AUTONOMIC RESPONSES TO STIMULATION OF PALEOCEREBELLUM—EFFECTS OF INTERCOLLICULAR SECTION

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Summary : Stimulation of rostromedial aspects of the fastigial nucleus in the anaesthetised cat produced an autonomic activity pattern in which marked rise in arterial pressure and initial respiratory apnoea followed by increase in depth and rate were a necessary accompaniment. Stimulation of more lateral and caudal region of the fastigial nucleus in general produced a varying degree of depressor response. The effects on heart rate and intravesical pressure in both cases were variable. Stimulation of cerebellar vermis produced a wide variety of autonomic responses which could not be grouped into distinctive patterns with respect to the morphological localization of stimulated points.

The intercollicular section in these animals decreased the mean arterial pressure and slowed the respiratory rhythm but increased its depth. Effects on heart rate and intravesical pressure were variable. The autonomic responses elicited on stimulation of the fastigial nucleus or of cerebellar vermis were not abolished after the intercollicular section. Instead, they underwent marked changes with respect to their quality, magnitude and temporal patterning. These experiments suggest not only the presence of tonic influence of rostral brain structures on the systemic arterial pressure, but also that moment to moment variable facilitatory and inhibitory influences from the rostral brain structures can markedly change the autonomic activity patterns induced by the stimulation of paleocerebellum.

Key words : paleocerebellum fastigial nucleus cerebellar vermis autonomic activities arterial pressure heart rate respiration intravesical pressure effect of intercollicular section.

INTRODUCTION

Paleocerebellum has a profound influence on the autonomic functions of the body (1,2,6,7,10,16). Zanchetti and Zoccolini (22) observed that the somatic and autonomic components of rage reactions elicited on stimulation of fastigial nucleus were abolished after precollicular decerebration. It has been suggested that the autonomic effects of cerebellar origin may be mediated through hypothalamus (2,22). Besides, Sawyer *et al.* (17) were not able to obtain cerebellar induced actonomic responses after diencephalic lesions. Nevertheless Moruzzi (7,14) had demonstrated the effects of cerebellar stimulation on carotid sinus reflex in the precollicular decerebrate animals. More recently Achari and Downman (1) found that fastigial stimulation effects remained unchanged after intercollicular section. Miura and Reis (12) reported similar conclusions.

In this study the fastigial nucleus and the vermal cortex of the cerebellum were stimulated before and after intercollicular sections. The results obtained indicate that the cerebellar stimulation responses do not disappear after the intercollicular section as reported earlier by some workers (2,17,22), nor do they remain unchanged as reported by Achari and Downman (1). Instead, if the higher nervous connections are broken by an intercollicular secton the cerebellar stimulation responses undergo marked changes with respect to the patterning of various autonomic parameters. Results of this investigation constituted a part the brief report published earlier (3).

MATERIALS AND METHODS

Experiments were conducted on 18 cats of either sex weighing between 2.5-4 *kg* and anaesthetized with 60 *mg/kg* of alpha chloralose which was administered intravenously after a preliminary induction with ether,

Recording Techniques : All recordings were done on a 6-channel Grass model 5 P Polygraph. Arterial pressure was recorded from the femoral artery by the use of a Statham strain gauge transducer (model P 23 AC). The rate and depth of respiration by registering the chest movements through a pneumographic belt by the use of a PT-5 pressure-volume transducer. Heart rate was continuously monitored by recording standard limb lead II of the electrocardiogram. The method of recording intravesical pressure changes was described in an earlier communication (16). Briefly it consisted of introducing two polythene catheters in the bladder through an abdominal cystostomy, and connecting one of these to a P23 AC Statham transducer for recording the pressure. The other catheter was normally kept blocked except when after a micturition, it became necessary to introduce more saline in the bladder so as to keep the bladder volume constant at 6 *ml.*

Stimulation Technique: Presence of bony tentorium cerebelli makes it difficult to introduce vertical stereotaxic electrodes. The deep nuclei of the cerebellum were therefore approached by employing angularly oriented electrodes as described earlier (16). Bipolar copper electrodes, insulated except at the tips and with an intertip distance of 0.5 mm were used for stimulation. Stimulation pulses of 4-8 volts, 0.5-2.0 msec at 50-200/sec were obtained from a Grass Model S4 square wave stimulator which was connected to the electrode through a grass isolation unit model S14-B4.

Intercollicular Section: With the head of the animal fixed in the stereotaxic instrument, a window of about 1 cm square was made on either side of the midline of the skull by careful drilling. A spatula blade (1 cm wide and 0.5 mm thick) mounted on an electrode carrier was gently lowered through this window in the antero-posterior plane ll it touched the base at a place which was between A_0 and P_1 (18). The procedure was peated 2-3 times on each side, every time the spatula being a little more lateral than e previous. This produced a complete and clean cut at the intercollicular level which as always confirmed postmortem at the end of the experiment.

The purpose of intercollicular section was to severe the higher brain connections to chieve a residual function of cerebellum and brainstem inter actions. But surgical severnce of these connections is necessarily accompanied by some trauma to the brain tissue d at times, may cause a slowly developing damage of the brainstem by the seeping haemorhage consequent to injury of blood vessels, and oedema formation. Evidently, with a lowly developing damage of the brainstem, the effects of cerebellar stimulation will vary ith the time interval that elapses after the intercollicular section. This is demonstrated in ig. 1 which consists of series of records depicting the change that occurs in the fastigial

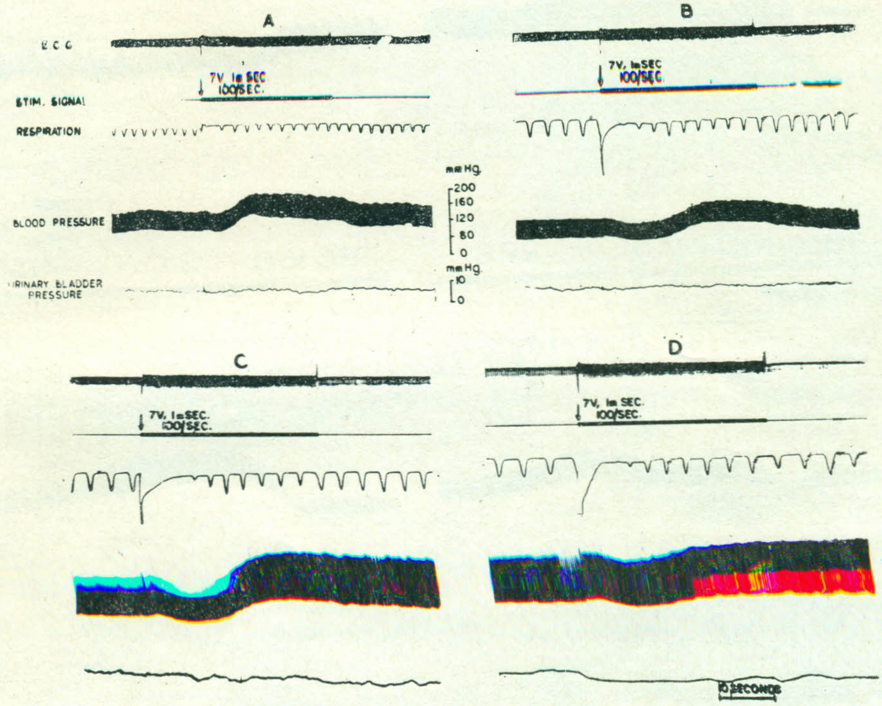

Fig. 1 : Polygraphic records obtained on stimulation of rostromedial part of fastigial nucleus before (A), and ½ hr (B), 1 hr (C) and 1½ hr (D) after the intercollicular section.

In A, stimulation of fastigial nucleus produced a minor initial fall of arterial pressure followed by a marked rise lasting throughout the stimulation period. This response underwent a progressive change in B, C, and D although the stimulation parameters remained constant at 7 V, 1 msec, and 100/sec. Note that the pressor component became less marked as the time passed and depressor component became progressively prominent till at D, only fall in pressure was elicited. Respiratory response pattern consisting of initial apnoea followed by later quickening of rate remained unchanged though the rate of the control period progressively decreased in B, C and D.

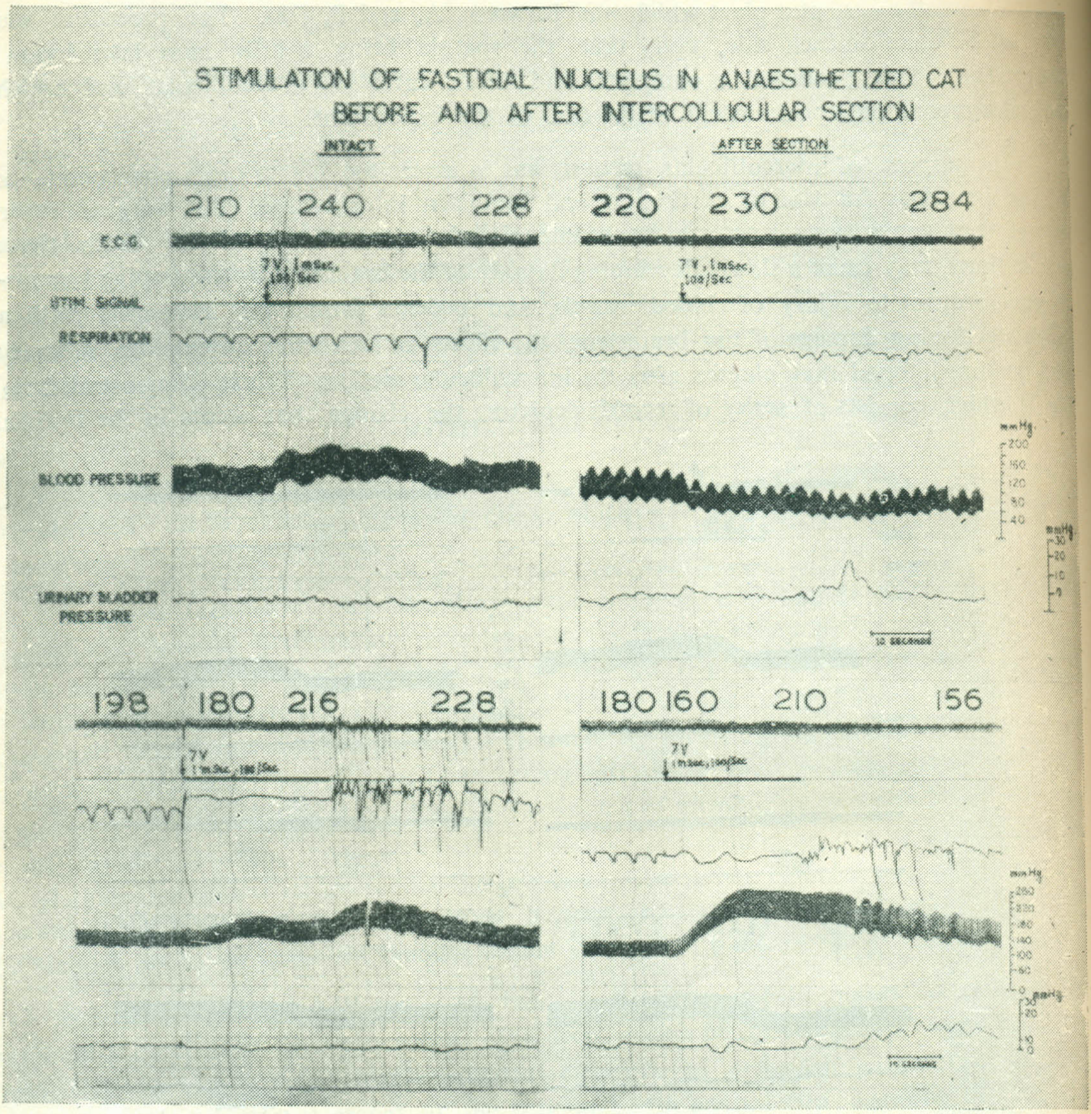

Fig 2 : Polygraphic records obtained on stimulation of fastigial nucleus (rostromedial) before (left hand panels) and after (right hand panels) the intercollicular section from two different cats. Upper tracings exhibit that the vasopressor response was converted into a vasodepressor response and the urinary bladder pressure showed a marked post-stimulation rise after the intercollicular section. In contrast the lower tracings demonstrate that the small rise of arterial pressure before the section became very prominent after the section. Although the response remained pressor in nature, the change in temporal patterning is markedly notable. The urinary bladder pressure as in the upper tracings showed post-stimulation rise. Also note the marked slowing of heart during the initial phase and after the stimulation period that occurs subsequent to the intercollicular section.

(Figure on the ECG tracings represent the calculated heart rates per min.)

ucleus stimulation response with the passage of time after the intercollicular section. t will be noticed that the depressor-pressor biphysic response obtained $\frac{1}{2}$ hr after the in- ercollicular section is converted to just a depressor response $1\frac{1}{2}$ hr after the section. While assembling the data of this study therefore, each cerebellar stimulation response was tested at least at 3 half hourly intervals after the section and was taken into considera- ion only if such testing produced identical responses.

Histological Confirmation: At the end of experiments an electrolytic lesion was pro- duced at the electrode tip by passing a constant current of 2 mamps for 10 seconds. The brain was perfused with 10% formal saline. Serial coronal sections of 12 μ thickness

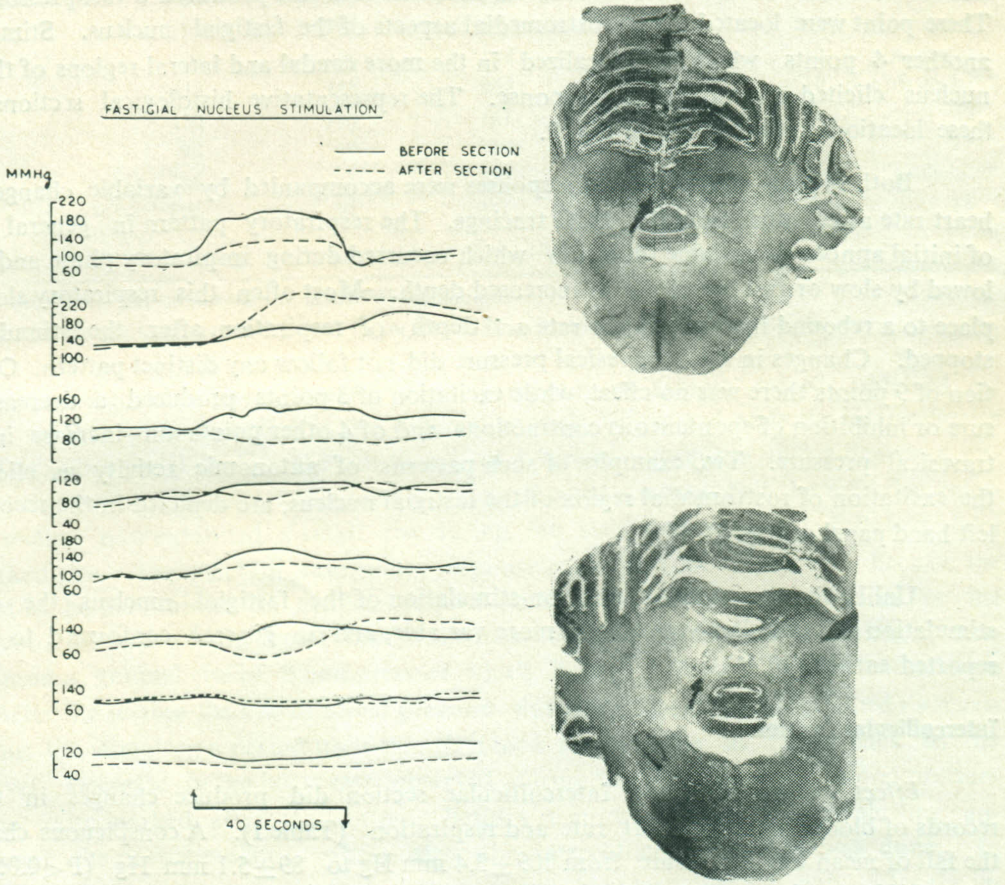

Fig 3 : Tracings of mean arterial pressure reflecting the effect of intercollicular section on fastigia stimula- lation response. Each set of 2 tracings represents repeated observations from one animal.

Histological Sections: the upper section shows the location of stimulation point which elicited pressor responses, and the lower section shows the stimulation point which produced depressor responses.

were cut, mounted and stained with haematoxylin and eosin. The section were enlarged by x 9 and the electrode placements confirmed.

Miscellaneous : Animal's body temperature was maintained by applying electrically heated pads with thermostatic control at 37°C. Whenever required, artificial respiration was instituted by connecting the tracheal cannula to a positive pressure respirtory pump. The depth and rate of respiration was regulated at 50-60ml/stroke and 16-20/min.

RESULTS

Autonomic Responses from Paleocerebellum: Stimulation of 16 points in the fastigial nucleus of either side of cerebellum in 12 anaesthetized cats produced a vasopressor response. These point were located in the rostromedial aspects of the fastigial nucleus. Stimulation of another 4 points which were localized in the more caudal and lateral regions of the fastigial nucleus elicited a vasodepressor response. The representative histological sections showing these locations are presented in Fig. 3.

Both pressor and depressor responses were accompanied by variable changes in the heart rate as counted from the ECG tracings. The respiratory pattern in general consisted of initial apnoea of variable duration which occurred during inspiratory phase and was followed by slow or fast breathing of increased depth. Most often this respiratory slowing gave place to a rebound increase in the rate and depth of respiration, after the stimulation was stopped. Changes in the intravesical pressure did not follow any distinct pattern. On stimulation of 9 points there was no effect, while excitation of 3 points produced a decrease of pressure or inhibition of spontaneous contractions and of 4 other points an increase in the intravesical pressure. Two examples of such patterns of autonomic activity as elicited from the excitation of rostromedial region of the fastigial nucleus, are depicted in the records on the left hand panel of Fig. 2.

Unlike the responses obtained on stimulation of the fastigial nmcleus the effects of stimulation of cerebellar vermis were more variable, and in general conformed to the results reported earlier (10,16),

Intercollicular Section

Effect on basal records : Intercollicular section did produce changes in the basal records of blood pressure, heart rate and respiration (Table I). A conspicuous change was the fall of mean blood pressure from 109$\pm$3.4 mm Hg to 89$\pm$5.1 mm Hg ($P<0.05$). Heart rate exhibited only small variations.

Effect on respiration however was more marked and manifested itself in terms of slowing and increase in depth. In 4 out of 12 animals it stopped altogether and artificial respiration was instituted to keep them alive.

ABLE I : Effect of intercollicular section on basal records of arterial pressure, heart rate and respiration.

	Arterial pressure (mm Hg)		Heart rate (per min)		Respiration (per min)	
	Before section	After section	Before section	After section	Before section	After section
17	95	85	—	—	14	10
18	110	90	—	—	16	12
22	115	110	—	—	12	Artificial**
23	93	73	184	160	16	7
24	95	95	200	202	18	6
25	95	85	156	176	10	6
26	95	75	194	192	10	Artificial**
37	115	105	256	232	16	Artificial**
38	130	130	167	148	16	12
39	95	60	226	234	26	17
40	105	85	220	194	20	Artificial**
41	120	80	237	231	20	14
ean :	109 ± 3.4	89 ± 5.1*	204 ± 10.7	197 ± 10.4		

*$P < 0.05$ (Student's test employed for statistical evaluation)

**In these animals artificial respiration had to be instituted after the intercollicular section.

Effect on fastigial nucleus response : Fig. 2 reporduces sample records obtained on imulation of the fastigial nucleus in two different animals before and after the intercollicular ection. The upper panel depicts the conversion of a pressor response into a depressor resonse after the section. Intravesical pressure which showed a minor fall before the interollicular section now exhibited a small rise during the stimulation period followed later y a marked rise. The effect on respiratory response could not be compared because the nimal had to be maintained on artificial respiration after the section. The records in the ower panel on the other hand depict that in the intact animal, stimulation of fastigial nuceus produced a gradual rise of blood pressure which increased further as the stimulation eased. After the section the rise of blood pressure was more marked, and attained its maximum during the stimulation period itself though it took longer time to come back to the ontrol level. Decrease in the heart rate observed during the early phase of blood pressure ise became more marked after the section. Besides, a more marked cardiac slowing appeared during the post-stimulatory phase after the intercollicullar section was done. In ddition, the post-stimulatory contraction of the urinary bladder appeared only after the inercollicular section. The intercollicular section did not make any appreciable change in the ecord of the respiratory response, except that the chloralose jerks which become markedly pparent on the record during the post-stimulatory phase disappear almost totally after the ntercollcular section.

The changes in the autonomic response with respect to mean arterial pressure that occur after the intercollicular section are summed up in Fig. 3 from which a wide variety of changes with respect to quality, magnitude and temporal patterning can be observed. Similar were the changes with respect to heart rate and intravesical pressure responses. Changes in the rhythmic patterning of respiratory response to fastigial stimulation, however were difficult to assess for the intercollicular section per se affected the basal respiratory records much morc than other parameters (Table I).

Effect on responses from the cerebellar vermis : In the intact preparation stimulation of cerbellar vermis produced a wide variety of autonomic activity patterns. After the intercollicular section different responses were affected differently. Like the effects on the fastigial nucleus stimulation responses, no consistent patterns of changes were observable.

DISCUSSION

Increase of systemic arterial pressure and heart rate on fastigial nucleus stimulation has been recently reported (1,4,14,15). Achari and Downman (1) do not mention about exact localizaltion of pressor points in the the fastigial nucleus but Miura and Reis (14,15) limit the pressor area to rostro-medial fastigial nucleus. The present study confirms these observations of Miura and Reis and in addition demonstrates that the caudal and lateral part of the fastigial nucleus can produce depressor effects. Fastigial connections with the brain stem nuclei are well documented (6,10,20). Miura and Reis (14,15) conclude that the efferent pathway for the fastigial pressor response operates through the paramedian reticular nuclei. It has been reported that the caudal portion of the fastigial nucleus projects to higher brain areas specially on the contralateral side (6,10). In that case the depressor responses obtained on stimulation of this area are likely to involve the higher brain regions. It may be noted that though frank sympathetic responses have been demonstrated to be obtained on stimulation of fastigial nucleus, Hare et al (9) had observed pupil constriction which is a parasympathetic response on stimulating the white matter beween nucleus fastigius and interpositus. It is likely that they were in effect also stimulating in close proximity to the caudo-lateral part of the fastigial nucleus. It is interesting to note that fastigial nucleus stimulation can produce synchronization of electrocortical activity leading to sleep (13) which seems to be occurring through the diffuse projection system of thalamic neurones (5). A functional difference between the rostromedial and caudo-lateral parts of the fastigial nucleus as evinced in this study, therefore is quite possible.

Intercollicular section led to statistically significant fall in the mean arterial pressure which supports the concept that the brainstem reticular formation is in continuum with the hypothalamus in providing tonicity to the smooth musculature of the vascular system (12). The slowing of respiration and increase in its depth in these preparations is not in consonance with Wang *et al.* (21) who have reported only eupnoeic breathing when the sections are made above the level of pons. Influences of higher brain areas on respiration however are well known, and are more likely to be exercised in the lightly anaesthetized animals as employed in this study.

The influences of the intercollicular section on the fastigial stimulation responses were quite variable. One thing is certain that these responses do not remain unaltered after the section as reported by some authors (1.14,15). Instead there is a definite change in terms of magnitude, and temporal pattening of all the recorded parameters which emphasizes that for the elaboration of a particular autonomic response pattern in all its details, activities of the higher brain areas and the paleocerebellum have to be employed in an integrated manner. Doba and Reis (7) have demonstrated that the fastigial nucleus is specially involved in the mediation of cardiovascular compensation which is reflexly employed consequent to change of posture. Bhattarai (4) has demonstrated that the autonomic response patterns induced by diencephalic stimulation undergo marked changes in their temporal patterning after decerebellation. Zanchetti and Zoccolini (22) using unanaesthetized cats produced a typical rage reaction on stimulation of the fastigial nucleus. The rage reaction disappeared after the midbrain section which essentially demonstrates that the fastigial stimulation effect is not exclusively mediated through the bulbar reticular formation. The level of neural heirrarchy involved in the elaboration of a particular autonomic response pattern will depend on the complexity of the response. Higher areas of the brain i.e. hypothalamus and limbic system, therefore, will be involved whenever an autonomic response pattern produced by fastigial stimulation is complex enough to warrant it.

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