

Superior cerebellar peduncle lesions selectively abolish the ipsilateral classically conditioned nictitating membrane/eyelid response of the rabbit

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Unilateral lesions of the ipsilateral superior cerebellar peduncle as it leaves the body of the cerebellum to enter the brainstem were found to abolish or severely impair a previously conditioned nictitating membrane (NM)/eyelid response without effecting the unconditioned response or conditioning of the contralateral NM/eyelid.

We have recently reported that large ablations of the ipsilateral, lateral cerebellum result in abolition of a previously conditioned nictitating membrane (NM)/eyelid response without effecting the amplitude of the unconditioned response or the ability to learn the response with the contralateral NM/eyelid^{14,16}. Similar lesions in naive animals were also found to prevent these animals from learning conditioned responses with the ipsilateral, but not the contralateral, NM/eyelid¹². Furthermore, lesions of the pontine brainstem, which included the lateral aspects of the brachium of the superior cerebellar peduncle (SCP, the main output pathway of the dentate and interpositus cerebellar nuclei²), abolished the retention of this response¹¹. The present study was performed to evaluate the effects of lesions of the superior cerebellar peduncle on retention and relearning of the classically conditioned NM/eyelid response.

The conditioning paradigm was similar to that of previous studies¹⁷. In brief, standard procedures for classical conditioning of the rabbit NM/eyelid response were used: acoustic conditioned stimulus (CS), 1000 Hz, 85 dB, on for 350 ms, coterminating with a 100 ms, 2.1 N/cm² (3 psi) corneal airpuff unconditioned stimulus (UCS), intertrial interval pseudorandom with a mean value of 30 s. Thirteen blocks of training were given per day, each block

consisting of 1 tone alone trial and 8 paired trials for a total of 117 trials per day. Extension of the NM was measured with a micropotentiometer and eyelid closure was also monitored; they behave essentially identically¹⁵ and all effects reported here occur equally for both responses. A unipolar lesioning electrode was implanted under halothane anesthesia in the region of the entry point of the superior cerebellar peduncle into the brainstem according to the following coordinates — 3.5 mm anterior to lambda, 3 mm lateral to the midline, and 14.0 mm ventral to dura, with the animal's head held such that the top of the skull at lambda was 1.5 mm below that of bregma. All animals were allowed at least 5 days post-operative recovery, then trained on the left side to a criterion of 8 conditioned responses on any 9 consecutive trials, overtrained one additional day and subjected to lesion of the ipsilateral (left) superior cerebellar peduncle (SCP) by passing 2 mA of DC current for 15 s under light halothane anesthesia. The animals were allowed to recover for 24 h and then subjected to 4 more days of training of the left NM/eyelid, then switched to training of the right NM/eyelid for 72 trials and switched back to the left NM/eyelid for the remaining 45 trials (see Fig. 1).

The mean amplitudes for conditioned responses (CR) and unconditioned responses (UCR) for the 5

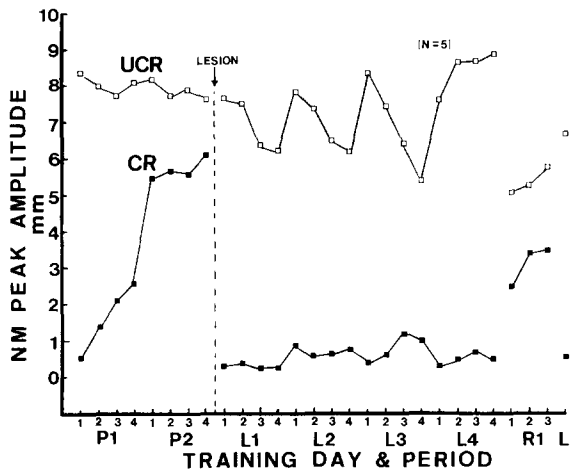


Fig. 1. Effect of lesion of the ipsilateral superior cerebellar peduncle (SCP) on retention and reacquisition of the nictitating membrane (and eyelid) responses, averaged for 5 animals. Solid squares, amplitude of conditioned response (CR); open squares, amplitude of unconditioned response (UCR). All training was to the left side except where labeled R1. The lesion abolished or severely impaired the ipsilateral CR with no effect upon the UCR. P1-P2 indicate the two days of training prior to the lesion. L1-L4 indicate the 4 days of training after the lesion. The contralateral (right) eye was then trained and learned quite rapidly (R1). The left eye was again trained (L) and still showed only very small responses. Numbers on abscissa represent approximately 27 trial blocks.

animals with lesions of the SCP are plotted over the course of training in Fig. 1. All animals learned the original response within two days of training. The mean number of trials to reach criterion was 108 ± 54.5 (\pm standard deviation). The lesion was found to abolish or drastically reduce the amplitude of the CR over the 4 days of post-lesion training as compared with the CR amplitudes of the day prior to the lesion ($F = 7.8$ $df = 19,76$ $P < 0.001$), without effecting the amplitude of the UCR ($F = 0.59$ NS). When shifted to training of the right NM/eyelid, all animals learned the response very rapidly, with the average trials to criterion being 15.8 ± 8.6 ; significantly less than for original acquisition of the left side ($t = 3.3$ $df = 8$ $P < 0.05$). An additional animal whose lesion was medial to the SCP (see Fig. 2) showed no effect of lesion on the amplitude of the ipsilateral CR (7.7 ± 3.8 mm before lesion, 7.6 ± 1.6 mm after lesion). Thus, lesion of the SCP is found to abolish or severely impair the ipsilateral, but not the contralateral, CR.

The extent of the lesion for each animal is reconstructed in Fig. 2. The lesions of 5 of the 6 animals

are seen to encompass a significant portion of the SCP as it leaves the body of the cerebellum and enters into the brainstem. The CRs of all 5 of these animals were abolished or severely impaired after the lesion (see Fig. 1). Other cell groups were occasionally disrupted. These cell groups included the superior vestibular nucleus ($n = 3$), the lateral vestibular nucleus ($n = 2$), the nucleus of the lateral lemniscus ($n = 2$), and lobes 3 and 4 of the cerebellum ($n = 1$). However, the only region common to all animals was that of the SCP and any immediately adjacent reticular cells. Given this, and the fact that both large ablations and stereotaxic lesions limited to the cerebellum can selectively abolish the ipsilateral CR^{14,16}, (and unpublished data), the most parsimonious conclusion is that the critical structure lesioned in the present study is the SCP.

The SCP contains mainly efferent fibers from the cerebellum to brainstem and thalamic structures (e.g. red nucleus, ventral lateral thalamus). Although there are some afferents to the cerebellum contained within the SCP, the majority of these fibers are from the ventral spinocerebellar tract and are involved with the hind limbs and trunk only². The present study therefore strongly suggests that the abolition of the conditioned response with large ablations and electrolytic lesions of the cerebellum also occurs with disruption of essential efferents from the cerebellum. In support of this, we have also recently found that lesions in more anterior portions of the brainstem abolish the conditioned response only when they impinge upon the lateral parts of the brachium of the SCP¹¹. In addition one other laboratory has found that lesions in several parts of the ipsilateral brainstem can selectively abolish the ipsilateral conditioned response. These lesion reconstructions have not yet been published but the authors have kindly made them available to us. It appears that all of their effective lesions included damage to the SCP⁴.

A number of theories have suggested that the cerebellum may be involved in the learning and memory of motor movements^{1,6,8,13}. Indeed, experiments have shown the cerebellum to be involved in various forms of behavioral modification^{3,5,7,9,10}. Our previous experiments have shown that the ipsilateral cerebellum is essential for acquisition, retention, and relearning of the classically conditioned

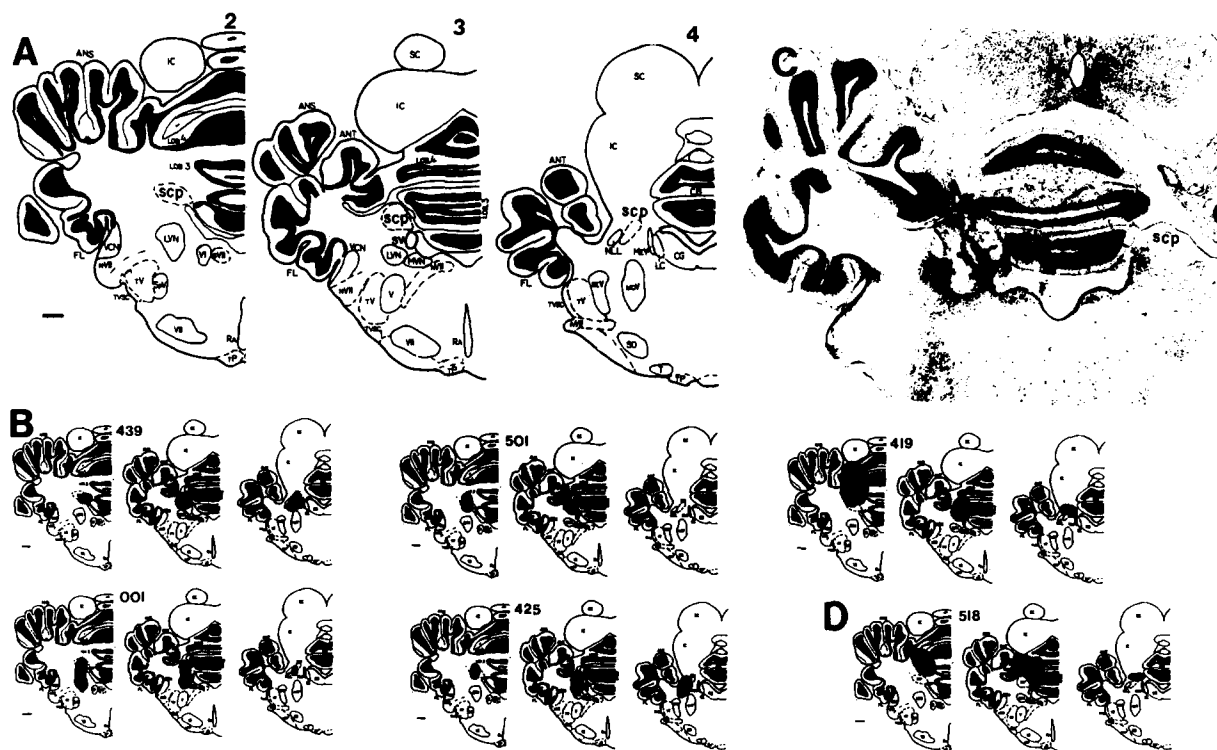


Fig. 2. Reconstructions of the electrolytic lesions of all 6 animals. A: the course of the superior cerebellar peduncle (SCP) as it leaves the cerebellum and enters the brainstem. The number above each section is the level of the section in millimeters anterior to lambda. The calibration bar in the lower left represents one millimeter. B: lesion reconstructions of the 5 animals exhibiting substantial damage to the SCP. The number above each set is the animal's identification number. C: photomicrograph of the lesion of animal number 439. D: lesion reconstruction of an animal whose lesion mostly spared the SCP (it damaged only the most medial part) and had no effect upon the ipsilateral CR. Abbreviations of structures near the SCP for part A are as follows: ANT, anterior lobe of the cerebellum; LC, locus coeruleus; LVN, lateral vestibular nucleus; MeV, mesencephalic fifth nucleus; MVN, medial vestibular nucleus; NLL, nuclei of the lateral lemniscus; SCP, superior cerebellar peduncle; SV, superior vestibular nucleus.

NM/eyelid response^{11,12,14,16}. The present study strongly suggests that efferents from the cerebellum essential for the performance of this learned response travel through the SCP. We would like to suggest that the primary memory trace for this response develops within the cerebellum. Indeed, preliminary unit recordings from the cerebellum have found regions which show stimulus evoked responses (tone, airpuff), regions which show neuronal models of the learned behavioral response, and regions which show both^{14,16}.

However, there are other possibilities. The cerebellum may be an essential afferent or efferent for a memory trace localized elsewhere in the nervous

system. It is also possible that ipsilateral cerebellar lesions somehow result in critical dysfunction of some other region of the nervous system that is itself the locus of the memory trace. At present, there is little evidence that such a process occurs. The fact that lesions of the SCP disrupt the CR indicates that if such a process does occur it must be efferent from the cerebellum.

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