

How the mesencephalic locomotor region recruits hindbrain neurons

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Abstract: This chapter summarizes experiments which were designed to reveal how repetitive electrical stimulation of the mesencephalic locomotor region (MLR) recruits nearby hindbrain neurons into activity, such that locomotion can ensue in the tiger salamander, *A. tigrinum*. The MLR stimulus strength was subthreshold or near-threshold for locomotor movements to ensue. Such relatively weak stimulation of the MLR produced locomotor movements after a relatively long delay, which featured neuronal interactions in the hindbrain. MLR-evoked spike responses of single hindbrain neurons were recorded before locomotor movements began. This allowed consideration of the build-up of the hindbrain neuronal activity, which was subsequently impressed upon the spinal cord such as to evoke locomotor movements. Each train of MLR stimulus pulses evoked monosynaptic responses in but a small proportion of the hindbrain's neurons. Rather, oligosynaptic responses were routinely evoked, even in the "input" neurons that were activated monosynaptically. Consecutive stimulus volleys recruited a given neuron after a variable number of synaptic translations. It is argued that the hindbrain's input neurons excited a much larger number of other hindbrain neurons. By this means, an MLR-evoked, short-lived propagating wave of excitation (i.e., ~2–4 successive synaptic activations) can be spread throughout the hindbrain.

Introduction

Several divisions of the brain participate in the control of a movement. Take, for example, the induction of locomotion in various vertebrates, including caudate amphibians, by repetitive stimulation of the mesencephalic locomotor region (MLR; Shik, 1997; Grillner and Wallén, Takakusaki et al., and S. Mori et al., this volume). The excited neurons project to the hindbrain (Orlovsky, 1970). At this site, monosynaptically excited neurons initiate the processing that leads to activation of the appropriate amount and composition of the hindbrain's neuronal population, which, in turn, activates the relevant spinal locomotor networks. To achieve this task at the hindbrain level, how many successive synaptic

excitations (translations) occur in relevant neurons after each input volley from the MLR?

In a previous study on the rough skin newt, *T. granulosa*, we recorded extracellularly the impulses of hindbrain neurons before MLR-induced locomotor movements began (Bar-Gad et al., 1999). The latency of time-locked synaptic responses was predominately at ~13, 18, 23 and 28 ms. These distinctive latencies appeared intermittently when the train of repetitive MLR stimulus pulses had an inter-stimulus (pulse) interval (ISTi) of 100–200 ms. Each volley from the MLR evoked a propagation of activity in hindbrain neurons with a characteristic synaptic translation time of 5–6 ms. The activity was short-lived and ceased after three or four translations, at which time hindbrain neuronal activity terminated or became disengaged from the MLR stimulus. In that study, however, we mostly used trains of MLR stimulus pulses that were subthreshold

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49 for evoking locomotor movements. Now, we are able
50 to record the activity of the same hindbrain neuron in
51 several successive periods of repetitive MLR stimula-
52 tion, including the period of transition from rest to
53 real locomotion.

54 In this chapter, we show how experiments on the
55 tiger salamander, *Ambystoma tigrinum*, have provided
56 an estimation of the processing of MLR stimulus
57 volleys in the hindbrain, using stimulus trains that
58 were both subthreshold and at the threshold for
59 evoking locomotor movements. The information so
60 gained provides insight into the nature of autonomous
61 hindbrain processing, this being a key component of
62 the multilevel control of locomotion.

64 Methods

65 Most of the methods have been described previously
66 (Bar-Gad et al., 1999) and are provided below only in
67 brief.

68 Locomotion was evoked in *A. tigrinum* by
69 repetitive electrical stimulation of the MLR. The
70 stimulus current and frequency were adjusted so that
71 the locomotor movements began ~ 15 s after stimulus
72 onset. It was assumed that the hindbrain neurons
73 recruited by a near-locomotor-threshold train of
74 stimulus pulses were mainly those that participated
75 in the preparation's transition from rest to loco-
76 motion. The distance between the sites of MLR
77 stimulation and the recorded hindbrain neurons
78 was ~ 4 –5 mm.

79 The stimulus train (trial) that was at the threshold
80 for locomotor movements usually consisted of
81 5–12 μA pulses at an IStI of 80–200 ms. It was
82 delivered for ~ 15 s, i.e., until locomotor movements
83 began. The inter-trial pauses were for 2 min, and the
84 total number of such trials per stimulus/recording
85 session was 2–11. The neuron's extracellularly
86 recorded impulses (i.e., spike discharges) were
87 discriminated off-line. Each set of impulses and its
88 corresponding train of stimulus pulses were then
89 converted into point processes.

93 Measurement abbreviations and terminology

94 We define: L_n , the latency of the n th impulse, as the
95 time between the impulse (neuronal spike) and the
96

immediately preceding stimulus pulse; IImI_n , the inter-
impulse interval between the n th and the $n+1$ th
impulse; IStI, inter-stimulus (pulse) interval of a train of
stimuli delivered to MLR; T , the duration of an IStI;
and k_n , the number of stimulus pulses ($0, 1, \dots, m$)
between the impulses n and $n+1$. Note that
 $\text{IImI}_n = k_n T + (L_{n+1} - L_n)$. All time variables are in ms.

An IImI of a duration approximately equal to an
integer multiple of T and containing k stimulus pulses
is termed integer kT interval. Integer intervals were
formed by the successive time-locked responses (e.g.,
intervals in Fig. 1 inset, *not marked* by asterisks:
 $k=1$). Delayed responses (see Results) could form
noninteger $(k+1/2)T$ and $[(k+1)-1/2]T$ intervals
(e.g., intervals in Fig. 1 inset, marked by asterisks:
 $k=1$, thus one-and-one half intervals were formed).
Such noninteger intervals are abbreviated $k+$ and
 $(k+1)-$ (e.g., $1+$ and $2-$ in Fig. 1 inset). The $k+$
and the $(k+1)-$ IImIs contain k and $k+1$ stimulus
pulses, respectively.

Finally, the firing ratio is defined as the inter-
stimulus interval divided by the average inter-impulse
interval.

Results

In this chapter, we focus on the behavior of 16
hindbrain neurons, which we studied in nine
experiments on four animals. In all, there were
 ~ 100 trials, 80 of which contained > 20 consecutive
impulse responses.

Basic variations in the impulse patterns

The following variations in the mode of firing were
observed routinely. As shown in Fig. 1, they included:
(1) an alternation of k values between successive
impulses; (2) fluctuations of the IImI and the latency
of time-locked impulses; and (3) the intermittent
presence of delayed (relative to the preceding
stimulus pulse) impulses.

The k value commonly alternated among two
or three adjacent integers. For example, at a firing
ratio of 0.3, k varied irregularly between 2, 3 and 4.
At a firing ratio of 0.5, k was 1, 2 or 3. At a firing
ratio of 0.8, k alternated between 1 and 2, or 0, 1 and
2 (Fig. 1). At an IStI of 100–200 ms, k normally

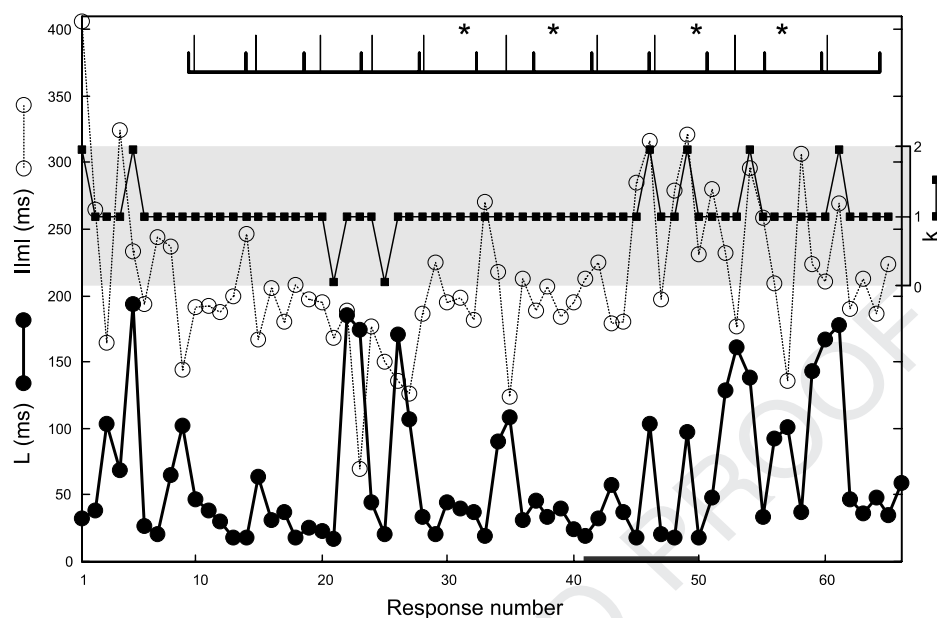


Fig. 1. Commonly observed variations in the firing of a hindbrain neuron during a train of stimulus pulses delivered to the MLR. This figure shows variations in the inter-impulse interval (IIMI) and response latency (L) values (left-side ordinates) for 65 consecutive impulses (neuronal spike responses) of a hindbrain neuron to a train of MLR stimulus pulses (ISTl = 200 ms). Also shown is the number of stimulus pulses (k) between successive impulse responses (right-side ordinate). Note that the delayed impulses prevented an increase of $k = 2$ intervals to more than 300 ms during alternating k discharge. The inset at the top of the figure shows a part of the stimulus train (short thick vertical lines) and its associated impulse train (longer thin vertical lines). The thick horizontal line under the latency values (i.e., starting after the 40th spike response) shows where the inset epoch occurred within the trial. In this inset, note the intermittent presence of delayed impulses (i.e., in the 6th and 10th ISTl). Four asterisks (*) denote the noninteger (1+) and (2-) inter-impulse intervals.

alternated around 1 (i.e., 1 to 2, or 1 to 0) during near-locomotor-threshold stimulus trains, but around 2 during subthreshold ones. At an ISTl of 300–500 ms, the evoking stimulus trains remained commonly sub-locomotor-threshold and k alternated between 1, 2 or 3 in a stimulus-strength-dependent manner. The firing ratio commonly decreased when the MLR stimulus threshold for evoking locomotion gradually increased in the later phases of the stimulus/recording sessions.

Figure 1 shows that variations in the k and latency values were exhibited during epochs of both steady-state discharge and either decreasing or increasing discharge. The k trend generally resulted from a gradual change in the occurrence of k and $k + 1$ intervals. The latency values fluctuated irregularly mainly among two ranges (see also Fig. 3C). Delayed impulses were encountered mostly either in the middle (e.g., 3rd and 9th impulses in Fig. 1)

or at the end (e.g., 5th and 22nd impulses in Fig. 1) of an ISTl. Therefore, they were usually recognized at an ISTl > 120 ms. In general, when a hindbrain neuron responded to a sub-locomotor-threshold stimulus train, it exhibited a longer average IIMI than when responding to a near-locomotor-threshold train.

Abrupt shifts in hindbrain neuronal discharge

Figure 2 shows that throughout a single trial, three types of abrupt shift in the firing of hindbrain neurons could occur either separately or in combination. They included: (1) a k shift in which a new k value could emerge, or one of the preexisting k values could disappear; (2) a shift in the modal or minimal latency value of time-locked impulses; and (3) the emergence of delayed impulses. These abrupt shifts

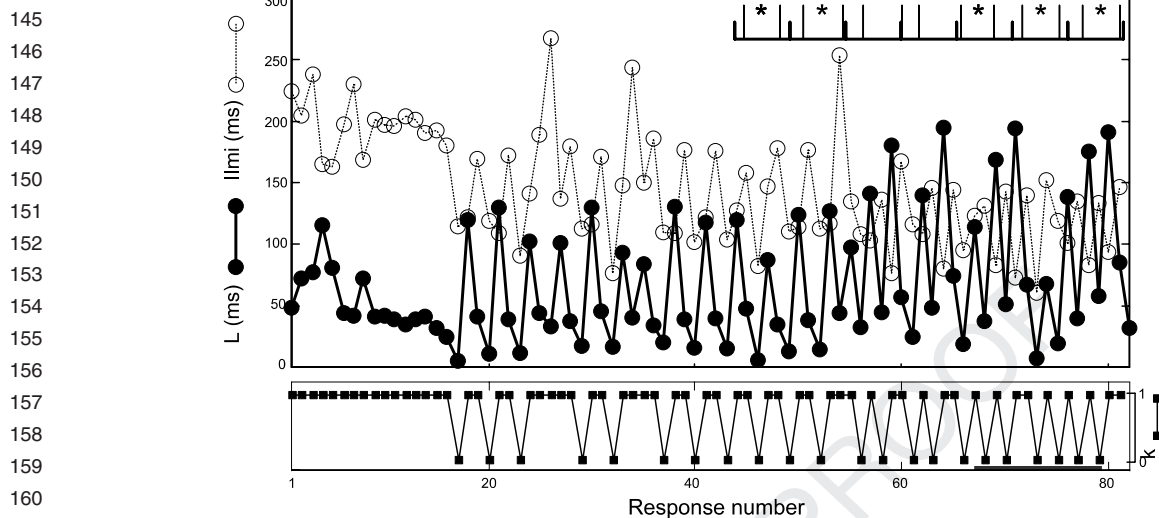


Fig. 2. An example of abrupt shifts in a hindbrain neuron's firing during MLR stimulation. This figure is organized like Fig. 1, except for the k values being presented at the bottom. For this sequence of impulses, the ISTI was 200 ms. The figure shows that after ~ 15 initial inter-impulse intervals at $k=1$, there was a near-regular k alternation from 1 to 0. The *inset* shows an epoch during which five $k=0$ inter-impulse intervals were interspersed with $k=1$ intervals. Note the two abrupt shifts in regular patterns of the response latency (L : i.e., shifts at 17th and 54th impulse).

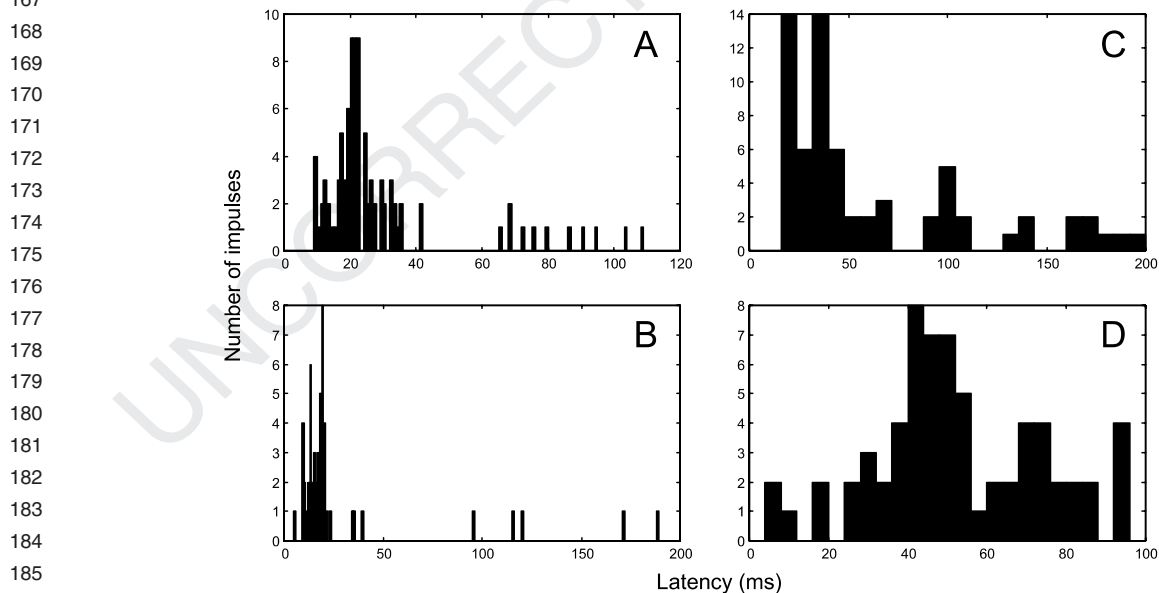


Fig. 3. Latency histograms for the impulses of four exemplary hindbrain neurons during MLR stimulation. (A) Responses (bin width, 1 ms) of the hindbrain neuron shown in Fig. 4 to MLR stimulation at an ISTI of 120 ms (6 μ A pulses). (B) Another neuron's responses (bin width, 1 ms) to MLR stimulation at an ISTI of 200 ms (7 μ A pulses). (C) Responses (bin width, 8 ms) of the hindbrain neuron shown in Fig. 1 to MLR stimulation at an ISTI of 200 ms (9 μ A pulses). (D) Responses (bin width, 4 ms) of a fourth neuron to MLR stimulation at an ISTI of 100 ms (7 μ A pulses). Two- or three-modal distribution of time-locked impulses (reflecting several synaptic translations of the propagating activity throughout the hindbrain) are seen in A–C but a broad unimodal distribution of nonlocked responses is seen in D. See text for discussion.

normally occurred during near-locomotor-threshold stimulus trains. They were also seen, however, in response to sub-locomotor-threshold stimulation.

A longer modal latency could be accompanied by an increase in the k value. For example, at an IStI of 500 ms, one hindbrain neuron exhibited a shift in its modal latency from 26 to 32 ms during $k=1$ firing. This shift was abruptly followed by an alternation of k to values that ranged from 1 to 4. At an IStI of 200 ms, the same cell's modal latency increased from 12 to 35 ms, and the k value changed from 1–2 to ≥ 3 . In yet another neuron, at IStIs of 120 ms there was a latency shift from 13–24 to 31–41 ms, and the abrupt appearance of delayed impulses.

Time-locked and delayed impulses of hindbrain neurons

The time-locked impulses mostly had a latency of 15–40 ms. Usually the range of latencies was 15–30 ms, with 1–3 modes (see examples in Figs. 1–3). A latency of 13–15 ms was characteristic of monosynaptic responses (Fig. 3A and B, first mode). About 7–9 ms of this value involved the conduction time from the point of stimulation (cf. Bar-Gad et al., 1999). Figure 3A shows that disynaptic responses (latency, 18–22 ms) predominated, however. The number of responses with a longer latency (oligosynaptic responses) could be either higher (Fig. 3B, third mode) or not (Fig. 3C, second mode).

Time-locked, mid-IStI and prestimulus impulses could usually be distinguished at an IStI ≥ 200 ms, but rarely at an IStI < 120 ms. At IStIs ≤ 200 ms, the latency of time-locked impulses of some neurons alternated between 15, 21, 28 and 35 ms. At IStIs of 500 ms, however, the time-locked impulses of these same neurons occurred at 28–55 ms. In other neurons, their time-locked impulses aggregated near 35 ms at an IStI of 200 ms, but around 21 and 35 ms at an IStI of 100 ms.

The successive time-locked impulses formed integer kT inter-impulse intervals. But the delayed mid-IStI impulses were commonly preceded and followed by noninteger IImIs (see Methods). The inset in Fig. 1 provides two examples of a delayed impulse that occurred in the middle of an IStI. Each of these mid-IStIs impulses terminated one

integer-and-one half $[k+1/2]T$ interval and began another one $[(k+1)-1/2]T$. These noninteger intervals are marked by asterisks in the Fig. 1 inset. These paired $(k+)$ and $[(k+1)-]$ intervals restrained fluctuations in the duration of IImIs during alternations of the k values. The IImIs within such a $[k+, (k+1)-]$ pair were usually of similar duration but some $k+1$ IImIs could have either a longer or shorter duration than the k ones. The neuron in Fig. 1 produced both time-locked and several delayed impulses at an IStI of 500 ms, too.

Doubling of the discharge rhythm of hindbrain neurons

A doubling of the firing rhythm of hindbrain neurons occurred when both a time-locked and a delayed impulse were generated in the same IStI. For example, in Fig. 2 note that after some mid-IStI impulses emerged, the duration of the IImIs began to alternate with 0+ and 1– IImIs, both with duration of about half the IStI. Then, prestimulus impulses also began to appear (see Fig. 2 inset). When this neuron was responding at an IStI of 500 ms, the delayed impulse was at a mid-IStI when the immediately previous impulse had a latency < 16 ms. If the latency of the time-locked impulse was > 16 ms, however, a delayed impulse appeared either near the end of the corresponding IStI, or it was not generated.

In another neuron (see Fig. 3B), time-locked impulses appeared mostly at 14, 19 and 24 ms, and the k value alternated around 2. Again, the impulses between the 0+ and 1– IImIs occurred at the mid-IStI when a time-locked impulse with a latency of ~ 14 ms began a 0+ IImI. Delayed impulses were prestimulus, however, when the latency of the preceding time-locked impulse was > 19 ms. Figure 4 shows that after this neuron displayed a period of time-locked impulses, two delayed (47th and 49th) impulses appeared. Shortly thereafter, the first 0+ IImI occurred, and, finally, IImIs with a $k > 1$ value disappeared altogether. Each delayed impulse now contributed to a 0+ IImI. All the 0+ IImIs, and some of the 1– ones, had a duration that was half that of the IStI.

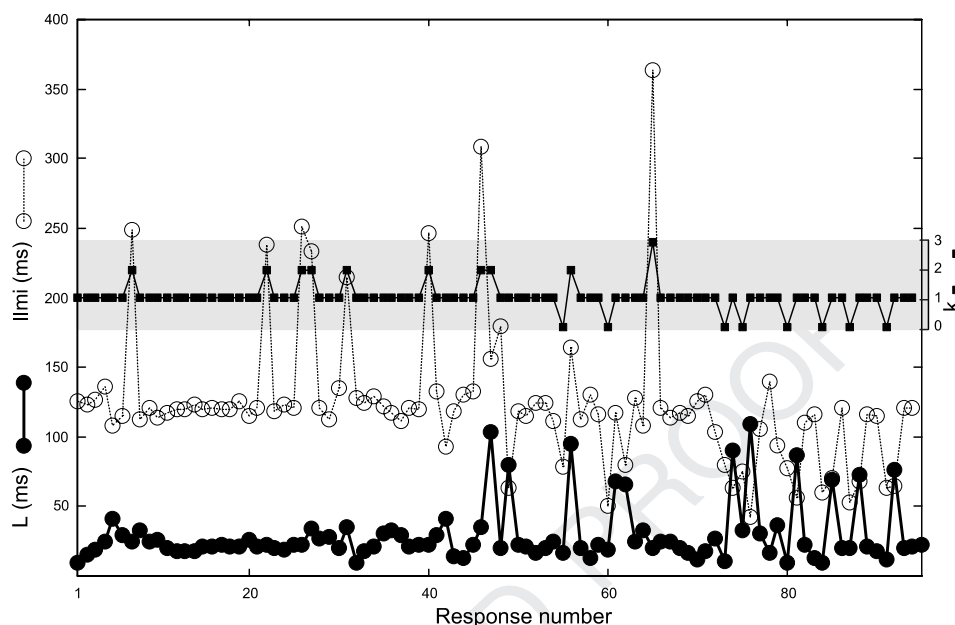


Fig. 4. An example of doubling the rhythm of a hindbrain neuron's discharge. This figure is organized as in Fig. 1 (but without an inset) and Fig. 5 below. The neuron's responses were to an IStI of 120 ms (6 μ A stimulus pulses). Note that the duration of the IImIs first alternated between values of near-120 ms and near-240 ms (i.e., the latter was 100% greater), and later, between near-120 ms and near-60 ms (i.e., the latter was 50% less).

Nonlocked responses of hindbrain neurons

For the present purposes, a nonlocked response was defined as one in which its *average* latency had a value of approximately half the duration of the IStI. Nonlocked impulses were usually distributed uniformly throughout IStI. In contrast to time-locked and delayed responses, they did not form regular patterns. Some neurons generated integer intervals at an IStI of 500 ms but noninteger ones also occurred at an IStI of 200 ms. At an IStI of 100 ms, the latency distribution of the responses could have a maximum of ~ 45 ms (see Fig. 3D). In such cases, categorizing the type of response became equivocal.

For nonlocked impulses, the duration of their IImIs was broadly distributed, with a modal duration that was not related to the duration of the IStI. For example, one neuron's impulses were nonlocked at an IStI of 1000 ms. The modal duration of $k=1$ IImIs was 250 ms, while that for $k=0$ IImIs was 350 ms. The latency of this neuron's time-locked responses was scattered across a span of 42–62 ms, at an IStI of 500 ms. The neuron's IImIs varied from

380 to 650 ms, even during a period of constant $k=1$ discharge. At an IStI of 200 ms, however, this cell's k value shifted from 1 to an alternation between 1 and 2, and its impulses divided into time-locked and delayed ones (Fig. 5). In this neuron, as in several others, firing continued at a slow rate during a few seconds after the conclusion of the stimulation train. Evidently, this neuron was being driven by some distinct sources, which could affect its firing under certain conditions.

Background discharge in the absence of stimulation was exhibited by three of the total sample of 16 neurons, and all three had nonlocked responses to MLR stimulation. At an IStI of 1000 ms, the mean IImI of one of them decreased from 94 to 54 ms, and the mean's standard deviation reduced from 50 to 25 ms. During this cell's background discharge, the distribution of the duration of its IImIs had two modes at 70 and 140 ms. During the stimulus train, this cell's corresponding modes shifted to 40 and 80 ms. For another of these three neurons, the distribution of IImIs of the background discharge had three modes at 100, ~ 220 and

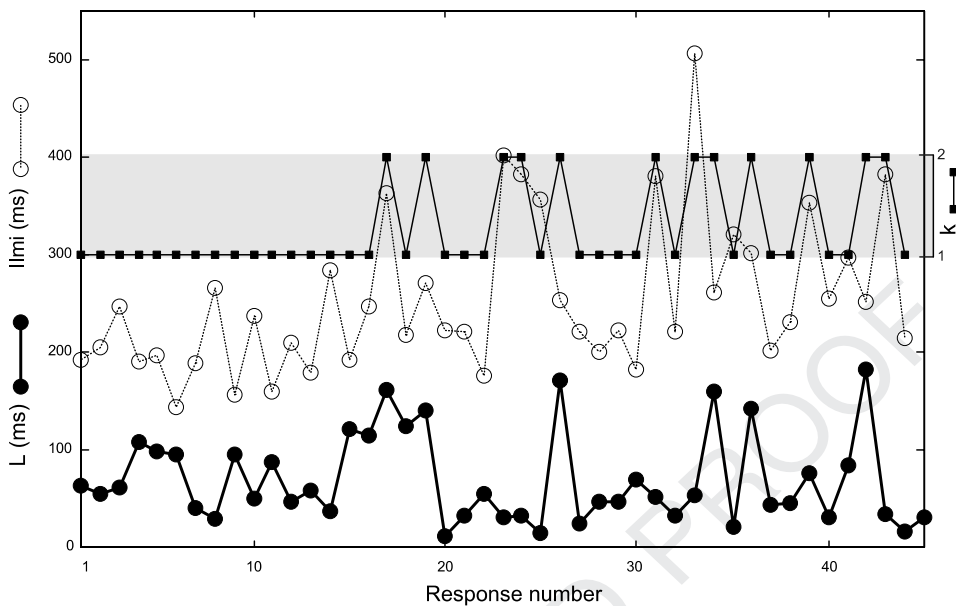


Fig. 5. An example of the progressively decreasing rate of a hindbrain neuron's firing during MLR stimulation. This figure is organized like Fig. 1 (but without an inset). The IStI was 200 ms (10 μ A stimulus pulses). Delayed impulses ($L > 100$ ms) became clearly distinct from time-locked ones when the k value began to alternate between 1 and 2. This neuron continued to fire at a slow rate after the end of the stimulation train.

~ 320 ms. The modal duration was of 140 ms, however, at an IStI of 500 and 200 ms. The duration of the third neuron's IIMIs during its background discharge had a mean value of 200 ms and one, two or three modes at ~ 130 , 260 and 380 ms, in different recordings. These values were the same during sub-locomotor-threshold MLR stimulus trains. During near-locomotor-threshold stimulation, however, the duration of the mean IIMI could decrease to 100 ms.

Discussion

Basic variations in hindbrain neuron responses to MLR stimulation

Some hindbrain neurons responded monosynaptically to at least a portion of the stimulus volleys from the MLR. Such cells presumably recruited other hindbrain neurons oligosynaptically. When near-threshold stimulus pulses were delivered, the synaptic translation time was 5–8 ms. A key point is that this

delay time depended on the time course of the excitatory postsynaptic potential rather than the synaptic delay (Babalian and Shapovalov, 1984; Matsushima et al., 1989; Wu and Wang, 1995).

Propagation of activity among hindbrain neurons initially increased but ceased sharply after 3–4 synaptic translations (Fig. 3A–C). The short-lived hindbrain wave of excitation, when involving a given neuron, could ordinarily not reexcite this neuron after additional translations. It would seem that the excitatory wave *propagated* (i.e., excited *new* neurons) rather than reverberated (reexcited the same neurons). During a given trial, the pathway of the wave (i.e., from neuron to neuron in the hindbrain) and the latency for activation of a given neuron varied. These basic variations prevented prediction of whether a hindbrain neuron would or would not be excited by a given MLR volley. Again, it would seem that a substantial and persistent variability of the amplitude and duration of postsynaptic potentials could have contributed to these variations (cf. Parker and Grillner, 2000; Hatta et al., 2001).

337 ***Significance of near-locomotor-threshold***
 338 ***MLR volleys***

339
 340 The hindbrain neurons activated by a near-locomotor-threshold MLR volley included a small subset of
 341 monosynaptically activated neurons. Even in these
 342 cells, the majority of responses were di- or
 343 oligosynaptic. Indeed, most hindbrain neurons were
 344 recruited after 2–4 translations. It would seem that
 345 the greater the excitation delay, the more the
 346 recruitment of hindbrain neurons must have
 347 depended on interactions among the latter, later-
 348 activated cells. We propose that the MLR facilitates
 349 such interactions by virtue of first monosynaptically
 350 activating the most appropriate ‘input’ hindbrain
 351 neurons. Subsequent translations would then result in
 352 recruitment of the appropriate amount and composition
 353 of hindbrain neurons to ensure that locomotion
 354 could then be brought about by the relevant spinal
 355 networks.
 356

357 We further propose that the stronger the MLR’s
 358 input volley to the hindbrain, the less the number of
 359 translations among the latter’s neurons, and the more
 360 definitive the role of the MLR. Application of
 361 suprathreshold stimuli to MLR engaged more of the
 362 hindbrain neurons monosynaptically. Correspond-
 363 ingly, the hindbrain becomes less autonomous. In
 364 such instance, the predominant and shortest pathway
 365 from the MLR to the spinal cord would be the
 366 reticulospinal one (see Orlovsky, 1970; Sirota et al.,
 367 2000).
 368

369
 370 ***Delayed and nonlocked impulses***

371
 372 Delayed impulses could not be generated by the
 373 short-lived, MLR-evoked excitatory wave in the
 374 hindbrain. Rather, we propose that such impulses
 375 revealed the active contribution of hindbrain neurons
 376 in processing the MLR volley. The results suggest
 377 that it was a matter of chance as to whether a given
 378 IImI, which had been initiated by a time-locked
 379 impulse, would be terminated by a similar or a
 380 delayed impulse. Nonetheless, when both a time-
 381 locked and delayed impulse occurred within the
 382 same IImI, certain rules were evident. These included:
 383 (1) a short-latency impulse could start a noninteger
 384 IImI, whereas a long-latency one could not; (2) an

IImI initiated by time-locked impulse could be designated random-like as an integer or noninteger one when its k value was > 2 ; and (3) if an IImI had a k value of < 1 , its final (closing) impulse could be time-locked or delayed, depending on the latency of the interval’s initial (opening) impulse. The relative degree to which these local rules applied to single hindbrain neurons contributed to their idiosyncratic responses to the MLR volleys.

Evolution of hindbrain neuronal behavior throughout a stimulus train delivered to MLR

In the MLR-activated hindbrain, changes in the firing pattern of single responding neurons, and the number of activated neurons throughout the time course of a single stimulus train, culminated when locomotor movements were about to ensue. This finding was supported by observations on the increase in the test neurons’ firing ratio throughout the evolution of a stimulus train. Such frequency facilitation of the responses of neurons with an initially low firing ratio was also observed previously in hindbrain neurons of the cat (Selionov and Shik, 1990) and rough skin newt (Bar-Gad et al., 1999). Similarly, repetitive stimulation of the cerebral-buccal neuron in *Aplysia californica* was shown to enhance monosynaptic excitatory postsynaptic potentials in its target neurons (Sanchez and Kirk, 2000). Note further that the stimulation of mossy fibers decreases spike threshold in granule cells in the rat cerebellum (Armano et al., 2000). Moreover, reticulospinal cells can exhibit nonlinear amplification and generate high-frequency discharge in the lamprey (Di Prisco et al., 2000). The balance of actions of ATP and adenosine (Dale, 1998), or serotonin modulation of glutamate receptors (Li and Zhuo, 1998), might contribute to the gradual evolution of neuronal discharge too.

The latency between arrival of the input volley from the MLR at the hindbrain and the response of one of the latter’s neurons could increase or decrease throughout a stimulus train. Different types of abrupt shifts might presumably influence distinct target neurons. Hindbrain neurons could experience facilitation, depression or both, throughout the time

course of the same repetitive input from the MLR. All of these behaviors were evident in the hindbrain and their cumulative effect was a key component of the preparation's transition from rest to MLR-evoked locomotion.

Contribution of a single hindbrain neuron to the initiation of locomotion

The results showed that for an MLT stimulus train to reach the threshold for locomotion to ensue there was a trade-off between the strength of the train's stimulus pulses and their inter-pulse interval. This inverse rule was not obeyed by the individual activated-hindbrain neurons, however. Such a neuron could exhibit a doubling of its firing frequency in one near-locomotor-threshold MLR stimulus train, but not in another. Similarly, a given hindbrain neuron could generate two impulses in the ISTIs of both near- and sub-locomotor-threshold trains. Such a neuron could exhibit either an augmented or decreased rate of firing during two *identical* stimulus trains, or during trials with the same *average* duration of IImIs. Similarly, a hindbrain neuron could exhibit a doubling of its firing rate while an adjacent one was generating nonlocked responses.

Concluding thoughts

In the authors' opinion, unstable neuronal discharge is a normal feature of neuronal behavior in the elaboration of movement. It reveals a way by which a single hindbrain neuron contributes to the processing of the input volley from the MLR. The experiments showed that when the MLR was stimulated at near-threshold strength for locomotion to ensue, the activation of hindbrain neurons occurred largely after 2–4 successive synaptic translations. During normal locomotion, it is likely that while interacting hindbrain neurons are developing their output to the spinal cord, they are responding to excitatory input from both the MLR and other higher command centers. Viewed in this light, the facultative nature of the MLR command to the locomotor hindbrain is functionally advantageous. To gain a better understanding of the origin and role of abrupt shifts in the firing of hindbrain neurons during MLR

stimulation, it will next be desirable to record simultaneously from several neurons.

Acknowledgments

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Abbreviations

IImI	inter-impulse (neuronal spike) interval
ISTi	inter-stimulus (pulse) interval
<i>k</i>	number of stimulus pulses between consecutive impulse (neuronal spike) responses
<i>L</i>	latency
MLR	mesencephalic (midbrain) locomotor region
T	duration of an ISTi

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