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INTERACTION OF EXTRACEREBELLAR AND CEREBELLAR CORTICAL INPUTS IN DENTATE NEURONS OF THE CAT

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Abstract. Interaction of afferent influences from pontine nuclei (NRTP, NPL and NPM) and inferior olive (IO) with influences from the cortex of neocerebellum (Crus I and II of hemisphere) was studied in dentate neurons (ND) in anesthetized and immobilized cats. Interaction of converging influences was tested with regard to response latencies. Activation of pontine nuclei (NP) and IO as well as cerebellar cortex affected all varieties of nuclear neurons regardless of their localization within the nucleus and their type (efferent or intranuclear). Stimulation of precerebellar nuclei (NP and IO) evoked in ND neurons an activity similar in firing patterns, displayed as bursts of excitation (S + S) lasting up to 10 ms. Initial excitation with following inhibition (S+ −S), or excitation changed into inhibition with "rebound" (S+ − $+_2$S) were also observed. Similar patterns of evoked activity were in neighbouring nuclear neurons. Stimulation of lateral parts of Crus I and Crus II was most effective for ND. Influences from different parts of stimulated cortex have points of maximal action onto the given nuclear neuron (discrete action); divergence and convergence of influences were also observed. Cerebellar cortex stimulation depressed background impulse activity of ND neuron with gradual return to an initial level (S−S) or through a "rebound" (S− $+_2$S). Interaction of cortical and precerebellar nuclei influences was determined by algebraic summation of excitatory and

inhibitory converging actions and the spontaneous activity. The latter persistently decreased in the course of repeated stimulation of the cerebellar cortex. The data show some peculiarities of that interaction and the role of the nuclear activity proper in forming the signals at the "output" of the cerebellum.

INTRODUCTION

The neocerebellar structures — hemisphere cortex and nucleus dentatus (ND) — are known to receive the main afferent inputs from the rostral parts of the brain, from cerebral cortex predominantly (1–3, 9). The pontine nuclei, medial (NPM) and lateral (NPL) and nucleus reticularis tegmenti pontis (NRTP) being the sources of cerebellar afferent fibers of mossy type (MF), are the main relay nuclei transmitting this activity to the cerebellum (1–3, 9, 17, 21, 23, 27). Olivary nuclei mediate to the cerebellum the corresponding impulsation from rostral or caudal regions of the brain via the axons distinguished by the climbing distribution of terminals (CF) on the cerebellar Purkinje cells (12, 13, 17, 20, 21, 24). The effects of direct activation of each of these afferent paths are first studied on cerebellar Purkinje cells, and two kinds of responses "simple" and "complex" spikes — according to the character of synaptic activation of Purkinje cells by MFs or CFs, were found (13, 22). Moreover, it was shown that both types of afferents converge onto the same Purkinje cell. Numerous versatile studies of the question were later generalized into a conclusion about the role of mossy and climbing afferent systems, their fine and harmonic cooperation in the complex functions of the cerebellar cortex (21), especially in movement control (3, 13, 19, 21, 25) as well as in the process of motor learning (18). However, the activity of cerebellar subcortical nuclei in the above conditions was studied in a limited number of experiments on interpositus (20, 23, 27) and fastigial (4, 5, 15) nuclei and on Deiters neurons in response to stimulation of IO (8). These experiments revealed both direct influences onto nuclear neurons and those mediated by cortical collaterals of cerebellar mossy and climbing afferent fibers, as well as some specific features of their organization. But so far, there is no comprehensive notion about the organization of afferent inputs from various precerebellar nuclei of the brainstem within the central cerebellar nuclei, and ND in particular. Moreover, according to recent concepts (13, 19, 21), the activity of cerebellar subcortical neurons in the course of processing of afferent input undergoes modulating inhibitory influence of the cerebellar cortex. Nevertheless, the experimental studies confirming this point of view and

describing the processes that take place at the nuclear level are very scarce.

The present experiments, as well as earlier ones (7), investigated various afferent influences-cerebellar and extracerebellar — onto the neurons of central cerebellar nuclei. These studies dealt with the nuclear activity, both background and evoked. As to the present experiments the unit activity of dentate nucleus was induced by direct stimulation of precerebellar nuclei — pontine and inferior olive, and of the cortex of the cerebellar hemisphere. The interaction of afferent influences thus evoked was also studied.

METHODS

Experiments were carried out on anesthetized (50 mg/kg — chloralose intraperitoneally and 5–10 mg/kg sodium pentobarbital supplementarily) and immobilized (10 mg/kg gallamine thriethiodide, Flaxedil, intravenously) cats. Combination and depth of anesthesia were kept so as to provide approximately the same level of background activity in nuclear neurons. Artificial respiration and CO_2 percentage in expired air (within 3.5–4%) were maintained at the same level during the experiment. Four to six silver ball electrodes, insulated except for the surface contacting the cerebellar tissue, were used for monopolar stimulation within Crus I and II of cerebellar hemisphere. Single rectangular pulses or series of three with frequency of 500 Hz, duration 0.1 ms and intensity 0.25–1 mA (more often 0.4–0.8 mA), were commonly used.

Identification of efferent nuclear neurons was carried out by stimulating them antidromically from the brainstem nuclei onto which the ND efferent neurons project (26): ventro-lateral nucleus of thalami (VL), pontine nuclei (NP) — medial (NPL), lateral (NPL), reticular tegmenti (NRTP), and inferior olive (IO). All stimulating electrodes were inserted into the brain stereotaxically. Three steel electrodes insulated except 0.2–0.5 mm at the tips (100 μm in diameter), were implanted in the contralateral thalamic nucleus (VL) in the sagittal plane. The middle electrode was common for the two outer ones. Contralateral NPM and NPL were stimulated monopolarly via tungsten insulated needles inserted stereotaxically at an angle of 12° in the rostro-caudal direction. An indifferent silver ball electrode was placed between them on the exposed brain surface. NRTP was stimulated bipolarly through a pair of steel insulated wires inserted under left tentorium. The contralateral IO was stimulated by a concentric electrode (interpolar distance 0.2 mm). Single pulses of 1/s lasting 0.1 ms with intensities 0.04–0.2 mA for VL and 0.1–0.4 mA for NP and IO were used for stimulation.

ND neurons were recorded extracellularly within coordinates P = 8.5–9.4; L = 6.8–7.2; H = +1.5–1.5 by means of glass micropipettes filled with 2M K-citrate. The neuronal activity was photographed from the oscillograph screen. Histograms of interspike intervals of neurons background activity (IH) and poststimulus time (PSTH) were constructed with the ANOPS 101 analyzer and later reproduced on an x-y recorded with analysis time of 0.5–5 s. In parallel with this IH and PSTH with another time of analysis (usually, 410 or 820 ms at bin widths 0.8 or 1.6 ms respectively) were performed by means of an ANOPS 2 analyzer. Usually 32–64 successive responses were superimposed. At the end of each experiment the cat was perfused with 10% formalin solution and the cerebellum and other parts under study removed for histological examination.

RESULTS

Fifty six neurons within ND were recorded; most of them (35) were identified as efferent neurons according to criteria of antidromic activation of neurons (stability of latencies with a scatter of not more than 0.2 ms, ability to reproduce high frequency stimuli (100–500 Hz) at superthreshold intensities of stimulating current, and collision of the response with spontaneous action potentials). Stimulation of ventralateral nucleus of thalami (VL) evoked antidromic focal potentials with latencies of 0.6–1.8 ms (31 neurons) and the reticular nucleus of tegmenti ponti (NRTP) — 0.4–0.6 ms latencies (4 neurons). Neurons activated antidromically from pontine lateral or medial nuclei (NPL and NPM) and inferior olive (IO) were not recorded. Neurons which projected to none of the brainstem regions under study were classified as intranuclear neurons.

Thirty two neurons (21 efferent and 11 intranuclear), displaying background impulse activity and affected by various afferent inputs were analyzed statistically. The frequency of background activity was found from IH recorded usually at the beginning and sometimes at the end of the neuron testing. Preponderant frequencies were 40–140 imp/s. The patterns of recorded IH displayed a large scatter of interspike intervals. Sometimes two or three modes of them could be clearly observed (Fig. 1*A*1, *B*2). As a rule, the level of neuronal background activity changed according to conditions of testing: it increased at the repeated activation of afferent inputs from the brainstem (Figs. 1*C*7,8; 3*E–G* and 4*A* 2–3) and decreased in the course of repeated cortical stimulation (Figs. 1*C*4, 5, 6; 3*A, C, D, H, I* and 4*C*1). In each case the level of background activity of the neuron reflected the predominance of tonic excitatory extracerebellar or inhibitory cerebellar actions.

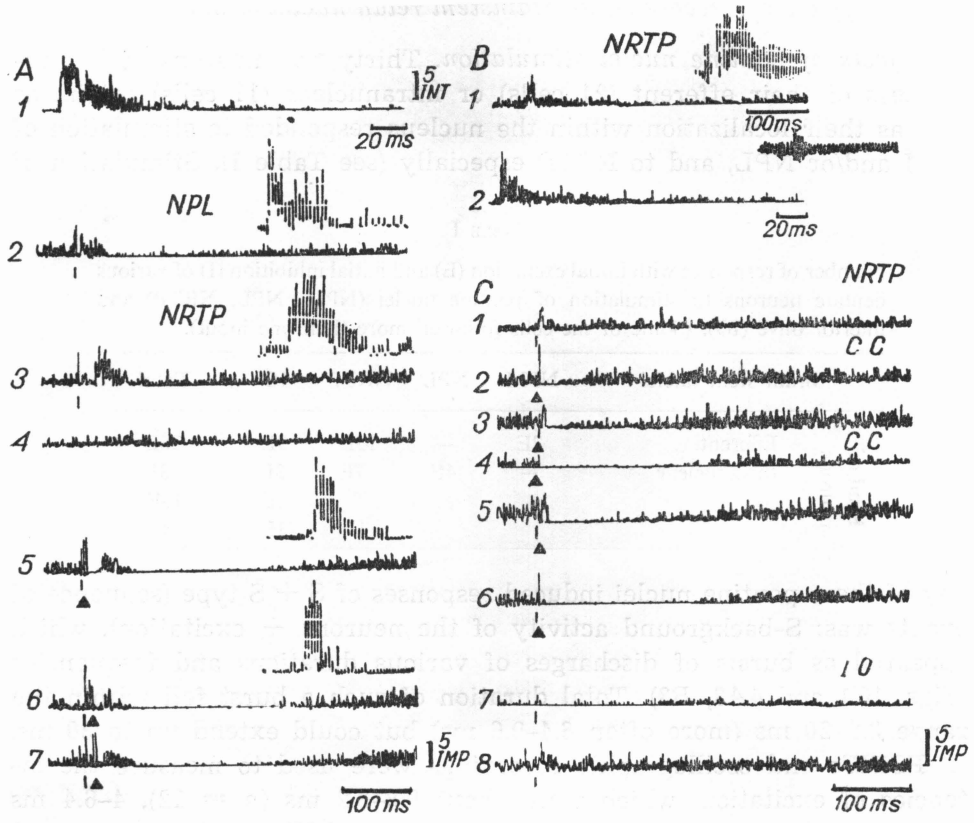

Fig. 1. Convergence of influences of various precerebellar nuclei on the dentate neurons (ND), presented as PSTH (32 repetitions). Here and in subsequent figures brainstem nuclei are marked as follows: NRTP, NPM, NPL and IO; stimulus application is marked by rods (for extracerebellar) and triangles (for cerebellar points); corresponding expanded PSTH's with another analysis time are included for some trials; it was synchronized with the second stimulus when paired stimuli were used (recording from ANOPS 2). Time and amplitude calibration: for IH and PSTH's presented in this and subsequent figures. In expanded PSTH the bin width is 1.6 (A) and 0.8 (B) ms. A instranuclear neuron; 1. interval histogram with prevalent frequencies 80 imp/s and 50 imp/s; 2,3 to NPL and NRTP stimulation; 4, in the absence of stimulation; 5, to NP and Crus I lateral part paired stimulation at intervals 2 ms; 6, 5 ms and 7, 10 ms. *B*, another intranuclear neuron in ventromedial--rostral part of ND. (1), PSTH the oscillogram of burst activity; (2) interval histogram frequency about 140 imp/s. *C*, another intranuclear neuron in the centre of the nucleus. (1), PSTH's in response to stimulation of NRTP; (7, 8), IO. (2), Crus I medialis; (4), lateralis; (3 and 5, 6), paired stimulation of NRTP and the cortex, test interval 1 ms.

Effects of precerebellar brainstem relay nuclei stimulation

Effects of pontine nuclei stimulation. Thirty two neurons of ND regardless of their efferent (21 cells) or intranuclear (11 cells) origin, as well as their localization within the nucleus responded to stimulation of NPM and/or NPL, and to NRTP especially (see Table I). Stimulation of

TABLE I

Number of responses with initial excitation (E) and initial inhibition (I) of various dentate neurons to stimulation of pontine nuclei (NPM, NPL, NRTP) and inferior olive (IO). (Some of the cells followed more than one input).

	Brain stem nuclei	NPM	NPL	NRTP	IO	Total
Kind of neurons	Efferent	2E	–	15E	9E	26E
	Intranuclear	–	4E	7E	3I	3I
					4E	15E
				1I	3I	4I

any of these pontine nuclei induced responses of S + S type (sequence of events was: S-background activity of the neurons + excitation), which appeared as bursts of discharges of various durations and frequencies (Figs. 1*C*1 and 4*A*3, *B*3). Total duration of such a burst fell within the range 3.2–20 ms (more often 6.4–9.6 ms) but could extend up to 30 ms.

PSTH's and oscillographic recordings were used to measure the latencies of excitation, which were about 0.8–3.2 ms (n = 12), 4–6.4 ms (n = 7) and 15.9 ms (n = 2) to stimulation of NRTP; 15.4 ms (mean) to stimulation of NPM and 20.8 ms (mean) to NPL.

In some cases initial excitation was followed by inhibition of neuronal activity with a gradual return to the background level (S+ −S) (Fig. 1*A*2, 3), or after a prolonged late excitation of a "rebound" type (noted by sequence S+ $-_2$S) (Figs. 2 and 3*G*). Responses of both S+S, or S+ −S types could be observed in the same ND neuron. In the neuron presented in Fig. 2 responses of both types — with initial excitation (S+ −S) and initial inhibition (S− +) were observed (Fig. 2*A*, *C*, *D*, *E*). Duration of inhibition was 18–25 ms. Repeated alteration of phases (S− $+_2-$ $+_2$S) can also be noticed (Fig. 2*A*). The effect was obtained by a single stimulus with a threshold intensity of 0.1 mA, in conditions of pure nembutal anesthesia, and the cat immobilized, which excluded any motor reactions and side effects possible under chloralose anesthesia.

It should be mentioned, however, that afferent inputs from NP, and especially those from NRTP, as a rule, initially produced the excitation of the neuronal activity, which after several repetition of NP stimulation led to a persisting rise of the background activity of the neuron.

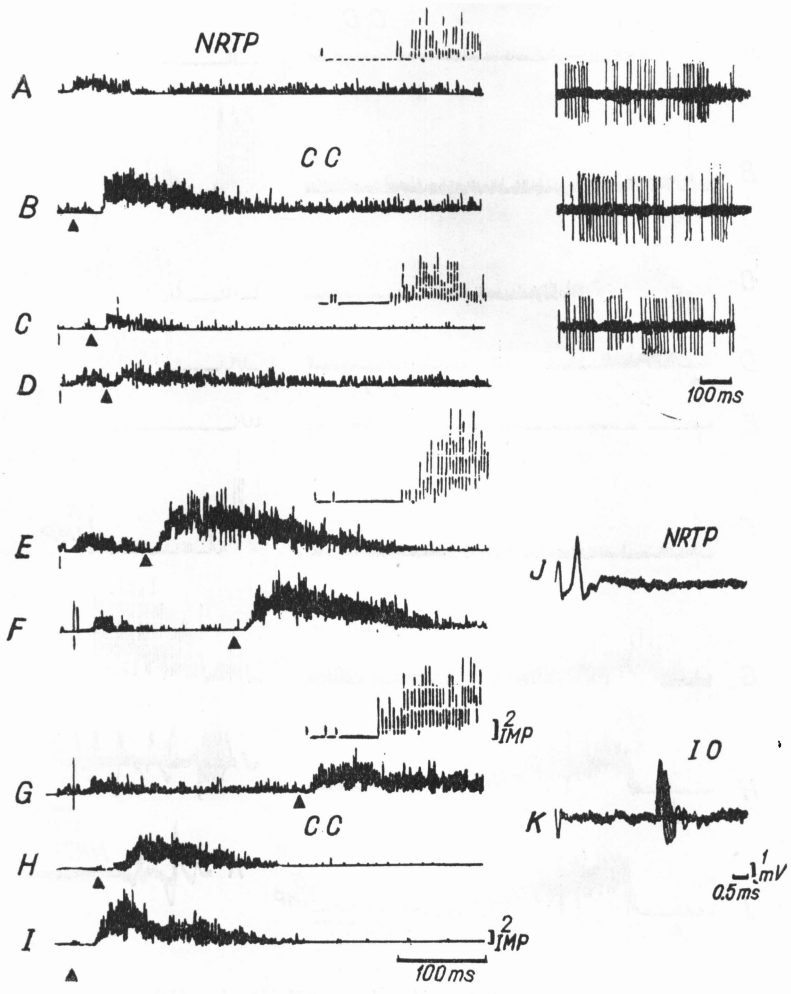

Fig. 2. Interaction of various converging extracerebellar and cerebellar cortical influences. PSTH and corresponding oscillograms in response to stimulation of NRTP (A). Crus II medial part (B). C–G, both of them at different intervals from 35 (C), to 240 (G) ms, H to cortical stimulation only; I without interval between stimuli. Bin width in expanded PSTH — 0.8 ms. (J), neuron projecting to NRTP and activated orthodromically from IO (K).

Effects of IO stimulation. In 13 ND neurons affected by IO stimulation, responses of S+S (Fig. 1C8 and 4A2), or S+ −S (Fig. 3E) types analogous to those evoked by pontine nuclei stimulation and consisting of 6–9 discharges in a burst were recorded. The latencies of responses to olivary stimulation were found to be within 1.47–2.4 ms and 4.8–8 ms (mean 4.3); the total duration of the multiple discharge was 3.2–17.6 ms

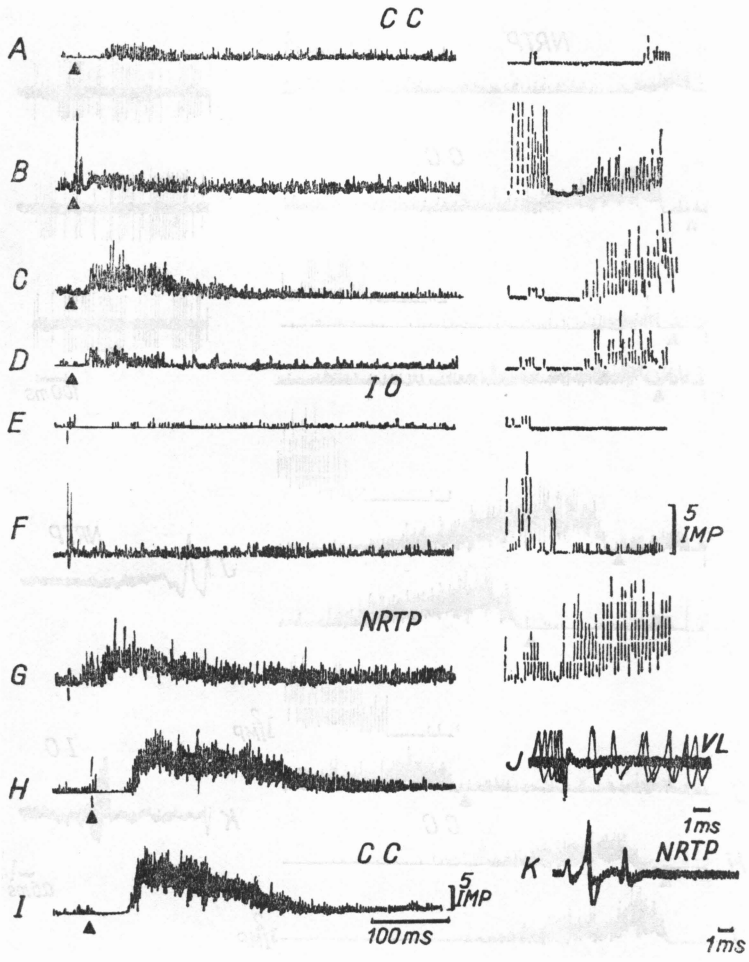

Fig. 3. Convergent action from different points of the cortex ND neuron. Efferent neuron activated antidromically from VL (collision of evoked AP with spontaneous discharges) (J) and monosynaptically from NRTP (K) and IO (PSTH) (E,F) PSTH — to stimulation of Crus I lateral part (A); lob. simplex rostral (B) and caudal (D) parts; Crus I medial part (C), effect of cortical stimulation increased during the repetition (cf. A and I); PSTH to stimulation of NRTP (G). (H) simultaneous stimulation of NRTP and Crus I lateral part. PSTH to Crus I lateral part (I). In expanded PSTHs bin width 0.8 ms.

(mean 6.9). Unlike the effects of NP stimulation the described neuronal activity was usually induced with larger variability of the response latency and appeared in an "all-or-none" fashion. For instance, it may be seen in Fig. 2*K* with orthodromic single action potentials. Such a manner of neuronal reaction remained unchanged, regardless of intensity of stimulation (both threshold and superthreshold). In oascilloscope recordings

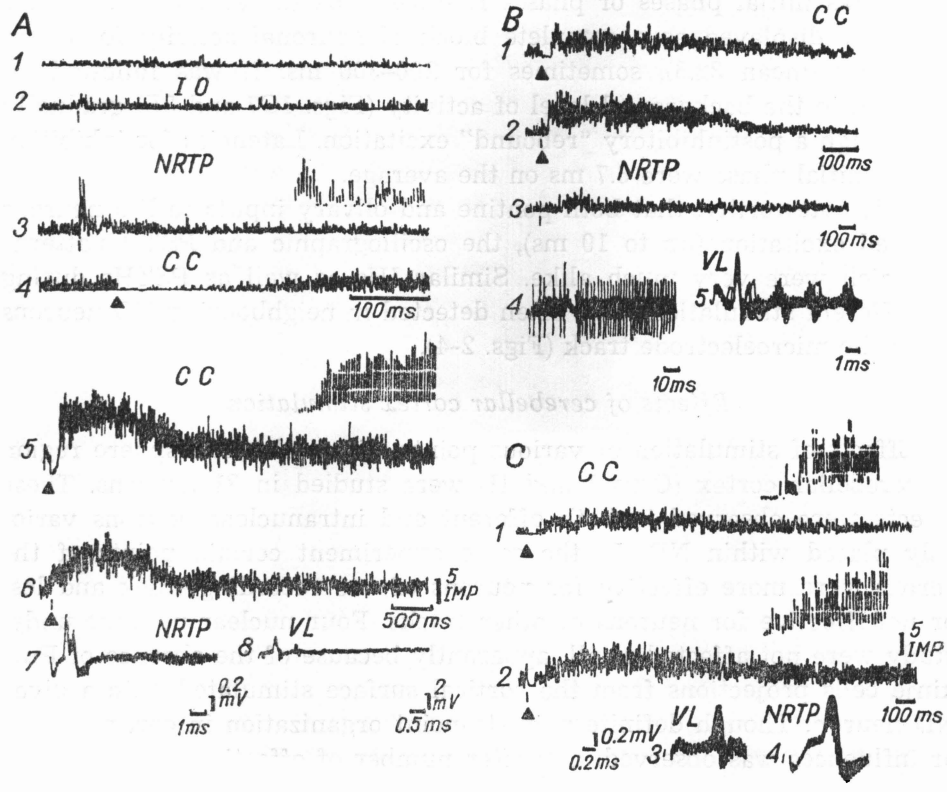

Fig. 4. Effects of interaction of precerebellar and cortical influences on ND neurons within one recording track. *A*, efferent neuron, activated antidromically from VL (8) and monosynaptically from NRTP (7). (1), background activity of the neuron; PSTH's (32 repetition) to stimulation of IO. (2), NRTP (3), Crus I lateral part (4), Crus II lateral part (5), to simultaneous application of stimuli in NRTP and Crus II (6). *B*, another efferent neuron activated antidromically from VL (5). PSTH's, to stimulation of Crus I medial part (1), NRTP (3), both of them with 5 ms interval between stimuli (2), oscilloscope trace (4). *C*, another efferent neuron, activated antidromically from VL (3) and monosynaptically from NRTP (4). PSTH's, to stimulation of Crus II lateral part (1), paired stimulation NRTP and the cortex with 5 ms interval (2). In expanded PSTH's the bin width is 1.6 (A3), 6.4 (C), 12.8 (A5) ms.

performed within the nucleus no responses like a "complex" spike were observed. As is known, the "complex" spikes characteristic of the climbing fiber activation of Purkinje cells of the cortex consist of an initial full sized spike and the following partial spikes varying in number, form and amplitude (13, 21, 22).

In case of IO stimulation responses with initial inhibition (S—S) in both efferent and intranuclear neurons appeared more often. Inhibitory

effects (as initial phases or phases following the initial excitation) were generally displayed as a complete block of neuronal activity for about 24–45 ms (mean 32.6), sometimes for 200–300 ms. It was followed by a return to the background level of activity (Figs. 1*C*7 and 3*E*) gradually or through a postinhibitory "rebound" excitation. Latencies for inhibition in the initial phase were 6.7 ms on the average.

It is noteworthy, that both pontine and olivary inputs to ND neurons induced excitation (up to 10 ms), the oscillographic and PSTH patterns of which were very much alike. Similar IHs as well as PSTHs during the afferent stimulation were often detected in neighbouring ND neurons along the microelectrode track (Figs. 2-4).

Effects of cerebellar cortex stimulation

Effects of stimulation of various points within the hemisphere region of cerebellar cortex (Crus I and II) were studied in 31 neurons. These effects were observed in both efferent and intranuclear neurons variously placed within ND. In the same experiment certain points of the cortex were more effective for neurons of one recording track and less or noneffective for neurons of other tracks. Four nuclear neurons under study were not affected at all, apparently because of the absence of Purkinje cells projections from the cortical surface stimulated onto a given ND neuron. Though definite point-to-point organization in cortico-nuclear influences was observed, a greater number of effective cortical points was localized within the lateral regions of Crus I and II.

Effects of stimulation were displayed as inhibition of various strength (S−S) (Figs. 1*C*2, 4 and 4*A*4) or inhibition followed by excitation of the "rebound" type (S− $+_2$S) (Figs. 2*B*; 3*AD* and 4*A*5, *B*1, *C*1). Inhibition usually produced a complete block of neuronal activity with a latency of 1 ms and duration of about 16–25 ms, for threshold single stimuli. Series of two or three stimuli or single stimuli of larger amplitude induced an inhibition of longer duration (100–150 ms). PSTH and corresponding oscillograms on the right in Fig. 2*A* and *B* display similarity in initial phases (S− $+_2$S) of responses to stimulation of both cerebellar cortex and NRTP. Duration of inhibition was 18–25 ms, but postinhibitory rebound excitation was more evident in the case of cortical stimulation (PSTH and oscillogram, Fig. 2*B*). As a rule, during a repeated testing of the cortex the effects of cortical action increased (Fig. 3*A*, *J*) and led gradually to a general decrease of nuclear neuronal activity (lasting sometimes 3–5 min).

Similar patterns of cortical influences were obtained from one of the stimulated points on neighbouring cells within the microelectrode tract (Figs. 2*B*, *H*, 3*C* and 4*A*5, *C*1). Besides this peculiarity of cortico-nuclear

interaction, another phenomena were observed: the given cortical region could exert its influence onto various parts of the nucleus (divergence of action), while influences from neighbouring cortical regions could converge onto the same nuclear neuron. In all cases, nevertheless, points of maximal cortical action on a particular nuclear neuron could always be detected (see for example Figs. 1*C*2, 4 and 3*A–D*).

Interaction of extracerebellar and cerebellar cortical inputs in ND neurons

In studying the interaction of barinstem afferent and cerebellar cortical inputs emphasis was laid on changes in the initial phase. The later events in neuronal activity were not analyzed in detail because of their dependence on the type and depth of anesthesia. In each nuclear neuron the interaction was studied after the following procedures: (i) registration of IH (before, in the course or at the end of testing) and (ii) PSTH of responses to each of testing stimuli in the brainstem and the four points within the cortex, (iii) selection of the most effective points for stimulation and its threshold. The interaction of predominantly monosynaptic influences was tested at intervals appropriate for latencies of responses to each of the testing stimuli; the intervals used provided almost simultaneous arrival of converging inputs at the nuclear neuron under study.

Twenty seven neurons in different parts of ND were analyzed this way. The interaction depended on how pronounced each of the converging inputs was. If the inhibitory influences of cerebellar cortex prevailed, a phenomena of cerebellar cortical excitation — inhibition (Fig. 1*A*5–7, *C*3,5,6) or inhibition with "rebound" (Figs. 2–4) were revealed in both background and evoked activity of nuclear neurons. Here the background activity was always completely suppressed, while evoked burst activity often remained with some changes in its configuration-increase of latency, shortening of duration and decrease in the number of discharges (PSTH peak was decreased and shortened). As is obvious from the examples presented in Figs. 1*C*5 and 4*A*6, the excitatory effect of the extracerebellar signal (Figs. 1*C*1 and 4*A*3) could overcome the strong inhibitory influence of the cerebellar cortex (Figs. 1*C*4 and 4*A*5). Their interaction somewhat changed the burst activity turning it into a more discrete flow (Fig. 1*C*5). Sometimes it extended the excitation if the burst of activity sumed up in time with the "rebound" excitation evoked by the stimulation of the cortex (Fig. 4*A*6). The latter effect is obvious in spite of the fact that the evoked burst activity of the neuron was smoothed down by inhibitory influence of the cortex, and of the "rebound" excitation which too became less pronounced. The described effect is in accordance with the above examples in which the same afferent volley indu-

ced different patterns of S+S, S+ − +S, or S+ − $+_2$S responses in the recorded neuron apparently due to the influences coming into the nucleus directly and via the cerebellar cortex. The development of one of the versions of the effects was determined by the presence of tonic excitatory extracerebellar or inhibitory cerebellar actions dominating in the testing period. For all that, in majority of neurons the burst of excitation at the nuclear level, being affected by inhibitory cortical action, became less intensive and more discrete.

In the case of two-phase action of the brain stem afferents (S+ −S) the direct stimulation of the cortex was accompanied by various effects depending on the sign of interacting phases and their intensity. Coincidence of two similar phases (for instance, the inhibitory actions and the following "rebound") intensified the effect (Figs. 1 and 2*A*). The output activity of the neuron seemed to repeat the pattern of responses to each of the converging volleys with greater emphasis. This resulted in longer inhibition and intensive prolonged late excitation of activity (Figs. 2*E*,*F* and 4*B*2,4, *C*2). A different result was observed in the situation when the phases of converging actions were opposite in sign (as is seen in Fig. 2*C*, *D* compared with *A*, *B*). In such cases the effect of the interaction was determined by the algebraic summation of converging excitatory and inhibitory actions. Here, the cortical effect could be smoothed down (Fig. 2*C*, *D*).

Similar effects of interaction were usually observed in neighbouring ND neurons. In Fig. 4 the responses of three neurons to stimulation of NRTP (in all the cases responses were of S+S type) and to the cerebellar cortex stimulation (S− $+_2$S) are shown, as well as their interaction in conditions of simultaneous application of testing stimuli. In these cases the inhibitory cortical effect was less pronounced, while the period of "rebound" became considerable.

DISCUSSION

In above experiments the changes of the neuronal activity within dentate nucleus of the cerebellum were investigated in conditions of direct stimulation of pontine nuclei (NRTP and NPM, NPL) and inferior olive, situated on the pathway from rostral parts of the brain to the lateral parts of the cerebellum, and which are the sources of cerebellar afferent fibers of mossy (MF) and climbing (CF) types. According to our results, NRTP is represented in ND more intensively than other pontine nuclei, apparently because of its reticular (non-specific) origin (3). It is possible that topically organized projections of pontine neurons proper (NPL and NPM) (9) are mainly distributed within the cerebellar cortex.

Stimulation of both NP and IO evoked in ND short (usually up to 10 ms) bursts of activity (S+S) with latencies (0.8–3.2 ms for NRTP and 1.5–2.4 ms and 4.8–8 ms for IO) suggesting monosynaptic afferent inputs to nuclear neurons. Similar data were obtained in interpositus (20, 23, 27) and fastigial (4, 5) nuclei.

An important result of the present study was the observation that excitatory inputs from NP and IO converge onto ND neurons and evoke similar patterns of activity. In this sense reactions of nuclear neurons are different from responses of cerebellar Purkinje cells to the activation of MF and CF paths. Analogous observations were made by other authors on NIA (20, 23). "Complex" spikes typical of CF activation of Purkinje cells (13, 21, 22), as a rule, were not recorded in nuclear neurons either in the present or in the above–mentioned experiments (4, 5, 20). It may be caused by another distribution of olivary axons on the nuclear neurons as compared with the terminal branching of CF on the Purkinje cells. In nuclear neurons the difference between the actions of MF and CF afferent systems was in the larger variability of the response latencies and appearance of responses to IO stimulation in an "all-or-none" fashion. The latter implies lack of convergence of some axons on one neuron of the nucleus. As is known, a specific feature of Purkinje cell response to CF activation is its appearance in an "all-or-none" fashion, as a result of synaptic contacts of one branch of CF onto a Purkinje cell (one-to-one connection) (13, 21, 22). The burst activity in nuclear neurons in response to a single stimulus applied to IO may be explained by the effect of repeated impulses which might arise in IO neurons, and be conducted to ND via their axons.

The observed scatter of latencies in responses to stimulation of NP can be explained by transmission of excitation via mossy fibers with "fast" and "slow" conduction velocities (1–3), while the preponderence of latencies above 1 ms assume transmission carried out mainly through "slow" fibers. Latencies of responses to stimulation of NRTP as well as NPL and NPM above 3 ms may be the result of polysynaptic transmission of excitation within the brainstem or ND. The values for latencies of responses to IO stimulation suggest the conduction of impulses from IO through the "slow" fibers of various calibre (13, 23).

The direct excitatory action of extracerebellar impulses in ND neurons did not depend on their localization within the nucleus, on their kind — efferent or intranuclear or on the on-going level of the background activity. The latter tonically increased during repeated stimulation of NP or IO. The responses of the same ND neurons to the direct excitatory action of extracerebellar impulsation (S+S) and responses complicated by the effect of the same volley via the cerebellar cortex

(S+ −S, or S+ − $+_2$S) (7, 13–15) should be regarded as a display of the action of collaterals of cerebellar afferent fibers within the central nuclei. Moreover, in the course of the experiments topical correspondence of inputs (from NP or IO), both direct and mediated via the cerebellar cortex, on the same ND neurons was indicated. Similar organization of afferent input from IO was found by other authors in studies on Deiters nucleus (8). According to the results of our experiments, the appearance of the inhibitory phase of the response to extracerebellar volley was facilitated by the usage of cortical stimulation in the course of neuron tests.

The direct stimulation of the cerebellar cortex was accompanied by the well known phenomenon of cortical excitation-inhibition (S−S) or inhibition with subsequent "disinhibition" (S− $+_2$S) of the underlying cerebellar nuclear activity (13, 19). This "sculeturing" effect of the cerebellar cortex stimulation was observed both in the background and evoked activity on the nuclear level. The former was more reactive and could usually be completely suppressed. Repeated stimulation of the cortex led to a tonic depression of nuclear activity on the whole. The inhibitory modulating influence of the cortex (in absence of direct stimulation) was displayed by the inhibitory effects of the extracerebellar afferent volleys as an initial inhibition (S−S), or an inhibition as a phase of the action following the initial excitation (S+ − $+_2$S). In the latter variant of response the period of excitation became shorter, than it was in the case when the inhibitory phase was not revealed (S+S).

The results of the interaction of cerebellar and extracerebellar inputs in dentate neurons depended on the localization of stimulating electrodes within the cortex and on the signs of phases of converging actions. Coincidence of two similar phases intensified the effect, while in the case of opposite phases the interaction was determined by the summation of excitatory and inhibitory processes and their potency. Sometimes the cortical effect could be smoothed down or did not show at all. "Restraining" of bursts of excitation on the output of the cerebellum by the cortical inhibitory action and turning them into more discrete packages of impulses (with "silence" phases of various duration) may be considered as a manifestation of modulating inhibitory action of the cerebellar cortex on the activity of underlying nuclear neurons in the process of coding the current afferent information (13, 19). The results of these and previous experiments (7) allow us to consider cerebellar central nuclei as structures where extracerebellar and cerebellar excitatory and inhibitory inputs are integrated thus forming signals going to the subsequent structures of the brain.

As it was pointed out, the majority of effective (for ND neurons) cor-

tical points were in the lateral parts of Crus I and II of the hemisphere, which is in accordance with the known morphological data (10). Meanwhile, one could always detect within the effective region of the cortex points with maximal effect onto the given nuclear neuron (discrete action). Together with this, divergence and convergence of influences could also be observed. These peculiarities of cortico-nuclear organization were also described in earlier experiments (6). Moreover, the study of nuclear neuron activity by means of IH and PSTH analyses showed that cortical projection to cerebellar nuclei organize the neurons in "column's". This conclusion was based on the similarity of patterns of background activity and effects of cortical stimulation in several nuclear neurons along the microelectrode track. Analogous observations were made in experiments on NI (7). They conform well to electron microscopic studies of ND (11), which discovered the multiple contacts of a descending Purkinje cell axon with neighbouring nuclear neurons together with wider distribution of axonal terminals within the nucleus (divergence) an, vice versa the termination of axons of several Purkinje cells on one nuclear neuron (convergence). The uniform innervation of neurons in "column" from a limited cortical area with maximal effectiveness of one separate zone within the stimulated cortex points out the discrete character of the cortico-nuclear projections in the cerebellum. Recent microphysiological studies of Deiters nucleus established their fine organization with the presence of microzones in cortico-nuclear action (8).

It should be mentioned that in these and previous experiments (7) similar patterns of activity were usually recorded in neighbouring neurons of the same microelectrode tract also in response to various extracellular sources of activation. Foci of similar nuclear activity appearing from the influx of information both extracerebellar and/or cerebellar are obviously necessary for reliability of cerebellar communications with other structures of the brain.

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