Research Paper

In previous studies, bilateral lesions of the rostral fastigial nucleus (rFN) of the cerebellum impaired recovery of mean arterial pressure (MAP) after many forms of hypotension. This study examined effects of cerebellar lesions on baroreflex responses during transient, isovolaemic, non-orthostatic changes in MAP in anaesthetized cats. Bilateral rFN lesions did not alter the rate or extent of fall in MAP induced by nitroprusside, but reduced by 39% the reflex increase in heart rate per unit decrease in pressure (AHR/ΔMAP). Femoral artery resistance remained below control levels. Lesions prolonged the time for 50% MAP recovery after nitroprusside by 93%. During phenylephrine-induced MAP increases, bilateral rFN lesions augmented reflex AHR/ΔMAP by 68%. In intact cats, the reflex decrease in HR after phenylephrine was blocked by electrical stimulation of the rFN, but appeared immediately after stimulation was stopped. Stimulation alone increased both MAP and HR. Propranolol failed to block either the increased HR or the suppression of reflex cardiodeceleration induced by rFN stimulation. Decreases in resting HR after rFN lesions may reflect removal of tonic cerebellar inhibition of cardiac parasympathetic tone. Thus, the cerebellum can influence autonomic output and modify baroreflex sensitivity by augmenting cardiovascular responses mediated by the sympathetic nervous system and inhibiting those mediated by the parasympathetic nervous system.

Key words: Cerebellum, Baroreflex sensitivity, Sympathetic, Parasympathetic, Fastigial nucleus, Hypotension

Introduction

Cerebellectomy or specific lesions of the rostral fastigial nucleus (rFN) impair recovery of blood pressure after orthostatic hypotension induced by head-up tilt.1-3 The compensatory cardiovascular responses to this transient, isovolaemic form of hypotension are initiated by vestibular and baroreflex pathways.

Similar cerebellar lesions also markedly impair the response to severe, long-term hypotension induced by haemorrhage or administration of endotoxin.4,6 Because of the actual or effective decrease in blood volume, respectively, in these latter models, both volume receptor and baroreflex pathways normally initiate and maintain the compensation. Volume receptor responses involving angiotensin and vasopressin are both blunted in animals with cerebellar lesions.5,7

The involvment of the cerebellum in these compensatory reflexes is poorly understood. Electrical stimulation of the rFN of the cerebellum produces a pressor response accompanied by an increase in heart rate8 which overrides the expected reflex cardiodeceleration. Evidence is contradictory as to whether electrical stimulation activates fibres of passage or cell bodies of origin.5,10 In either case, however, there is a cerebellar output influencing the autonomic nervous system. Electrical stimulation of the rFN increases sympathetic nervous system activity,8 but the expression of the marked increase in heart rate together with the prominent pressor response may suggest that stimulation of the rFN also inhibits activity of the parasympathetic nervous system. Other early studies8,11-15 suggested an interrelationship between the cerebellum and baroreflexes, but this relationship has not been closely examined.

In the present study, we examined the influence of the cerebellum on the baroreflex during recovery from transient, non-orthostatic, isovolaemic changes in arterial pressure. Transient decreases in arterial pressure were induced by bolus administration of nitroprusside. Increases in arterial pressure were induced by bolus administration of phenylephrine and/or electrical stimulation of the rFN. We compared the recovery of arterial pressure and the accompanying heart rate changes before and after lesions of the rFN or administration of pharmacological agents.

Materials and Methods

General methods: Experiments were performed in mongrel cats of either sex that weighed between 2.5 to 3.5 kg. Anaesthesia was induced by intramuscular injection of ketamine hydrochloride (20 mg/kg) and maintained by intravenous infusion of α-chloralose and urethane (20 and 350 mg/kg, respectively). Supplemental anaesthetic was administered routinely throughout the experiment. Catheters were intro-
duced via femoral vessels into the abdominal aorta and inferior vena cava for monitoring arterial blood pressure and arterial blood gases and for infusion of drugs and anaesthetic, respectively. A tracheostomy was performed for insertion of a tracheal tube to ensure a patent airway and permit mechanical ventilation.

As a standard procedure, cats were positioned in a Kopf stereotaxic apparatus, and a small hole was made in the skull and dura overlying the cerebellum. A stainless steel, concentric, bipolar electrode (Rhodes Medical Instruments, NE-100) was advanced slowly into the cerebellum at a 45° angle into the ventromedial region of the rFN. A localized region was identified bilaterally where the maximum stimulus-locked increase in MAP occurred during minimal, constant-current stimulation (Grass SD9 and WPI model 305) of 25–50 μA (50 Hz, 1.0 ms pulse width) using 3-s trains.

In cats used to test the effects of lesions or sham-lesions, the coordinates were noted, and the electrode was withdrawn. After testing control responses, the electrode was reintroduced to the original coordinates with final placement again determined by the site of maximal pressor response. Pressor responses at this time were equivalent to those obtained originally. Lesions of the rFN were made bilaterally by passing a cathodal current through the outer pole of the electrode using a standardized DC voltage (25 V). After the experiment, the extent and location of the lesions were evaluated from 50 μm frozen sections stained with cresyl violet. The lesions were considered adequate if histological examination confirmed that 50–100% of the ventromedial portion of the rFN was ablated on both sides (Fig. 1).

After general preparation, mechanical ventilation was started, and the cats were paralyzed with gallamine triethiodide (5 mg/kg i.v., initial dose). The paralytic agent was used to eliminate spontaneous respiration and any prominent influence on blood pressure from somatic afferents. This dose of gallamine did not induce an increase in resting heart rate (HR) and did not prevent a significant, vagally mediated, reflex bradycardia in response to an increase in MAP induced by phenylephrine. The mechanical ventilator was adjusted to maintain end-tidal CO₂ at approximately 5%. Rectal temperature was maintained at 37–38°C by infrared lamps.

Responses to transient decreases in arterial pressure: The compensatory HR response to a transient, isovolaemic, non-orthostatic hypotension was examined in the cats in Groups A–D. Compensatory changes in peripheral vascular resistance were examined in some cats in Group A. Hypotension was induced by bolus administration of sodium nitroprusside (10 μg/kg i.v. in 5% dextrose).

In Group A (n = 12), changes in MAP and HR were measured during and after administration of nitroprusside before and 60 min after bilateral lesions of the rFN. Femoral artery blood flow was measured in six of these cats. Data obtained from some additional animals (n = 6) prepared as part of Group A was excluded from final analysis, because the lesions were found not to meet the defined criteria on histological examination. Group B (n = 6) served as a time-matched control group. In these cats, the electrode was reintroduced after the first infusion, but no lesions were made.

In Group C (n = 6), the response to nitroprusside was tested before and 5 min after blocking the angiotensin converting enzyme with captopril (0.2 mg/kg i.v.) to rule out a contribution to the compensation by the renin-angiotensin system. The effectiveness of blockade was confirmed by the absence of any of the significant pressor response previously induced by the administration of angiotensin I (0.5 μg/kg i.v.).

In Group D (n = 6), nitroprusside was administered before and after β-adrenergic blockade (propranolol, 0.3 mg/kg i.v.) to assess the extent to which elimination of sympathetic activation mimicked post-lesion changes in the HR responses. Blockade was vali-