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# Participation of the Cerebellar Dentate Nucleus in the Control of a Goal-directed Movement in Monkeys

## Effects of Reversible or Permanent Dentate Lesion on the Duration and Accuracy of a Pointing Response*

D. Beaubaton and E. Trouche

Institut de Neurophysiologie et Psychophysiologie, C.N.R.S. – INP – 31, Chemin Joseph Aiguier – B.P. 71, F–13277 Marseille Cedex 9, France

**Summary.** Experiments carried out on seven adult baboons were addressed at specifying the participation of the cerebellar dentate nucleus (DN) in the control of duration and accuracy of a goal-directed movement. The visuo-motor task used in this experiment involved trained pointing movement towards stationary target.

The monkeys trained to point with the index finger to a target light were required to perform stereotyped movements of constant amplitude and direction, or movements with variable amplitude and direction. Duration of response execution was measured by movement time and accuracy by terminal spatial errors. We analysed the effects of excluding the DN on the arm ipsilateral or contralateral to the partially inactivated nucleus.

Two techniques have been used to impair the DN activity: in three monkeys the structure was reversibly cooled with a chronically implanted thermode; in four others partial electrolytic destruction of the DN was performed.

In the arm ipsilateral to the lesioned DN we observed modifications of movement times, appearance of systematic errors with increased dispersion. Contralateral effects were restricted to movement times. Changes in movement times and spatial errors were studied over time (4 months) in permanently lesioned animals. Only the spatial dispersion presented a total recovery.

These data show that the DN is concerned with the control of speed and accuracy during the execution of visually triggered movements in monkeys. Moreover comparison of results concerning ipsilateral and contralateral effects of DN dysfunction on movement times and errors, and evidence of different time course of recovery in these variables, suggest a differential control exerted by the DN on speed and accuracy of goal directed movements.

**Key words:** Dentate nucleus – Movement time – Spatial error – Goal-directed movement – Cooling – Lesion – Monkey

## Introduction

Following Fitts' experiments (1954) numerous psychological studies have been devoted to research, in human subjects, of the relationships between speed and accuracy of arm movement (Keele 1973). The neurophysiological basis of such dual control of speed and accuracy has recently been discussed by Brooks (1979a). In this connection, systematic analysis of movement execution can contribute to qualify the central processes underlying motor control. The organization of reaching has been described as involving different components (Paillard and Beaubaton 1976): a phase for the ballistic transport of the hand towards the target and afterwards a terminal stage with the final guiding of the movement to ensure the correct placement of the hand. In spite of this heterogeneity the pointing task used in the present experiments can be considered as a valid experimental model to investigate the spatiotemporal disturbances resulting from nervous lesions. In particular such standardized goal-directed responses make it possible to analyse the movement execution time and its spatial accuracy (Paillard and Beaubaton 1978). Moreover the pointing response, involving several limb joints, may be viewed as a "compound movement" according to Holmes' terminology (1939). In this context, the existence of specific impairments for these movements was questioned

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*Offprint requests to:* D. Beaubaton (address see above)

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compared to dyskinesias observed in simple monoarticular responses (Brooks 1979b).

In the monkey the participation of DN in motor initiation has been evidenced (Meyer-Lohman et al. 1977). We showed previously in baboons performing the pointing task that the DN was involved in the triggering of goal-directed responses (Trouche and Beaubaton 1980; Beaubaton et al. 1980). The problem was now to find whether the DN intervenes in the course of movement execution as suggested by the increased discharges in DN units during the motor act (Meyer-Lohman et al. 1975; Robertson and Grimm 1975; Thach 1978). This question was tackled by varying the amplitude and direction of the pointing response and comparing the effects of DN absence in different paradigms.

Spatial impairments have been described in human cerebellar patients (Holmes 1939) and in animals, either after large cerebellar destruction (Dow and Moruzzi 1958) or limited nuclear exclusion (Horvarth et al. 1970; Brooks et al. 1973; Goldberger and Growdon 1973). However, lesion studies have shown that dentatotomy induced, in spatially oriented movements, more severe disturbances in monkeys than in cats (Liu and Chambers 1971). A quantitative analysis of limb trajectories was provided by Gilman et al. (1976) in decerebellated monkeys but no quantitative approach has been undertaken to study the speed and accuracy of compound movements after lesions limited to the DN. This series of investigations was aimed at analysing the spatial errors following dentatomy; the duration of movement was also considered in order to appreciate the modifications concerning speed of execution and the relationships between defects affecting the velocity of the limb response and spatial inaccuracy.

It is generally assumed that unilateral DN exclusion induces strictly ipsilateral impairments in the monkey. However, some clinical observations (Heimburger 1970) and experimental results (Robertson and Grimm 1975) suggest the possibility of a bilateral control exerted by the DN. These observations are corroborated by anatomical data (Chan Palay 1977) showing bilateral dentatofugal projections. The eventuality and the nature of such disturbances was investigated in the present experiment by recording the performances of the limb contralateral to the excluded DN in some cases. Finally, in permanently lesioned monkeys, the occurrence of functional recovery from impairment of movement execution was investigated. Any change in the rate of recovery concerning either the temporal or spatial variables could contribute to knowledge of the specificity of the control exerted by the DN on the speed and accuracy of the movement studied.

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

## Material and Methods

### *Subjects*

Seven adult baboons (Papio papio) were used. Three of the animals had cryoprobes chronically implanted unilaterally in the DN. The other four underwent unilateral electrolytic lesions of the DN. In all seven cases the limb ipsilateral to the DN excluded was tested. In addition the performance of the contralateral limb was analysed in two of these cases.

### *Cooling and Lesion Procedures*

Implantation of thermodes and electrocoagulation were carried out under nembutal (35 mg/kg i.v.) in aseptic surgical conditions. The DN was located stereotaxically using the atlas of Riche et al. (1971) and electrophysiologically by recording its spontaneous activity.

The probes and the cooling device were of the type developed and described by Dondey et al. (1962) and Bénita and Condé (1972). Cooling of the nervous tissue along the probe (1.1 mm in diameter) was prevented by a vacuum sheath extending 3 mm from the tip. 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 the nucleus interpositus. The probe was held by a special holder (Massarino et al. 1979) fixed to the skull by a series of screws cemented into the bone.

In the present experiment we utilised a cooling temperature of 0° C at the tip of the probe. A tip temperature of 25° C was used as control; this temperature is known to have no effect on nervous transmission (Bénita and Condé 1972). Previous data obtained with the same task showed that cryoprobe implantation in itself did not cause any change in performance and that the observed changes could not be attributed to mechanical disturbances associated with the cooling device (Trouche and Beaubaton 1980).

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

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

### *Experimental Apparatus*

In each session the baboon was placed in a cage located in a dimly lit and soundproof room. 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 working panel. This arrangement made it possible to standardize the posture of the animals and easy to connect the thermode with the tubes coming from the cooling apparatus. Reinforcement, for successful trials, consisted of apple juice (2 ml), delivered directly to the mask in which the animal's muzzle was positioned.

In the pointing task a vertical panel (60 cm × 45 cm) was placed about 20 cm away from the animal. On its lower part was a

lever which opened a microswitch when pressed by the hand. On the upper part of the board was a square screen (17 cm × 17 cm) 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 the reinforcement were controlled on-line by a microprocessor system (Motorola) which also recorded the data and carried out the statistical treatment.

*Behavioral Procedure: The Pointing Movement*

*1. Description of a Trial.* The task used in this experiment was previously described (Paillard and Beaubaton 1978; Trouche and Beaubaton 1980). The animals were trained to extend their forelimb and to press the lever with their hand. On appearance of the luminous signal the subject had to release the lever and point at the target with its index finger. This response may be considered as a multijoint movement with a differential involvement of limb joints according to the position of the target. It must however be noted that the limb displacement was mainly dependent on the shoulder, responsible for the raising of the arm from the lever to the target.

*2. Description of a Session.* In the monkeys implanted with probes, the effects of cooling on the performance were studied in each session. Each session consisted of 96 trials, the normal, the control (25° C) and the blocking temperature (0° C) 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 temperature, in a latin square, minimised any possible effects due to order of presentation. Furthermore, the random use of a non-blocking temperature (25° C) made it possible to avoid conditioning effects.

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

*3. Description of the Different Conditions.* The monkeys 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 centre of the screen at each trial. The single position of the target imposed stereotyped pointing movements having essentially the same amplitude and direction. The only uncertainty was the moment of occurrence of the signal.

Condition 2: Variable Target Position. In this condition the position of the target was varied from trial to trial in a pseudo-random fashion of rectangular frequency. The signal could appear in any one of four places. Two points were situated on the same vertical meridian 16 and 20 cm respectively from the lever, 2 cm on each side of the centre of the screen. Two other points are situated on the same horizontal axis 4 cm to either side of the centre of the screen.

The animals with implanted probes were confronted with each experimental condition in sequence, while the animals with permanent lesions were studied in condition 1 and 2 on alternate days. In this latter group, 5 sessions preceding coagulation were taken as controls (Pre-op). A series of 5 experimental sessions were carried out on the coagulated animals as soon as they had recovered from the operative shock (Post-op I). Five further sessions, corresponding to Post-op II were carried out about 20 days after operation. Finally, a last series (Post-op III) of 5 sessions was performed 100 days post operatively.

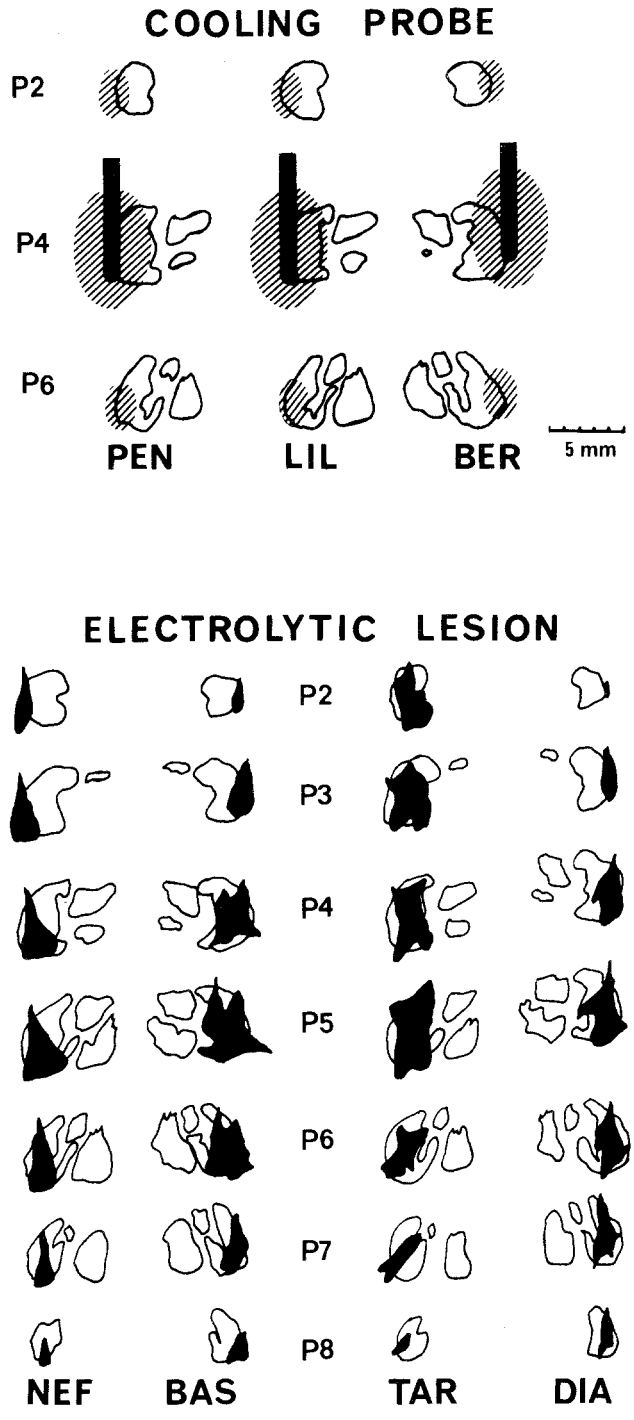


**Fig. 1.** Histological controls of cooling probe positions and electrolytic lesions. On top: frontal sections of cerebellar nuclei (dentate nucleus and interpositus nucleus) in three probe-implanted monkeys. The sections correspond to three planes of the atlas of Riche et al. (1971). The medial diagram (*P4*) shows the actual probe placement. Estimated 20° C isotherms indicate the extent of cooled zone (hatched) from *P2* to *P6* when the tip of the probe is 0° C (Bénita and Condé 1972). Below, size and extent of the electrolytic lesions in four monkeys. Rostro-caudal diagrams, represented from top to bottom, correspond to sections of cerebellar nuclei from *P2* to *P8*

**Table 1.** Effects of dentate dysfunction on movement times

| Dentate dysfunction | Operant arm | Subjects | Condition 1 Single target position | | | Condition 2 Variable target positions | | |
|---|---|---|---|---|---|---|---|---|
| | | | Control | – | Dysfunction | Control | – | Dysfunction |
| Cooling | Ipsi. | LIL | 167.96[a] (65.32)[b] | *2.49*[c] | 145.12 (37.60) | 171.36 (43.86) | *2.68* | 137.14 (40.98) |
| | | PEN | 212.33 (51.96) | 1.20 | 221.28 (37.57) | 193.48 (50.01) | *3.57* | 221.71 (46.10) |
| | | BER | 254.46 (58.92) | 0.73 | 244.93 (52.86) | 219.49 (64.15) | 0.17 | 216.71 (70.23) |
| Lesion | Ipsi. | BAS | 240.52 (20.50) | *1.97* | 230.24 (72.74) | 249.83 (41.30) | 1.35 | 257.97 (59.37) |
| | | NEF | 162.21 (36.91) | *7.39* | 204.92 (48.63) | 165.05 (37.06) | *7.81* | 201.68 (37.19) |
| | | DIA | 217.59 (28.84) | 1.64 | 212.06 (51.87) | 225.29 (39.48) | *6.17* | 245.19 (42.70) |
| Lesion | Contra. | TAR | 279.54 (95.43) | *3.78* | 350.81 (105.23) | 284.05 (85.75) | *4.44* | 354.87 (117.07) |
| | | DIA | 189.84 (22.37) | *16.87* | 156.41 (24.77) | 193.49 (22.10) | *11.27* | 170.10 (24.55) |

[a] Averaged MTs (ms)
[b] Standard deviation
[c] Student's *t*-value (Italics when significant at $p = 0.05$)

*Data Analysis*

In the pointing task, speed and accuracy of the operant response were studied by recording the movement time and the spatial pointing error. The movement time (MT) was defined as the time interval between the release of the lever and the first contact of the finger on the screen. The error was expressed by the distance between the computed mean point of pointing coordinates and the target. For each subject and each experimental condition averaged MTs and errors were afterwards computed. Statistical differences between control conditions and DN exclusions were tested by Student's *t*-test.

*Training*

Learning the pointing movement was started by allowing the animal to locate the target by touching with the index finger a button sticking out of the panel. This button was then removed which suppressed the tactile guidance associated with the luminous signal. In a second stage, the animals learned to activate the luminous signal by putting the flat of the hand on the lever situated on the lower part of the panel. When the motor sequence had been learned the subjects successively underwent the various experimental paradigms. Cryoprobe implantation or electrocoagulation were carried out when the performances were judged to be stable, which generally meant ten consecutive experimental sessions without statistically significant variation in the results. Familiarisation with the experimental material, acceptance of head immobilisation, adoption of a stereotyped posture, learning of the motor sequence and stability of performance generally ocurred after some six months. During the training period, both limbs were utilized, with a daily alternance. In the experimental sessions, only one limb was tested, except in one case (DIA). It must be noted that some changes in response execution occurred during learning. These changes are mainly characterized by reduction of hand movement; the limb displacement being more dependent on the shoulder joint.

*Histological Control*

After completion of the experiments, the animals were killed under deep Nembutal anaesthesia by intracarotid perfusion of 10% formol. The cerebellum was subsequently cut in transverse or horizontal frozen sections at 50 μm. The sections were alternately stained by the Nissl and the Klüver and Barrera methods.

*1. Cryoprobe Placement.* Histological examination (Fig. 1) showed that in LIL, PEN and BER, the probe was essentially situated in the same antero-posterior plane corresponding to P 5 in the atlas of Riche et al. (1971). In BER, the tip of the probe was situated more anteriorly and was more lateral in the nucleus. The isotherms represented in Fig. 1 show that in no case was the interpositus nucleus affected by cooling.

*2. Location and Size of Electrolytic Lesions.* Electrolytic unilateral lesion of the DN was carried out in NEF, BAS, TAR and DIA (Fig. 1). In all subjects the lesion extended anteroposteriorly from P2 to P8.

In permanently lesioned animals, the lesioned zone of the DN seemed to have a more rostro-caudal extent than in probe-implanted monkeys.

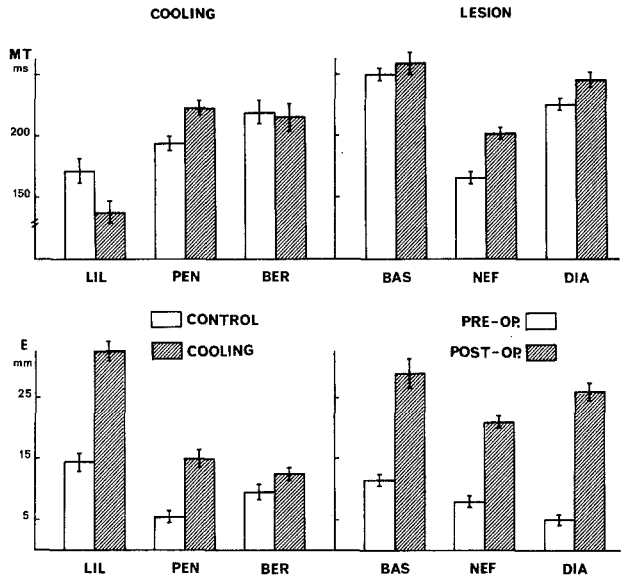


**Fig. 2.** Effects of DN dysfunction on movement time (*MT*) and spatial error (*E*). Effects of eliminating the DN, lesion ipsilateral to the active hand, in the six subjects. For animals *LIL, PEN, BER* the cooling period is compared to the control one, without cooling. Each histogram corresponds to the mean of 250 trials. For animals *BAS, NEF, DIA* the preoperative period is compared to the postoperative period after lesioning the DN. Each histogram corresponds to the mean of 300 trials. *MT* and *E* values on ordinates. *MT* and *E* recorded during experimental condition 2: multiple target position. Averaged values are shown with their confidence limites at $p = 0.05$ probability threshold

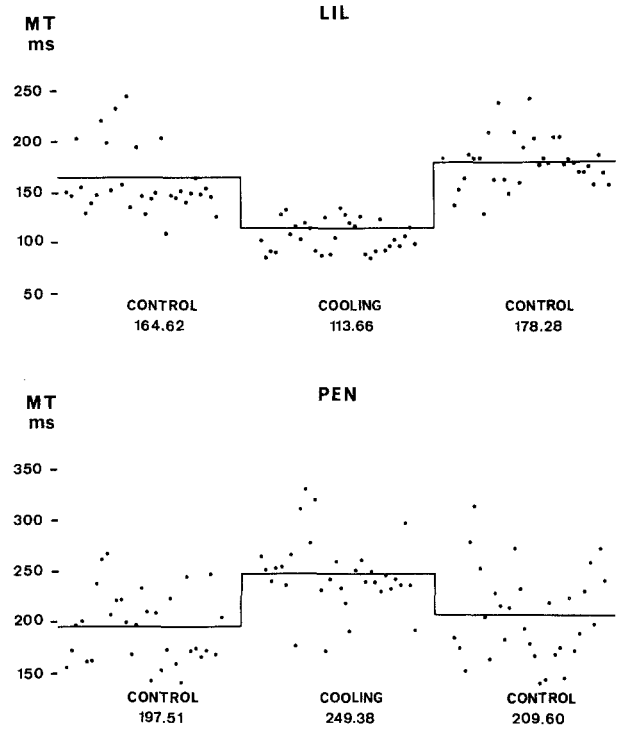


**Fig. 3.** Reversibility of cooling effects on movement time (*MT*). Trials recorded in a same session, in two thermode-implanted animals (*LIL, PEN*). The cooling condition is preceded and followed by a control condition without efficient cooling. Each of the points ranked along the abcissa correspond to a trial. Solid lines indicate for each period (32 trials) the averaged MTs. Each block is separated by a 3 min rest-period. Mean value of MTs in each block is indicated below

## Results

### *General Observations*

All animals were immediately active upon recovery from anaesthesia; a preference for feeding with the arm contralateral to the excluded DN subsided after a few days. In NEF and TAR, slight dysmetria and intention tremor were seen. These signs were particularly observed in the limb ipsilateral to the lesioned DN during tasks such as picking up small pieces of food. BAS and DIA presented a more marked ataxia with tremor in reaching for food and placing it in the mouth. In BAS the gait was jerky, and a mild hypotonia was observed in arm and leg. All these symptoms disappeared about two weeks after the lesion. No animals exhibited any obvious disturbances of ocular movements.

Concerning the thermode-implanted monkeys, observations made during the experimental sessions revealed no motor impairment due to the probe implantation or the functioning of the cooling device (Trouche and Beaubaton 1980). During the cooling periods one animal (PEN) exhibited slight oscillations at the end of the pointing movement, close to the target.

A lower frequency of lever pressing was also noted as a general effect of dentate dysfunction. Moreover the monkeys exhibited some difficulty in retrieving the position of the lever.

### *Effects of DN Dysfunction on Movement Times and Pointing Errors*

The first obvious observation is that DN dysfunction either by electrolytic destruction or by cooling never stopped the monkey's performance. All animals continued to execute the pointing movement in the required sequence, without necessity of retraining.

*I. Movement Times.* The mean MT values recorded in the control trials varied from 162 ms (NEF) to 284 ms (TAR). Such inter-individual variations could be attributed to differences in response strategies or learning levels.

a) Ipsilateral Effects. The results presented in Table 1 and Fig. 2 show that in all animals, except BER, DN

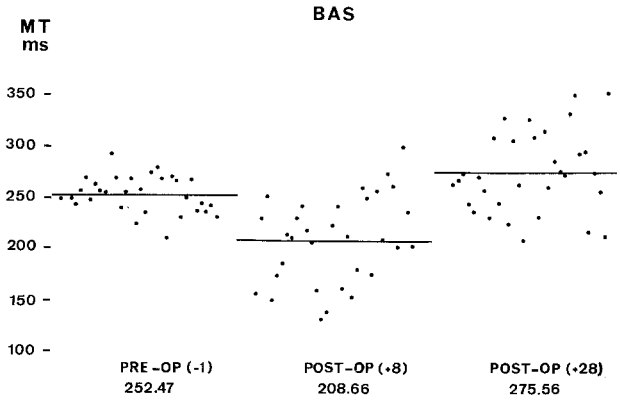


**Fig. 4.** Evolution with time of movement times (MTs) after permanent lesion of DN. MTs recorded in one animal (*BAS*) during three different sessions: one day before the operation (preop 1), 8 days postoperatively (postop +8), 28 days postoperatively (postop +28). Each point corresponds to a trial. Solid lines indicate for each period the averaged MTs. Mean value of MTs in each session (32 trials) is indicated below

dysfunction brought about significant changes in MTs, in one or both experimental conditions. However, different patterns of modification could be observed. The changes consisted in MT increase, as for example in PEN and NEF or in MT decrease, like in LIL or BAS in condition 1 (Table 1).

Figure 3 illustrates typical examples of such changes in the MTs caused by DN cooling. During the session a diminution in MTs could be observed in LIL after the initiation of cooling. Conversely DN exclusion in PEN induced longer MTs. In both monkeys cessation of cooling was followed by the return of MTs values comparable to those recorded prior to exclusion. This last point clearly illustrates the reversibility of the cooling method.

It must be noted that both types of MT modification could be observed in the same subject. In a case (BAS) with a permanent DN lesion the direction of the exclusion effect was dependent on the observation period (Table 3). In Fig. 4 three blocks of trials are presented, recorded in one preoperative session and two postoperative sessions, about one and four weeks after surgery. These results of BAS show decreased MTs in the first postoperative period, then increased MTs in the late postoperative session.

The overall data obtained in the two experimental conditions: single target position vs variable target position (Table 1) showed that with the exception of BER and NEF which presented similar results in both conditions, the remaining four monkeys evidenced different effects of DN lesion when the spatial position of the target was randomly modified (Condition 2).

**Table 2.** Effects of dentate dysfunction on spatial errors

| Dentate dysfunction | Operant arm | Subjects | Condition 1 Single target position | | | Condition 2 Variable target positions | | |
|---|---|---|---|---|---|---|---|---|
| | | | Control | – | Dysfunction | Control | – | Dysfunction |
| Cooling | Ipsi. | LIL | 12.90[a] (8.45)[b] | 0.59[c] | 13.85 (9.95) | 14.60 (10.94) | *9.29* | 36.58 (11.16) |
| | | PEN | 5.76 (11.48) | *3.29* | 12.81 (13.18) | 5.53 (7.61) | *6.09* | 15.06 (10.16) |
| | | BER | 6.40 (6.03) | 0.03 | 6.36 (8.03) | 9.43 (7.53) | 1.43 | 12.50 (13.79) |
| Lesion | Ipsi. | BAS | 8.90 (7.20) | *11.30* | 28.45 (26.38) | 11.55 (7.63) | *9.24* | 29.25 (25.01) |
| | | NEF | 5.66 (5.50) | *13.64* | 14.05 (12.40) | 8.34 (6.96) | *12.87* | 21.18 (10.52) |
| | | DIA | 5.31 (5.67) | *23.71* | 25.86 (13.97) | 4.82 (6.39) | *23.93* | 25.95 (12.52) |
| Lesion | Contra. | TAR | 3.59 (7.30) | 0.18 | 3.39 (5.58) | 5.18 (7.81) | 1.64 | 3.49 (5.14) |
| | | DIA | 3.34 (5.73) | 1.92 | 5.14 (5.72) | 3.41 (7.99) | 1.70 | 5.17 (7.53) |

[a] Averaged Es (mm)
[b] Standard deviation
[c] Student's *t*-value (Italics when significant at $p = 0.05$)

**Table 3.** Evolution of movement times after permanent lesion

| Operant arm | Subjects | Single target position (Condition 1) Pre-op | Post-op I | Post-op II | Post-op III | Variable target positions (Condition 2) Pre-op | Post-op I | Post-op II | Post-op III |
|---|---|---|---|---|---|---|---|---|---|
| Ipsi | BAS | 240.52[a] (20.50)[b] | 230.24[+c] (72.74) | 268.23[+] (60.80) | 256.89[+] (60.64) | 249.83 (41.30) | 257.97 (52.37) | 268.67[+] (67.05) | 245.92 (58.39) |
| | NEF | 162.21 (36.91) | 204.92[+] (48.63) | 192.07[+] (42.91) | 177.24[+] (28.15) | 165.05 (37.06) | 201.68[+] (37.19) | 182.08[+] (44.54) | 175.72[+] (42.07) |
| | DIA | 217.59 (28.84) | 212.06 (51.87) | 254.13[+] (54.98) | 247.22[+] (47.13) | 225.29 (39.48) | 245.19[+] (42.70) | 283.84[+] (48.88) | 253.22[+] (33.39) |
| | TAR | 279.54 (95.43) | 350.81[+] (105.23) | 314.76[+] (96.79) | 297.57[+] (107.12) | 284.05 (85.75) | 354.87[+] (117.07) | 326.02[+] (91.13) | 291.62 (108.58) |
| Contra | DIA | 189.84 (22.37) | 156.41[+] (24.77) | 186.29 (26.22) | 172.30[+] (21.58) | 193.49 (22.10) | 170.10[+] (24.55) | 206.41[+] (28.22) | 187.93 (22.80) |

[a] Averaged Mts (ms)
[b] Standard deviation
[c] +: Mean value statistically different ($p = 0.05$) from the pre-operative mean

b) Contralateral Effects. The effects of unilateral DN lesions on the performance of the contralateral limb were studied in two monkeys (TAR – DIA). As shown in Table 1, the dysfunction modified MTs in both cases.

As for the ipsilateral effect, two types of changes were observed. They consisted of MT increase (TAR) or MT decrease (DIA). In the latter case the decrease concerned mainly the first postoperative period, MTs tending to become longer in the later periods. No significant differences appeared between the two experimental conditions (Table 3).

*II. Pointing Errors*

a) Ipsilateral Effects. The data collected together in Fig. 2 and Table 2 indicate an impairment of pointing accuracy when control by the DN was impaired. In all subjects, with the exception of BER, the errors significantly increased during cooling, or after lesion, of the DN. This effect is greater in lesioned than in probe-implanted monkeys. It must be noted that cooling blocks of trials are characterized by an increased dispersion. This general effect of DN lesion on spatial dispersion is indicated by the increased standard deviations in Table 2.

A typical representation of spatial pointing distribution is given in Fig. 5. During the cooling period, the pointing surface significantly increased. Moreover a shift of the spatial distribution appeared, mainly characterized by pointing responses above the targets.

The comparison of the results obtained in the two experimental conditions (Table 2) shows a general trend to make greater errors when the position of the target was randomly modified from trial to trial (condition 2). Moreover the overall data show that the more marked effects of DN exclusion on the pointing errors are also observed in condition 2, with variable target positions.

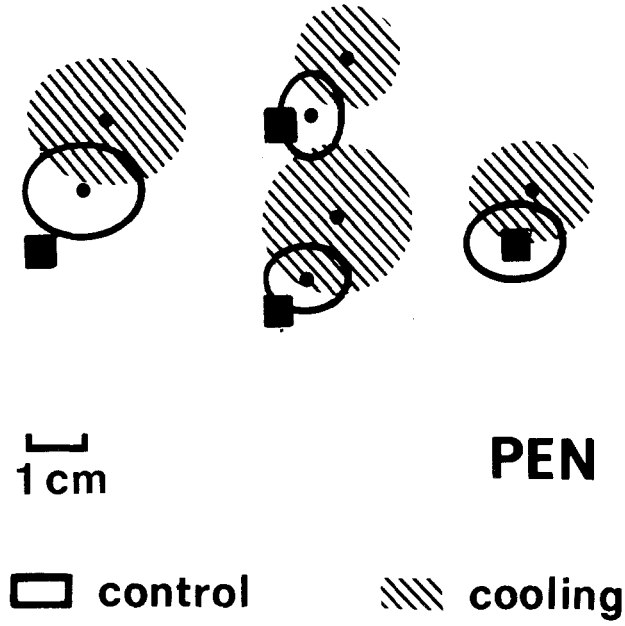


**Fig. 5.** Spatial distribution of pointing responses in a thermode-implanted animal: *PEN*. Black squares indicate the four possible positions of the luminous target. White: pointing surface without cooling. Each pointing surface corresponds to 64 trials. The standard deviations are given by the radius of the ellipses drawn around the averaged values. Hatched: pointing surface during DN cooling

**Table 4.** Evolution of spatial errors after permanent lesion

| Operant arm | Subjects | Single target position (Condition 1) Pre-op | Post-op I | Post-op II | Post-op III | Variable target positions (Condition 2) Pre-op | Post-op I | Post-op II | Post-op III |
|---|---|---|---|---|---|---|---|---|---|
| Ipsi | BAS | 8.90[a] (7.20)[b] | 28.45[+c] (26.38) | 20.16[+] (15.65) | 16.63[+] (8.93) | 11.55 (7.63) | 29.25[+] (25.01) | 24.05[+] (17.25) | 20.40[+] (9.47) |
| | NEF | 5.66 (5.50) | 14.05[+] (12.40) | 18.04[+] (7.95) | 17.45[+] (3.88) | 8.34 (6.96) | 21.18[+] (10.52) | 22.55[+] (9.17) | 19.48[+] (5.36) |
| | DIA | 5.31 (5.67) | 25.86[+] (13.97) | 19.10[+] (15.45) | 8.72 (13.28) | 4.82 (6.39) | 25.95[+] (12.52) | 5.67 (10.24) | 6.21 (9.60) |
| Contra | TAR | 3.59 (7.30) | 3.39 (5.58) | 3.85 (3.75) | 5.28 (5.07) | 5.18 (7.81) | 3.49 (5.14) | 6.87 (3.06) | 9.25 (9.36) |
| | DIA | 3.34 (5.73) | 5.14 (5.72) | 2.83 (6.09) | 4.06 (5.59) | 3.41 (7.99) | 5.17 (7.53) | 2.60 (6.78) | 3.55 (7.52) |

[a] Averaged Es (mm)
[b] Standard deviation
[c] +: Mean value statistically different ($p = 0.05$) from the pre-operative value

b) Contralateral Effects. The performances of TAR and DIA obtained with the limbs contralateral to the destroyed DN are given in Table 2. In both monkeys DN exclusion never produced any significant modification in errors, either in the averaged values or in the pointing dispersion.

*III. Timing of Recovery After Permanent Lesions.* Speed and accuracy of the pointing responses were studied over a period of four months in the four monkeys which had undergone unilateral destruction of DN. Recording sessions took place at various intervals after the operation: about 15 days, 1 month and 4 months.

a) Ipsilateral Effects. The results collected together in Tables 3 and 4 show different time courses of recovery for MTs and errors. The pointing dispersion recovered first: the scattering increase observed immediately after dentatotomy diminished during the first month and totally recovered after three months in BAS and NEF, a slight impairment being still present in DIA. Concerning the MTs, the significant modifications produced by the DN lesion had not disappeared about 120 days after DN lesion. However a slight recovery seemed to occur in this latest period, some sessions presenting MT values comparable to preoperative levels. Finally, in BAS and NEF, errors were still significant four months after dentatotomy, no signs of recovery appearing during this period. In one monkey (DIA), which performed the pointing task alternatively with both arms, the spatial errors decreased during the first postoperative month, although there remained a spatial impairment, as evidenced by an increased dispersion.

b) Contralateral Effects. As shown previously no significant impairment could be observed in the pointing accuracy of the contralateral limb. The only changes concerned the MTs. Table 3 indicates that in both monkeys, TAR and DIA, the modification in the MTs disappeared some three months after the DN lesion. Moreover, a more rapid recovery of MTs is observed in this contralateral limb.

## Discussion

The purpose of this study was to compare the effects of DN dysfunction on the duration and the accuracy of a learned goal-directed movement performed by baboons. Two main results may be stressed: firstly, the partial, permanent or reversible, lesion of a single dentate nucleus (DN) brings about significant changes in movement times (MTs). This effect concerns both arms. Secondly, the DN dysfunction induces significant increase in pointing errors. This effect is strictly limited to the ipsilateral limb. Moreover the recovery after permanent lesion is faster for MTs than for errors. These data suggest a differential involvement of the cerebellar DN in control of the speed and accuracy of a goal-directed movement in the monkey.

### *Dentate Nucleus and Control of Speed*

The data we have obtained show that partial inactivation of a single DN brings about complex modifica-

tions of MTs, affecting both arms. The complex characteristic of this impairment is mainly related to the presence of opposite effects. In our experiment the response duration is reduced or increased according to the subjects, or in the same subject according to the experimental conditions or the time after the lesion, it could even be hypothesized that in some cases the absence of significant effect on MTs is due to the average of opposite influences during the same session. This interpretation may be reinforced by the presence of an increased MT dispersion after DN exclusion (see for instance DIA in condition 1, Table 1).

As a matter of fact the presence in a goal-directed movement of different stages (Paillard and Beaubaton 1976) obviously leads to a consideration of the heterogeneity of this kind of motor response: the organization of reaching has been described as involving different components: a phase for the balistic transport of the hand towards the target and a subsequent braking phase. All kind of MT impairments may be the result of different effects affecting the various phases of the movement. After cerebellar ablation Gilman et al. (1976) noted that the lack of changes in the mean velocity of reaching responses was in fact reflecting an increase in speed of the initial portion of the trajectory with decreased speed in the latter portion. These data clearly illustrate that the MT can be differently modified according to the importance of the effects affecting either the initial impulse or the braking phase.

Assuming that cerebellar dysfunction produces an exaggerated acceleration and an inappropriate deceleration (Brooks et al. 1973; Gilman et al. 1976; Vilis and Hore 1980), the balance of these effects may explain some of the disparities in this study. Important disturbance in the terminal phase would explain the reasons why, in spite of an exaggerated acceleration, the total duration of the movement may be increased. The increased MTs could be explained by a marked acceleration followed by an abnormally long terminal phase. In this context, oscillations are obviously one of the factors responsible for the lengthening of the terminal phase. Cooling the DN (Cooke and Thomas 1976; Vilis and Hore 1980) provokes in monkeys an increase in the amplitude of the oscillations observed under normal conditions. When oscillations were clinically observed in these experiments, they always concerned monkeys presenting increased MTs.

The prevalence of slowing of movement in cerebellar patients was often emphasized. This observation led us to hypothesize a slowing strategy allowing a better movement control. The increased MTs obtained in the present experiment after DN cooling or lesion could, in some cases, be explained by such a slowing strategy. In this respect it must be noted that in some monkeys with permanent lesion (cf. BAS), increased MTs are prevalent in late postoperative periods. This effect can be concomitant with an improvement in the spatial accuracy which can be observed in the pointing dispersion.

According to Brooks (1979b) it cannot be ruled out that neocerebellar dysfunction would be determined by the balance of two processes: impaired feedback guidance and inappropriate feed-forward command. The DN can be considered as a critical link in the organization of motor programs responsible for the initial or the braking phases of the movement (Massion and Sasaki 1979). But the cerebellar dysfunction may also be induced by an impaired control of the ongoing movement. In a previous study (Trouche and Beaubaton 1980) data concerning the reaction times preceding the execution of pointing movements led us to conclude that the DN was not critically involved in the encoding of direction and amplitude parameters. Conversely, in the present experiment the MT modification provoked by DN inactivation are stressed by the variation of the response trajectories (condition 1 vs condition 2). This result would suggest the intervention of DN control during the execution of the movement.

Finally, the results of the present experiment show that the effects of DN dysfunction are not only unilateral. MT modifications were also observed with the limb contralateral to the lesioned structure. These modifications are similar to those obtained with the ipsilateral arm. The data obtained from primates after DN lesion (Goldberger and Growdon 1973; Brooks et al. 1973) always evidence ipsilateral effects. However Heimburger (1970) described bilateral modifications in tone after dentatotomy in spastic patients. According to Chan Palay (1977), whereas dentatofugal projections are predominantly contralateral, strong ipsilateral recrossed components exist. Moreover electroanatomical studies (Sasaki et al. 1976) demonstrated dentate projections towards cortical areas 4 and 6 in the monkey. As shown by Brinkman and Kuypers (1973), these areas exert a bilateral control of arm muscles. These different pathways could possibly provide an anatomical support for the bilateral modifications of movement velocity observed in the present experiment.

### *Dentate Nucleus and Terminal Accuracy*

The results of the present experiment show that partial inactivation of the DN induces significant

pointing errors with an increase in their dispersion. This effect is strictly limited to the limb ipsilateral to the inactivated DN.

Defects in movement accuracy such as hyper- or hypometric responses have often been described in cerebellar patients (Holmes 1939) or in lesioned animals (Dow and Moruzzi 1958). But, in general, the pathological and experimental data cannot clearly indicate the exact involvement of the neocerebellum in this spatial impairment. From the present results it may be suggested that the DN exclusion is sufficient to modify the spatial accuracy of the limb movement.

The role of cerebello-cerebral connexions in motor synergy has been stressed (Rispal-Padel et al. 1979). Therefore a wrong coordination between different muscle groups may explain the difficulties in spatial control of this kind of multijoint movement. But the disturbances of braking mechanisms after cerebellar lesions must also be taken into account and the overshoot observed in this experiment (Fig. 5) considered as a direct consequence of belatedly braked movements.

The question then arises as to whether the spatial impairments are strictly related to the dynamic disturbances of the movement. The relation between the hypermetric characteristics of the responses and the faulty braking would be in that direction. Our data, however, show that such explanations have to be qualified. Indeed, modifications of MTs, observed in the contralateral limb, are not accompanied by pointing errors. Conversely we observed during the experiment pointing errors without modifications of movement duration: such was the case in the late postoperative periods of lesioned monkeys. Therefore the independence of velocity and accuracy controls may be a relevant point of interpretation (Polit and Bizzi 1979).

If the range errors brought about by velocity disturbances are accepted one may consider the possibility of a specific spatial impairment resulting in directional errors. The contribution of proprioceptive information in spatial calibration of the moving limb has been emphasized by Paillard and Brouchon (1974). Taking into account the role of the neocerebellum in the modulation of proprioceptive loops (MacKay and Murphy 1979) it may be proposed that the impairment of DN activity would have, for this reason, a direct consequence on the terminal accuracy of the pointing response. Moreover in precision tasks, as used in our experiment, the relative positions of finger and target, visually and proprioceptively localized, determine error estimation. This "terminal" feedback is certainly responsible for program corrections. Therefore DN dysfunction, besides amplitude errors related to braking disturbances, may provoke directional errors resulting from a specific spatial impairment. In this sense, a likely interpretation of the constant errors observed in the present experiment consists in systematic misdirection of the limb towards wrongly located spatial targets.

If the proprioceptive inflow may be partly responsible for this spatial disturbance, other cues, such as the visual ones, must be considered. One can logically suspect the importance of oculomotricity in the accuracy of visually triggered and guided movements. The relationships between the DN and the oculomotor mechanisms have often been discussed (Chan Palay 1977). Besides the problem of the very existence of an oculomotor defect induced by DN exclusion, the question remains open of impaired spatial localization induced by abnormal eye movements.

Finally, the interpretation of spatial disturbances, like that of speed, must differentiate errors in the control of ongoing movements and defects resulting from wrong motor programs. The increased pointing dispersion during DN inactivation may be related to terminal oscillations which express the difficulties in the final control of the evolving movement. But pointing errors can also be explained on the basis of incorrect velocity programming and erroneous stored information about target localization. However, it must be noted that the modifications of movement characteristics (condition 1 vs 2), which do not influence the effects of DN inactivation on motor initiation (Trouche and Beaubaton 1980), present a significant effect on the movement execution. The lack of DN induces, in our experiment, maximal pointing errors when the response trajectories have to be modified at each trial (condition 2). Such a result could be an indication of the effective involvement of the neocerebellum in motor adjustment.

### *Rate of Recovery After Permanent Unilateral Lesion*

Simple clinical examination reveals that gross motor disorders, such as oscillations, reluctance to use the ipsilateral limb, disappear some two weeks after the unilateral DN lesion. As regards the learned pointing task the record made during the first four postoperative months show different time course and rate of recovery concerning the different experimental variables. The only variable exhibiting total recovery is the pointing dispersion. The MTs present a slight improvement without return to prelesion values. The spatial errors are still significant 120 days after the DN destruction.

The recovery of pointing dispersion may be related to the progress-improvement of MTs, and raises the question of the mechanism responsible for the recovery. The recovery phenomena after DN lesion can be attributed to vicarious functioning of the interpositus nucleus (Goldberger 1974). However in our experiment it must be noted that the lesion never concerned the whole nucleus. The remaining intact zones could be responsible for the improvement with time. Another possible interpretation of recovery phenomena consists in the intervention of the intact contralateral DN. The present experiment actually shows that destruction of a single DN brought about bilateral modifications of MTs. The fact that each DN can control the movement velocity of both limbs would explain the progressive decrease in MTs in the weeks following the lesion.

Finally, the lack of any modifications of the pointing errors must be considered. During the four months postoperative period, the striking stability of misdirection affecting the ipsilateral limb suggests a specific spatial defect due to the DN exclusion. In the same way, the faster recovery in the contralateral limb (Table 3) evidences the involvement of the remaining DN which certainly has a preponderant role in the control of this limb.

This observation suggests a specific role of the neocerebellum in the complex processes underlying the target localization in relation to a spatial reference system. Even if such an hypothesis may be proposed, the problem of motor strategies remains to be taken into account. The different rate of recovery observed in the experimental variables as interindividual differences in movement duration suggests the adoption of motor strategies favouring specific task instructions. At this stage of the experiments we do not yet know why, in the absence of DN, the control of speed would be privileged compared to that of accuracy. Further investigations, differentiating learning and reinforcement conditions, could contribute to the interpretation of this heterogeneity in the choice of motor strategies.

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