MLR-induced inhibition of barosensory cells in the NTS

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Degtyarenko, Alexandr M., and Marc P. Kaufman. MLR-induced inhibition of barosensory cells in the NTS. Am J Physiol Heart Circ Physiol 289: H2575–H2584, 2005.—A central motor command arising from the mesencephalic locomotor region (MLR) is widely believed to be one of the neural mechanisms that reset the baroreceptor reflex upward during exercise. We therefore examined the effect of electrical stimulation of the MLR on the impulse activity of cells in the NTS in decerebrate paralyzed cats. Of 129 NTS cells tested for baroreceptor input, 108 cells (84%) were inhibited by MLR stimulation. MLR stimulation (80–150 µA) inhibited the discharge of 48 of the 58 cells stimulated by baroreceptor input. MLR stimulation had no effect on the discharge of the remaining 10 cells, each of which displayed no spontaneous activity. In contrast to the 77 NTS cells responsive to baroreceptor input, there was no change in activity of 52 cells when arterial pressure was increased by phenylephrine injection or balloon inflation. MLR stimulation activated each of the 52 NTS cells. For 23 of the cells, the onset latency to MLR stimulation was clearly discernable, averaging 6.4 ± 0.4 ms. Our findings provide electrophysiological evidence for the hypothesis that the MLR inhibits the baroreceptor reflex by activating NTS interneurons unresponsive to baroreceptor input. In turn, these interneurons may release an inhibitory neurotransmitter onto NTS cells receiving baroreceptor input.

BOTH STATIC AND MODERATE DYNAMIC exercise are well known to increase arterial blood pressure, heart rate, and ventilation (32, 41). Two neural mechanisms, namely, central command and the exercise pressor reflex, are believed to be responsible for these increases in cardiovascular and ventilatory function (18, 47). Central command is defined as the parallel activation of the central neural circuits controlling locomotor, cardiovascular, and ventilatory function. Central command is a feedforward process that does not requireafferent input from contracting muscles (9). The exercise pressor reflex, in contrast, is evoked by the contraction-induced stimulation of group III and IV afferents (24), which are believed to be activated by mechanical and metabolic factors arising in the working muscles (18, 19).

The cardiovascular and ventilatory responses to exercise should be expected to be countered by the baroreceptor reflex. During exercise, however, the baroreceptor reflex is reset upward, thereby allowing arterial blood pressure, heart rate, and ventilation to increase. Recently, in decerebrate cats, central command, induced by electrical stimulation of the mesencephalic locomotor region, and the exercise pressor reflex, induced by static contraction of the triceps surae muscles, were found to reset the baroreceptor reflex upward (25). The central site where baroreceptor reflex resetting occurs is unknown, but the nucleus tractus solitarius (NTS) is a strong candidate, because this dorsal medullary site receives synaptic input from carotid and aortic baroreceptors as well as from cardiac mechanoreceptors (4, 27). Moreover, the NTS receives inhibitory input from the hypothalamic defense area, a site that is capable of suppressing the baroreceptor reflex (31, 31) but is distinct from the areas of the brain evoking central command.

We have sought to provide electrophysiological evidence consistent with the view that the NTS is the site where the baroreceptor reflex is reset upward during exercise. We have focused on baroreceptor resetting induced by central command, because this neural mechanism is believed to contribute significantly to the cardiovascular and ventilatory adjustments to exercise. Recently, Komine et al. (20) provided important evidence in support of resetting of the baroreceptor reflex by central command. Using conscious cats, they showed that the bradycardic component of the baroreceptor reflex was suppressed immediately before the initiation of forelimb extension (20). This recent finding can be explained by central command, and it prompted us to seek electrophysiological evidence to support it.

METHODS

General. The Institutional Care and Use Committee of the University of California, Davis, approved all procedures. Cats of both genders (2.1–3.6 kg) were initially anesthetized with 5% halothane and oxygen. The trachea, left jugular vein, and one common carotid artery were cannulated. The lungs were then ventilated mechanically with the halothane-oxygen gas mixture through the tracheal cannula. The remaining carotid artery was ligated. Body temperature was maintained near 37°C with a heating pad and lamp. The cat was placed in a Kopf stereotaxic and spinal unit, and the common peroneal nerve was dissected free and cut and its central end was placed on a hook recording electrode. In all cats, a precollicular-postmamillary decerebration was performed, and in most cats, a cerebellotomy was also performed to allow access to the dorsal medulla. All neural tissue rostral to the section was removed, bleeding was controlled, and the cranial vault was filled with agar. After the decerebration was completed, the lungs were ventilated with a mixture of room air and oxygen. Skin flaps surrounding the peroneal nerves were tied to brass bars, thereby forming the walls of pools, which were filled with warm mineral oil (37°C). Arterial blood gases were sampled and subsequently adjusted to normal values by injection of 8.5% sodium bicarbonate and/or by a change in ventilation.

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A stainless steel monopolar electrode was placed stereotaxically into the mesencephalic locomotor region (MLR) having the following coordinates: P2, L4, and HC1. The electrode was used to deliver monophasic electrical pulses (20–50 Hz, 0.2–0.5 ms, 80–150 μA) to the MLR. The electrode was considered to be optimally placed when low-intensity stimulation induced efferent activity in the peroneal nerve while the cat was paralyzed. The criterion for identifying the MLR in the decerebrate paralyzed cat closely parallels that described by Grillner and Shik (14).

In our experiments, we found that, in most cases, electrical stimulation of the MLR evoked tonic activity in the peroneal (i.e., flexor) nerve, an effect that was similar to the late and long-lasting discharges evoked by stimulation of thin-fiber muscle and skin afferents in spinal cats given DOPA as well as in decerebrate cats (1, 14, 16, 17). These late discharges were considered to be a stage of activation of the central command for locomotion (1, 2, 14). In addition, the spinal cord interneurons activated by spontaneous fictive locomotion were also found to be activated by the long-lasting tonic discharges evoked by stimulation of thin-fiber muscle and skin afferents in decerebrate paralyzed cats, with the only difference being that the level of activity was higher during fictive locomotion than during the long-lasting tonic discharges (1, 2). Furthermore, the cardiovascular and respiratory responses to MLR stimulation, whether it evoked fictive locomotion or tonic efferent activity, were identical (9).

Extracellular impulses were recorded from cells in the NTS with tungsten microelectrodes (FHC; tip impedances at 1,000 Hz of 4–6 MΩ). The tungsten electrodes were connected to a high-impedance probe (model HIP511, Grass), which in turn was connected to a preamplifier (model P511, Grass). Filters were set at 100–3,000 Hz. Arterial blood pressure was measured from the carotid arterial cannula, which was connected to a Statham transducer (model P23 XL). All signals were recorded and displayed using Spike 2 software. Similarly, all neural signals were also displayed on a storage oscilloscope.

Protocol. The cats were paralyzed with vecuronium bromide (0.1 mg/kg iv), which was supplemented every 30 min. The tungsten recording electrode was advanced through the NTS until the extracellular impulse activity of a cell was clearly identifiable. Next, phenylephrine (7–25 μg/kg), an α-adrenergic agonist, was injected intravenously, and the response, if any, of the cell was recorded. Phenylephrine was injected to increase arterial blood pressure, which in turn stimulated arterial baroreceptors as well as cardiac mechanoreceptors innervated by vagal afferent fibers. In a few experiments, sodium nitroprusside (30 μg/kg), a vascular smooth muscle relaxant, was injected intravenously. Finally, in other experiments, a balloon attached to a catheter (5F) was inserted into a common carotid artery and advanced into the carotid sinus. Placement of the balloon was manipulated after withdrawal of anesthesia. Successful placement was evidenced by balloon inflation causing a decrease in arterial pressure, which was attributed to the reflex evoked by stimulation of carotid sinus baroreceptors.

After determining whether the discharge of a cell was stimulated or inhibited by an increase in arterial pressure, we determined its response to electrical stimulation of the MLR. Single-pulse (1 Hz, 0.2–0.5 ms) and train (20–50 Hz, 0.2–0.5 ms, 2–10 s) stimulation recording efferent activity from the peroneal nerve was connected to a high-impedance probe (model HIP511, Grass), which in turn was connected to a preamplifier (model P511, Grass). Filters were set at 100–3,000 Hz. Arterial blood pressure was measured from the carotid arterial cannula, which was connected to a Statham transducer (model P23 XL). All signals were recorded and displayed using Spike 2 software. Similarly, all neural signals were also displayed on a storage oscilloscope.
were used. At times, we tried to evoke impulse activity in silent cells by stimulation of the MLR or by injection of phenylephrine or balloon inflation. Neither of the three maneuvers was performed in a systematic manner; therefore, the possibility that relevant silent cells were overlooked cannot be excluded. We marked the locations of some cells by passing anodal direct current through the recording electrode. The medullas were removed from the cat and sectioned (40 μm) for identification of these sites, which in turn were used as landmarks to identify, using stereotaxic coordinates, each of the remaining sites.

Data analysis. The artifacts evoked by electrical stimulation of the MLR were removed by the Spike 2 program ARTREM. The shape recognition package of the Spike 2 program was used to identify single units. Recordings in which the shape of the impulse was changed during increases in arterial blood pressure were discarded. Poststimulus time histograms were constructed from ≥30 presentations of the single-pulse stimulus applied to the MLR. Pulse synchronous time histograms were constructed from ≥40 heartbeats, the triggering event being end diastole. Values are means ± SE. Statistical significance was determined with t-tests. Pearson product-moment correlation coefficients were calculated where appropriate. The criterion for significance was set at \( P < 0.05 \).

RESULTS

NTS cells tested with phenylephrine. Of the 103 NTS cells tested, 63 responded to phenylephrine-induced increases in mean arterial pressure that averaged 67 ± 3 mmHg (baseline = 120 ± 3 mmHg). Only 5 of the 63 cells discharged in synchrony with the systolic phase of the arterial pressure pulse. The discharge of these five cells averaged 2.2 ± 0.7 impulses per cardiac cycle and ranged from one to five impulses per cardiac cycle. Although distribution of the cells responding to increases in arterial pressure was widespread within the NTS, there was a tendency for them to be found in the caudal part of this nucleus (Fig. 1).

Of the 63 NTS cells that responded to phenylephrine, 44 increased their discharge (from 5.3 ± 1.0 to 14.1 ± 2.2 impulses/s, \( P < 0.001 \); Fig. 2) and 19 decreased their discharge (from 7.3 ± 1.8 to 1.2 ± 0.5 impulses/s, \( P = 0.002 \)). Of the 44 NTS cells in which activity was increased by phenylephrine, 7 were also tested for their responses to

![Fig. 2. Effects of phenylephrine (25 μg/kg iv) and nitroprusside (30 μg/kg iv) injection on discharge of an NTS cell.](http://ajpheart.physiology.org/)

**A:** stimulation by phenylephrine. **B:** inhibition by nitroprusside. **C:** mean discharge frequency of cell in **A** vs. mean arterial blood pressure (ABP) when phenylephrine was injected in **A**. Correlation coefficient was significant (\( P < 0.001 \)). EC, extracellular activity; R, discharge rate (impulses/s).
sodium nitroprusside injection (30 μg/kg iv). Each of the seven cells decreased their discharge in response to nitroprusside injection (from 8.5 ± 1.3 to 1.0 ± 0.7 impulses/s, \( P < 0.001 \); Fig. 2). In addition, mean arterial pressure decreased by 53 ± 3 mmHg (baseline = 116 ± 4 mmHg). The discharge frequency of the seven cells in response to phenylephrine and nitroprusside injections was significantly correlated with mean arterial pressure. Specifically, the

Fig. 3. Activity of an NTS cell discharging in synchrony with arterial pressure pulse is inhibited by MLR stimulation. \( A \): inhibition of NTS cell discharge by MLR stimulation. Horizontal bar, duration of discharge. Inhibition of NTS cell discharge occurred before increase in arterial pressure. \( B \) and \( C \): expanded traces showing that cell discharged in synchrony with systole and its discharge increased in response to spontaneous increases in arterial pressure. \( D \): pulse synchronous nature of discharge of the cell over 50 heartbeats in \( A-C \). Top trace, averaged arterial pressure pulse for 50 heartbeats.

Fig. 4. Activities of 2 NTS cells not discharging in synchrony with arterial pressure pulse were inhibited by MLR stimulation (horizontal bar). Activities of both cells were increased by intravenous injection of phenylephrine. \( A \): activity of the cell (same as cell in Fig. 2) remained inhibited after the end of MLR stimulation. \( B \): activity of the cell increased after the end of MLR stimulation.
correlation coefficients were 0.60–0.81 (n = 7, P < 0.001; Fig. 2).

Of the 44 cells of which the activity was increased by phenylephrine, 34 (77%), including the 5 discharging in synchrony with the arterial pressure pulse, were inhibited by MLR stimulation (Fig. 3). The inhibition displayed by these 34 cells was immediate and almost always occurred before the onset of the MLR-induced increase in arterial pressure (Figs. 3 and 4). The pressor response to MLR stimulation averaged 64 ± 4 mmHg (baseline = 108 ± 4 mmHg) and remained above baseline levels for 37.0 ± 3.1 s after the end of stimulation. The remaining 10 cells (23%), which had no baseline discharge, remained silent when the MLR was stimulated but did show an increase in activity after the stimulation ended (duration = 29.5 ± 8.3 s; Fig. 5). The increase in discharge after the end of MLR stimulation may have been caused by the elevated arterial pressure, which in turn stimulated baroreceptors.

Of the 34 cells of which the activity was inhibited by MLR stimulation, 24 continued to be inhibited after the stimulation ended (duration = 16.5 ± 2.0 s), even though mean arterial pressure remained elevated above baseline levels (Figs. 3–5). The remaining 10 cells were activated after the stimulation ended (duration = 29.5 ± 8.3 s; Figs. 4 and 5). Of the 19 NTS cells in which activity was decreased by phenylephrine, 13 were inhibited by MLR stimulation, 5 were activated by MLR stimulation, and 1 showed no change. The inhibition displayed by the 13 NTS cells in response to MLR stimulation was immediate and occurred before the increase in arterial pressure. For each of the 103 NTS cells tested, MLR stimulation evoked an obvious increase in efferent discharge from the central cut end of the peroneal nerve.

Of the 103 NTS cells tested, 40 did not respond to the phenylephrine-induced increase in arterial pressure. None discharged in synchrony with the arterial pressure pulse. MLR stimulation increased the discharge of each of these 40 NTS cells (Figs. 6 and 7). On average, activity increased from 9.6 ± 2.1 to 40.6 ± 4.6 impulses/s (P < 0.001, n = 40). Of the 40 NTS cells activated by MLR stimulation, 15 continued to respond for 12.5 ± 2.9 s after the end of stimulation, 15 were inhibited for 14.9 ± 3.1 s after the end of stimulation, and the remaining 10 returned immediately to their baseline levels after the end of stimulation (Figs. 6 and 7E).

In 23 of the 40 cells activated by MLR stimulation, we were able to precisely determine the onset latency of the response to repetitive single-pulse stimulation of this region (Fig. 7, B and C). This onset latency averaged 6.4 ± 0.4 ms (range 3.1–10.4 ms, n = 23). The onset latency of the remaining 17 cells was variable and difficult to determine with any specificity. The distribution of the 40 cells within the NTS was widespread, but there was a tendency for them to be located within the caudal part of this nucleus (Fig. 1).

NTS cells tested with carotid sinus balloon inflation. Of the 26 cells tested, 14 responded to inflation of a balloon in the carotid sinus, a maneuver that decreased mean arterial pressure by 22 ± 2 mmHg (baseline = 130 ± 3 mmHg). Each of the 14 cells was spontaneously active and displayed an increase in activity when the balloon was inflated (Fig. 8). On average, activity increased from 1.7 ± 0.3 to 4.1 ± 0.7 impulses/s (P < 0.001). The discharge characteristics of these 14 cells were similar to those of cells displaying the second pattern of responsiveness to carotid sinus baroreceptor input, which was described by Seagard et al. (42). Of the 14 cells responding to balloon inflation, 4 were tested for their response to phenylephrine injection (25 μg/kg iv). Each of these 4 cells responded, increasing their discharge from 2.5 ± 0.8 to 7.8 ± 2.4 impulses/s. Most importantly, the activity of each of the 14 cells was inhibited by MLR stimulation (from 4.1 ± 0.8 to 1.0 ± 0.2 impulses/s, P < 0.001).

Of the 26 NTS cells tested, 12 did not respond to distension of the carotid sinus. Similarly, none of the four cells tested responded to phenylephrine injection (25 μg/kg iv). MLR stimulation increased the discharge of each of the 12 NTS cells. On average, activity increased from 5.7 ± 1.5 to 37.3 ± 6.5 impulses/s (P < 0.001, n = 12).

DISCUSSION

Two findings from our experiments are particularly relevant to baroreflex resetting by central command during exercise. 1) MLR stimulation decreased the discharge of 83% of the NTS cells responsive to baroreceptor stimulation that was induced by intravenous phenylephrine injection or carotid sinus distension. 2) MLR stimulation increased the discharge of 100% of the NTS cells tested that were not responsive to baroreceptor stimulation.

We did not electrically stimulate the aortic or carotid sinus nerve to identify NTS cells receiving arterial baroreceptor

![Fig. 5. Effect of MLR stimulation on discharge of 44 NTS cells in which discharge was increased by intravenous injection of phenylephrine. A: effects of MLR stimulation on 24 cells in which activity remained decreased from baseline levels after the end of stimulation. B: effects of MLR stimulation on 10 cells in which activity was increased over baseline levels after stimulation ended. C: effects of MLR stimulation on 10 cells that were silent before and during stimulation but discharged after stimulation ended. Pre, 30 s before MLR stimulation; during, MLR stimulation; post, after stimulation ended and when cells were still responding to stimulus; recovery, 30 s after “post” response. *P < 0.05 vs. Pre.](http://ajpheart.physiology.org/0)

![Fig. 5](http://ajpheart.physiology.org/0)
input, and clearly this must be considered a limitation. Instead, we identified these cells by intravenously injecting pharmacological agents as well as by inflating a balloon in the carotid sinus. Both methods produced results that were clearly consistent with the NTS cells receiving arterial baroreceptor input. Intravenous injection of phenylephrine or nitroprusside, which raises or lowers arterial blood pressure, respectively, has been shown to activate NTS cells that were driven by single-pulse stimulation of the aortic nerve (40, 48). Moreover, our data found a strong positive correlation between the discharge frequency of NTS cells and the change in mean arterial pressure induced by pharmacological agents. This correlation could be interpreted as evidence of baroreceptor input to these cells.

One might argue that the stimulation of NTS cells by phenylephrine injection in our experiments was caused by a mechanical disturbance arising from the proximity of the recording electrode to the cells as arterial pressure increased. If this were the case, one should expect that the cells would also be activated by MLR stimulation. Instead, the discharge of the cells was inhibited, even though MLR stimulation and phenylephrine injection increased arterial pressure to a similar extent. Finally, phenylephrine could not have had a direct stimulatory effect on NTS cells, because when this α-adrenergic agonist was injected into the NTS, it had an inhibitory action on the discharge of cells receiving baroreceptor input (46).

Our two findings need to be placed in a framework that explains baroreflex function during exercise. Fortunately, such a framework already exists (37, 38). This framework postulates that an NTS interneuron, which is unresponsive to baroreceptor input, releases an inhibitory neurotransmitter onto NTS cells stimulated by this input. This framework further postulates that this inhibitory interneuron is activated by input arising from central command or the group III and IV muscle afferents, evoking the exercise pressor reflex (Fig. 9). Both of our findings fit easily into this framework. For example, our first finding, i.e., that MLR stimulation inhibited the discharge of NTS cells receiving baroreceptor input, is consistent with central command resetting the baroreceptor reflex during exercise. Similarly, our second finding, i.e., that MLR stimulation excited NTS cells that did not receive baroreceptor input, is consistent with these cells being interneurons that release an inhibitory neurotransmitter.

There is substantial evidence that GABA might be the inhibitory neurotransmitter in the NTS. For example, ionto-
phoretic application of GABA markedly reduced or abolished the responses of NTS cells to electrical stimulation of the carotid sinus nerve in cats (27). Similarly, iontophoretic application of GABA markedly reduced or abolished the responses of NTS cells to electrical stimulation of the cardiac branches of the vagus nerve or to electrical stimulation of the aortic nerve in cats (5). In addition, potassium-induced depolarization of cells in the NTS has been shown to release GABA in vitro in a slice preparation from rats (30). Finally, cells in the NTS have been shown by immunocytochemistry to contain GABA (22, 23).

Neurotransmitters other than GABA may also play roles in inhibiting the discharge of NTS cells receiving arterial baroreceptor input. For example, blockade of 5-HT₃ receptors or NK-1 receptors in the NTS prevented the inhibition of baroreflex-induced bradycardia induced by stimulation of the periaqueductal area (7, 8). Similarly, iontophoretic injection of noradrenaline into the NTS inhibited the discharge of NTS cells, an effect that was antagonized by an antagonist to α₂-adrenergic receptors (10).

The anatomic pathway from the MLR to the NTS is not known. In rats, one report has shown that the cuneiform nucleus, which is an anatomic locus of the MLR, projected monosynaptically to the NTS (21). No evidence, however, was offered in this report that the injected sites caused locomotion or static contraction (21). Moreover, stimulation of the cuneiform nucleus evoked pressor and bradycardia responses (21), the latter of which is not characteristic of the response evoked from the MLR (3, 9). On the other hand, the MLR does project monosynaptically to the rostral ventromedial medulla, an area that includes the gigantocellular and magnocellular reticular formation as well as the nucleus raphe magnus (13, 43). These anatomic findings were supported by the electrophysiological finding that MLR stimulation in cats monosynaptically activated cells in the gigantocellular reticular formation with a latency of 1.0–1.5 ms (34). This latter finding is consistent with our finding that stimulation of the MLR activated NTS cells with an average latency of ~6 ms and raises the possibility that several synapses intervene in the pathway from the MLR to the NTS.
NTS, with the first possibly being in the rostral ventromedial reticular formation.

There is convincing evidence that central command inhibits the baroreflex in animals and humans. Specifically, in decerebrate paralyzed cats, electrical stimulation of the MLR caused an upward shift in the curve relating carotid sinus pressure to either mean arterial pressure or heart rate (25). In addition, in conscious cats, the bradycardia elicited by electrical stimulation of the aortic depressor nerve, which contains the axons of aortic baroreceptors, was attenuated immediately before the initiation of forelimb extension (20). In humans, attempted exercise during partial paralysis with curare caused an upward shift in the curves relating carotid sinus pressure to either mean arterial pressure or heart rate (12). Similarly, in humans, tendon vibration of an antagonist muscle, a maneuver that increased the central command needed to exercise its corresponding opposing muscle, shifted these curves upward (33).

There is also considerable evidence that the exercise pressor reflex inhibits the baroreceptor reflex. For example, static contraction of the triceps surae muscles and electrical stimulation of group III and IV muscle afferents inhibited the cardiac slowing induced by increases in carotid sinus pressure in cats (25, 26, 28, 29), dogs (36), and rats (38). In addition, activation of the muscle metaboreflex in humans by postexercise circulatory occlusion reset the sigmoid relation between mean arterial pressure and heart rate to a higher level (15). Moreover, activation of muscle afferents by compression during exercise resulted in a rightward shift in this relation (11).

In contrast to the sparse electrophysiological information about MLR input to the NTS, there is considerable information

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**Fig. 8.** Activity of an NTS cell was increased by inflation of a balloon in carotid sinus (A) and inhibited by MLR stimulation (B). C: anatomic locations of NTS cells in which discharge was changed by inflation of carotid sinus balloon. ○, cells in which discharge was increased by MLR stimulation (n = 12); ●, cells in which discharge was increased by inflation of carotid sinus balloon (n = 14).
about thin-fiber muscle afferent input to the NTS. For example, electrical stimulation of group III afferents has been shown to activate cells in the NTS of cats (35) and rats (44). Similarly, contraction of hindlimb muscles has been shown to activate cells in the NTS of rats (38, 45), and in some cases the input was shown to arise from group III and IV afferents (45). When tested, NTS cells, receiving input from thin-fiber muscle afferents, did not respond to increases in arterial pressure (39, 44), a finding consistent with the framework previously articulated (37, 38).

In conclusion, our study is the first to demonstrate electrophysiologically that stimulation of the MLR activates cells in the NTS that are not responsive to baroreceptor stimulation and inhibits cells in the NTS that are responsive to baroreceptor stimulation. Our findings are consistent with the hypothesis that exercise-induced baroreflex resetting occurs in the NTS (38, 45) and that central command is one of the neural mechanisms responsible for this resetting. According to this hypothesis, the barosensitive NTS cells that are excited by MLR stimulation release the inhibitory neurotransmitter GABA onto barosensitive cells in the NTS to reset the reflex. Nevertheless, the neurotransmitter released by barosensitive NTS cells excited by MLR input remains to be proven.

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GRANTS

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Inhibition of Baroreflex