion. Post-op 1 = between 5 and 19 days after DN destruction; Post-op 2 = between 20 and 40 days; Post-op 3 = between 100 and 120 days. RTs recorded during experimental condition 1: single target position (left) and condition 3: multiple target position (right). RT values on ordinates. Each column corresponds to the mean of 300 trials. Averaged values are shown with confidence limits at $p = 0.05$ probability threshold

Recovery Phenomena

Reaction times were studied over a period of 4 months in two animals (NEF and BAS) which had undergone unilateral ND destruction, followed in the case of BAS by a lesion of the contralateral DN.

Recovery after Unilateral Lesion. The results shown in Fig. 5 correspond to RTs for the hand ipsilateral to the lesion at various intervals after operation: about 15 days, 1 month and 4 months. It can be noted that the RT increase observed immediately after the operation diminished and entirely disappeared 4 months after unilateral coagulation. Differences in RTs recorded before operation and in the final postoperative period were not statistically significant. Furthermore, the results obtained in these two animals show that there is no relationship between speed of recovery and type of experimental conditions (single vs. multiple target position).

Recovery after Bilateral Lesions. In animal (BAS), the second DN lesion was performed after total recovery from the first one. The pointing task was carried out with the hand ipsilateral to the second lesion; the experimental protocol and duration of study were the same as for animals with unilateral DN lesion. As can be seen in Fig. 5, a bilateral lesion gave rise to a greater prolongation of RTs than did a unilateral one (65 ms, as opposed to 35 ms). Secondly, it may be noted that the increase in reaction time remained significant for 4 months after the second operation. However, some diminution in reaction time occurred between the immediate postoperative period and 4 months, suggesting that recovery after a second lesion is much slower than after a unilateral one.

Discussion

Dentate Inactivation and Reaction Time Increase

The results obtained in the experiments reported here show that permanent or temporary DN exclusion in the baboon causes an increase in reaction time in a finger pointing task. Delay in the initiation of movement is one of the components of the cerebellar syndrome as first noted by Holmes (1917, 1939) and more recently by Hallet et al. (1975) and Rondot et al. (1979) in human patients with extensive cerebellar lesions. Such a disturbance in the initiation of movement has been reproduced in the rhesus monkey by Meyer-Lohmann et al. (1977) through cold block of the dentate and interpositus cerebellar nuclei. The deficit is specifically one of movement initiation and is essentially distinct from abnormalities which become apparent in the course of the movement, such as an impairment in movement time (Trouche et al. 1979; Beaubaton et al. 1980) or a slowing of the initial speed movement (Meyer-Lohmann et al. 1977). This delay does not appear to be a consequence of the hypotonia which follows cerebellar lesions (Rondot et al. 1979). Our results clearly show that cerebellar inactivation strictly limited to DN provokes this major symptom of the cerebellar syndrome in the monkey, thus proving the importance of DN in movement initiation in this species.

This result is in agreement with electrophysiological findings (Thach 1975) showing that the earliest changes in cerebellar unit activity preceding the discharge of the motor cortex occurs in the dentate nucleus. However, the causative mechanisms of the increase in movement latency following DN inactiva-

tion remain a matter of some controversy. The phenomenon has frequently been attributed to the suppression of a tonic facilitatory effect of DN on the motor cortex – in other words, to a disfacilitation (Holmes 1939; Thach 1972). In fact, Meyer-Lohmann et al. (1977) found electrophysiologically that few cells in the motor cortex have their tonic background activity modified by inactivation of the cerebellar nuclei. These authors suggest that the increase in movement latency may rather be due to an interruption in the transmission of phasic instructions from the cerebellum to the motor cortical areas. This however raises the question of the involvement of DN in a system responsible for the rapid release of movement (Meyer-Lohmann et al. 1977; Lamarre et al. 1979; Wiesendanger et al. 1979a). A number of experimental findings lead to the conclusion that the dentato-thalamo-cortical system may underlie the control exerted by DN on the release of programmed movement. In addition to changes of electrophysiological activity in DN during the phase preceding the execution of a motor response (Thach 1975), such changes have also been observed in VL (Strick 1976; Schmied et al. 1979) and in the motor cortex (Evarts 1968). Furthermore, recent evidence suggests that the cerebello-thalamo-cortical system might provide the input for the "intentional component" of pyramidal tract neurone discharge (Meyer-Lohmann et al. 1975). Finally, cooling of VL in the cat leads to increases in reaction time (Benita et al. 1979). The fact that this finding could not be repeated in the monkey (Miller and Brooks 1977) may be explained by species differences. This possibility is made more likely by recent anatomical findings which demonstrate important differences between carnivores and primates in cortico-cerebellar interrelations (Angaut 1979; Sasaki 1979).

Finally, the control exerted by DN on the initiation of movement may be explained by an influence on motoneurones by way of subcortical structures. The direct dentato-spinal pathway described by Bantli and Bloedel (1976) appears to be involved in such a mechanism, as shown by the triggering of limb flexion movement by DN microstimulation in a monkey with motor cortex removed (Schultz et al. 1979). If DN plays an effective part in postural adjustment in primates, this type of control may be exerted through brainstem structures (Schultz et al. 1979), or by the cerebello-thalamo-cortical system (Massion and Sasaki 1979). The increased RTs observed in this experiment after dentate exclusion could reveal an impairment in postural reorganization underlying the initiation of movement.

The cerebellar syndrome is also evident by its effect in slowing the initiation of eye movements (Rondot et al. 1979). The question therefore arises as to whether or not an ocular component intervenes in the prolongation of reaction times in visual tasks such as those used in the experiments reported here. Anatomical data (Carpenter and Strominger 1964; Chan-Palay 1977) and microstimulation experiments (Ron and Robinson 1973) suggest direct connections between the DN and oculomotor centers. It may also be noted that the initiation of saccades is preceded by unitary discharges in DN (Grimm and Rushmer 1974; Gardner and Fuchs 1975; Thach 1978). Taken together, these data lead to the conclusion that lack of cerebellar control of oculomotor centers may cause a delayed saccadic eye movement or disturbances of oculomotor mechanisms involved in the visual localization necessary for the programming of limb movement.

Recovery of Reaction Time After Permanent Lesions

The recovery of RTs which has been observed after permanent unilateral DN lesions shows that the deficit in motor initiation is transitory, animals with DN destruction on the same side as the active hand displaying recovery of RTs to their original value four months after operation.

Such penomena have frequently been reported in monkeys after more or less extensive lesions of DN; however, studies of recovery have only described abnormal execution of movement, such as dyskinesia and intention tremor (Zervas et al. 1967; Zervas 1970; Goldberger and Growdon 1973). With respect to deficits related to movement execution, Goldberger (1974) has put forward interpretations whose validity should be discussed as concerns the initiation of movement.

Two possible mechanisms for recovery could be discussed. Firstly, recovery may be due to vicarious functioning of the interpositus nucleus (IN). It is in fact known that lesions, limited to either DN or to IN cause only few deficits in comparison with those appearing after combined destruction of both nuclei (Zervas 1970). Relationships may therefore exist between these nuclei, each being able to compensate for the absence of the other (Goldberger 1974). However, anatomical observations show that there is only partial overlapping between the thalamic projection zones of DN and IN in the monkey (Stanton 1973). Furthermore, even though both nuclei seem to control the execution of movement (Brooks et al. 1973; Uno et al. 1973), IN plays only a negligible role in the initiation of voluntary movement in the monkey. IN cells are activated later than those of DN (Thach 1972) and there is no strict correlation

between the changes of cell discharge in IN and the characteristics of ongoing movement (Thach 1978).

Secondly, after unilateral DN lesion, recovery from the deficit involving movement initiation may be due to intervention of the intact contralateral DN. There are, however, few experimental data suggesting bilateral control by DN. Bilateral postural effects after unilateral dentatotomy in man were described by Nashold and Slaughter (1969), and Zervas (1970) could notice an aggravation of the deficits seen after unilateral destruction, particularly in the lack of motor initiative, following bilateral DN lesions in the monkey. It is possible that the bilateral dentatothalamic connections described by Chan-Palay (1977) may subserve this action. This is supported by the results reported here following bilateral DN destruction, especially the persistence of RT increase, which implies that the intact DN could partly compensate for the destroyed one. This type of functional compensation, even given the existence of an anatomical substrate, can nevertheless not be considered as proof that such bilateral control of motor activity in the limbs occurs under normal circumstances with both DNs intact.

Dentate Nucleus and Preparation of Goal-directed Movements

The results obtained in the present study suggest that DN is involved in the initiation of goal-directed movements. It is difficult however to say exactly how this occurs; it is not known whether DN sets off programs elaborated in other motor integrative structures, or whether it intervenes more directly in motor preparation (Massion and Sasaki 1979).

Our data suggest that programming of movements in different directions brings about an increase in reaction time, but that this is not the case when only movement amplitude changes. This result, in agreement with the findings of Semjen and Requin (1976), confirms the diversity of mechanisms responsible for separately programming the amplitude and direction parameters, and justifies the experimental protocol chosen for the present study. In addition, our results show that the increase in reaction time following DN exclusion is not accentuated when different biomechanical variables such as amplitude and direction of the impending movement are randomly changed. In other words, the increase in reaction time is independent of the amplitude and direction of the response to be carried out. It may therefore be concluded that the presence of DN is not indispensable for the selection of the spatial parameters defining the motor program.

There are few experimental data concerning the possible role of DN in programming movement amplitude. Thach (1978), however, has described neuronal discharges in DN which are correlated with the amplitude of the response to be carried out. On the other hand, the intervention of DN in the evaluation of directional parameters is at present a matter of some controversy. Grimm and Rushmer (1974) and Robertson and Grimm (1975) were unable to establish a positive correlation between these changes in neuronal activity in DN and the spatial characteristics of trajectories of the monkey forelimb. Contrarily, a number of recent experimental results lead to the conclusion that DN may be involved in the establishment of a directional program (Thach 1978; Strick 1979).

The important question is to determine whether the correlation between neuronal activity and directional parameters is specific to DN or whether it is only a reflection of changes in other neural structures, for example, through corollary discharges or efference copies.

In this context, consideration should be given to anatomical (Wiesendanger et al. 1979b) and electrophysiological (Allen et al. 1978; Sasaki et al. 1979) studies demonstrating relationships between DN and cortical areas to which a role in the specification of the directional parameters of voluntary movement is attributed (cf. Requin 1980).

Our experimental results are in agreement with a number of recent findings which tend to modify the role classically attributed to DN in the control of voluntary movement, particularly with respect to its role in "long range planning of movement" (Evarts and Thach 1969; Allen and Tsukahara 1974). The results of Meyer-Lohmann et al. (1977), suggesting that DN is more concerned in the transmission of signals to the motor cortex than in their elaboration, support the conclusions of Wiesendanger et al. (1979a) on the functional role of the dentatothalamo-cortical system in the control of fast-triggered movement. The present results on the latency of goal-directed movement suggest that the effects of eliminating DN are independent of the spatial characteristics of the movement to be executed. Although it may be difficult to attribute a role to DN in the programming of the directional parameters of movement, it is equally difficult to reduce its function to simple transmission. The possible integration of sensory messages in this nucleus (Allen and Tsukahara 1974; Chan-Palay 1977) and the possibilities of rapid intervention at cortical and/or subcortical levels (Evarts and Thach 1969) should encourage research on its role in other aspects of motor control, such as postural reorganization preceding limb movement

(Schultz et al. 1979) or the activation of proximo-distal muscular sequences (Massion 1973). Moreover, any participation of the cerebellar structures in motor initiation cannot be considered without reference to an intervention of the basal ganglia system. Experimental data indeed suggest that complementary strio-pallidal and cerebellar influences could determine an integrated activity able to trigger an appropriate motor response (Beaubaton et al. 1980).

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