

The monosynaptic reflex: a tool to investigate motor control in humans. Interest and limits

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Summary – The principle of the monosynaptic reflex used as a tool to explore the excitability of the motoneurons (MNs) is explained and the general methodology of the H reflex is described. The different drawbacks inherent in the technique are then considered: mechanisms other than the monosynaptic excitation of MNs contributing to the H reflex size (limitation of the H reflex size by disynaptic IPSPs, presynaptic inhibition of the terminals, post-activation depression); non-linearity and changes in the 'recruitment gain' in the MN pool; and poor time resolution of the method. Despite these drawbacks, it is emphasized that the H reflex is the only available technique enabling one to investigate changes in transmission in spinal pathways during motor tasks. © 2000 Éditions scientifiques et médicales Elsevier SAS

H reflex / motor control / tendon jerk

Résumé – Le réflexe monosynaptique : un outil pour explorer le contrôle moteur chez l'homme. Le principe du réflexe monosynaptique utilisé comme un outil permettant d'explorer l'excitabilité des motoneurones (MN) est expliqué et la méthodologie générale du réflexe H est décrite. Les différents inconvénients inhérents à la méthode sont considérés : mécanismes autres que l'excitation monosynaptique de la des MN contribuant à l'amplitude du réflexe (limitation de la taille du réflexe H par des PPSI disynaptiques, inhibition présynaptique des fibres la ou post-activation dépression) ; non-linéarité et modifications du gain de recrutement dans la population de MN ; mauvaise résolution temporelle de la méthode. En dépit de ces inconvénients, il est souligné que cette méthode est la seule qui permette d'explorer les modifications de la transmission dans les circuits spinaux au cours du mouvement. © 2000 Éditions scientifiques et médicales Elsevier SAS

réflexe H / contrôle moteur / réflexe tendineux

INTRODUCTION

In the early 1940s the monosynaptic reflex (MSR) was introduced in animal studies as a tool for investigating excitability changes in the motoneuron (MN) pool [53]. When used as a test reflex, it allows one to assess the effect on the MN pool of conditioning volleys in peripheral afferents or descending tracts. During the

1940s and early 1950s this method was used to reveal important features of the input to spinal MNs. The main conclusions emerging from the experiments employing the MSR technique were not changed by experiments using intracellular recordings, which shows the reliability of the method.

In man, percutaneous electrical stimulation of the posterior tibial (PT) nerve evokes in the soleus (Sol)

muscle a well synchronised response [21], the H reflex, which was demonstrated to be monosynaptic by Magladery et al. [35]. The H reflex technique, which is the equivalent of the MSR method in animals, has been extensively used in physiological [56] and pathophysiological investigations [13] in humans. This review focuses on the interest of the H reflex in physiological investigations. The principle of the method and the general methodology are presented and particular attention is then paid to the different drawbacks inherent in the method and to their prevention.

PRINCIPLE OF THE METHOD

The monosynaptic reflex arc

Ia fibres from muscle spindle primary endings of a muscle have monosynaptic excitatory projections onto MNs of this muscle (homonymous projections). This pathway (*figure 1A*) is responsible for the tendon jerk (see the history of the laborious demonstration of this pathway in [38]).

The principle of the monosynaptic test

In a control situation, a test Ia volley, elicited by a constant stimulation, causes the discharge of some MNs (the control test reflex) and creates test EPSPs in other MNs, which are the subliminal fringe of excitation of the reflex (*figure 1B*). If MNs are facilitated (i.e., subliminally excited) by a conditioning stimulation, the size of the test reflex increases because more MNs are fired by the summation of conditioning and test EPSPs. In contrast, if MNs receive conditioning IPSPs, the constant test Ia volley could recruit fewer MNs than in the control situation and the size of the test reflex will be decreased. The method allows one to distinguish between: i) conditioning stimuli without effect on the excitability of the MNs; ii) those which evoke a subliminal excitation of the MNs when applied alone; and iii) those which elicit an inhibition of the MNs. A variant of the method is to compare the amplitude of the MSR in two situations, e.g., rest and voluntary contraction.

The orderly recruitment of MNs in the MSR

Figure 1B also shows that the size of the test Ia EPSP evoked in individual MNs by a constant afferent volley is larger in small MNs supplying slow motor units

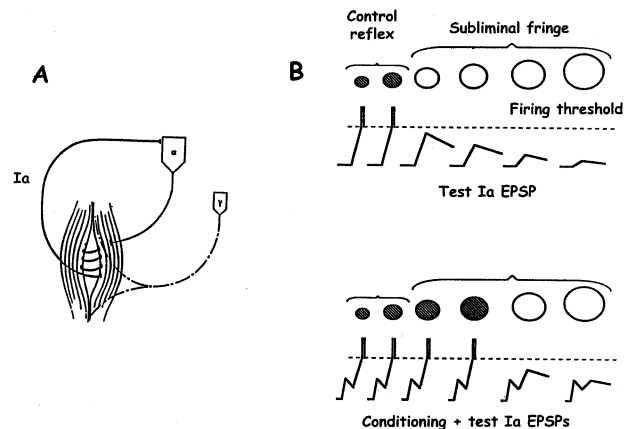


Figure 1. **A:** sketch representing the pathway of the monosynaptic reflex: Ia afferents from muscle spindle primary endings project monosynaptically onto homonymous motoneurons (MNs); the control by γ MNs of the sensitivity to stretch of primary endings is also represented. **B:** sketch representing the principle of the monosynaptic reflex (MSR). In each panel, the circles show the MNs (filled circles representing the MNs discharging in the MSR) and the underlying PSPs are sketched beneath (test Ia EPSPs in the upper panel, conditioning and test EPSPs in the lower panel). The size of the Ia EPSP evoked by a constant stimulation is shown to decrease from the small to the large MNs.

(MUs) than in large MNs supplying fast MUs. As a result, MNs are recruited in an orderly way by the Ia input from the smallest to the largest ones, according to the size principle [20]. Because this orderly recruitment of MNs is preserved when using a variety of excitatory and inhibitory inputs (but not all, see below) facilitation and inhibition will initially affect those MNs that just failed to discharge or were just recruited in the control reflex.

METHODOLOGICAL CONSIDERATIONS

In most healthy subjects at rest, H reflexes can be recorded from Sol, quadriceps (Q), and flexor carpi radialis (FCR) muscles, and tendon jerks can be elicited from Sol, Q, the short head of biceps femoris (Bi), semitendinosus, biceps and triceps brachii. In addition, H reflexes can be recorded from virtually all limb muscles whose parent nerve is accessible to electrical stimulation when a weak voluntary contraction potentiates the reflex by raising the MN pool close to firing threshold.

Recording

Bipolar surface electrodes, placed 1.5–2 cm apart over the corresponding muscle belly, are most commonly used for recording H and tendon reflexes (for the Q the best place is on the anterior aspect of the thigh, 5–10 cm above the patella). In the forearm, a selective voluntary contraction can be used to focus on the desired muscle, since the contraction allows the reflex discharge to occur predominantly or only in the contracting muscle.

Monopolar recordings, with an ‘active’ electrode over the mid-belly of the muscle and a ‘remote’ electrode over its tendon, have been recommended for measurements during voluntary contraction to minimize the changes in geometry of the muscle [19]. In fact, these changes are well taken into account if the reflex is expressed as a percentage of the maximum M wave measured in the same conditions.

Measurement. In practice it makes little difference whether the amplitude or the surface of the reflex is assessed. Whichever way the H reflex is measured, the same method should be used for the maximum M wave (see below).

Stimulation

H reflex

H reflexes are obtained by electrical percutaneous stimulation of Ia afferents contained in the corresponding mixed nerve. The technique to elicit H reflexes is now well codified [4].

Duration of the stimulus. Because the diameter of Ia afferents is larger than that of motor axons, it is generally possible, in Sol, Q and FCR, to evoke an H reflex with stimuli below motor threshold (MT). The strength-duration curves for motor axons and Ia afferents differ, such that the optimal stimulus duration for eliciting the H reflex is long (1 ms, [49]).

Uni- and bipolar stimulation. The best method for ensuring that Ia afferents are excited at lower threshold than motor axons involves placing the cathode over the nerve and the anode on the opposite side of the limb [23], so that current passes transversely through the nerve: thus Sol and Q H reflexes are evoked by monopolar stimulation of the PT nerve in the popliteal fossa and of the femoral nerve (FN) in the femoral triangle, respectively. However, in areas where there are many nerves, bipolar stimulations must be used in

order to avoid the stimulus from encroaching upon another nerve: the median (FCR) is so stimulated at the elbow.

H and M waves. Recruitment curve

Figure 2 summarizes the events occurring in the Sol when increasing the electrical stimulus intensity to the PT nerve (which is generally expressed in multiples of motor threshold). There is first a progressive increase in the reflex amplitude (*figure 2A, B*). When the motor threshold is reached, the short-latency direct motor response (M wave), due to stimulation of motor axons, appears in the EMG. Further increases in the test stimulus intensity cause the M wave to increase while the H reflex decreases (*figure 2C, D*). Finally, when the direct motor response is maximum, the reflex response has totally disappeared (*figure 2E, F*). This is because the antidromic motor volley set up in motor axons collides with and eliminates the H reflex ([22], *figure 2F*). These variations of the H and M responses with the test stimulus intensity are shown in the recruitment curve of *figure 2G*.

M max. M max is evoked by the recruitment of all motor axons and provides an estimate of the response given by the whole MN pool.

In fact, this is often an overestimation because it is impossible to restrict the stimulus to only motor axons of the muscle tested: e.g., the M max response following median nerve stimulation comes from the FCR, plus finger flexors plus pronator teres.

M max must always be measured since: i) it provides an estimate of the proportion of the MN pool tested by the MSR; ii) expressing the reflex as a percentage of M max (assessed in the same conditions) enables one to get rid of the changes in muscle geometry related to muscle length and contraction.

Small M wave to monitor the stability of the stimulation conditions. If the H reflex is performed during a manoeuvre which can alter the test stimulation (e.g., muscle contraction), it is necessary to ensure that any changes in the test H reflex are not due to a change in the position of the electrode with respect to the nerve. To that end, the site and intensity of stimulation must be adjusted so that the test stimulus also evokes an M wave, the constancy of which is used to monitor the stability of the stimulation conditions.

Descending part of the recruitment curve. However, the control test reflex should never be chosen in the descending part of the recruitment curve (see *figure 2G*), since, as explained below, slow MNs responsible for the

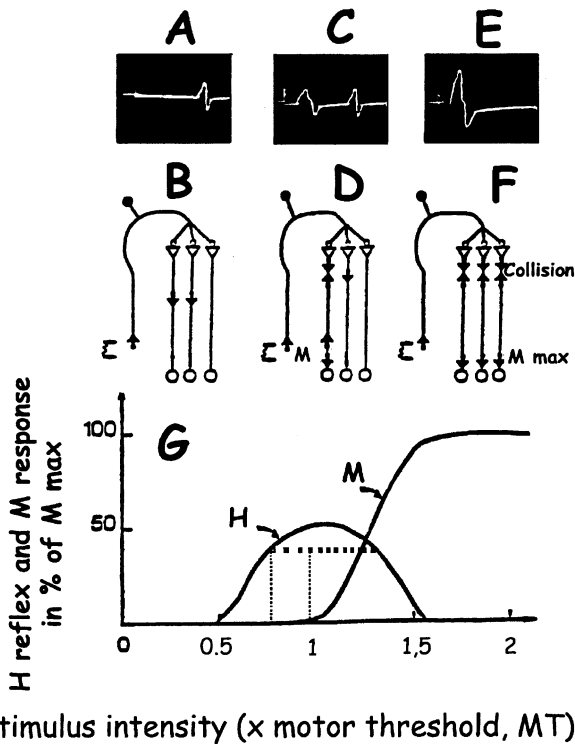


Figure 2. Diagram summarizing the events resulting in the production of reflex and motor responses. **A, C** and **E**: EMG responses in soleus following electrical stimulations of the posterior tibial nerve (PTN) at increasing stimulus intensities. **B, D**, and **F**: illustrations of impulses (arrows) propagating along Ia afferents and motor axons: **A-B**: the stimulus activates only Ia fibres and results in some MNs in an H reflex; **C-D**: the stimulus is increased and activates both Ia fibres and some motor axons and results in a direct motor response (M) and a reflex (H); **E-F**: the SM stimulus is supramaximal for all motor axons and results only in a maximum direct motor response, the reflex response being blocked by a collision with the antidromic motor volley. **G**: the amplitude of the motor (M) and reflex (H) responses (expressed as a percentage of M max) is plotted against the intensity of the electrical stimulation of the PTN (expressed in multiples of motor threshold). The dotted line shows that in some subjects the reflex stops to increase at stimulus intensities below 1.2 MT. (From [30].)

H reflex visible in the EMG are then insensitive to excitation or inhibition.

The H reflex and the M wave do not recruit the same MNs: small MNs innervating slow MUs are first recruited in the H reflex (see The orderly recruitment of MNs in the MSR), whereas electrical stimulation giving rise to the M wave first activates axons with a large diameter innervating fast MUs. As a result, in the descending part of the recruitment curve, reflexes ap-

pearing in the EMG are produced by small MNs, in which the collision in motor axons has not taken place. The reflex response given by the fastest MUs of the H reflex, i.e., those that are the most sensitive to excitation and inhibition (see The orderly recruitment of MNs in the MSR), has collided in motor axons with the antidromic motor volley (*figure 2C, D* and *G*) and has been eliminated from the EMG.

Tendon jerk

In some proximal muscles, where the H reflex is not easily distinguishable from the M wave (e.g., biceps and triceps brachii), the excitability of the MN pool may be tested by eliciting tendon reflexes using an electromagnetic hammer producing reproducible transient stretches.

The interpretation then is complicated by the fact that the amplitude of the reflex response elicited by the tap also depends on the γ fusimotor drive controlling the sensitivity to stretch of muscle spindle primary endings (see *figure 1*). In this respect, it has been proposed to use differences in H and tendon reflexes as reflecting the action of the γ drive on the tendon jerk [49], since both reflexes are mediated through the same pathway, except that the tendon jerk is elicited through activation of primary endings, the sensitivity of which is controlled by γ efferents. In fact, in addition to γ activity, H and tendon reflexes differ in several respects (involvement of more Ib afferents, better synchronization and shorter duration of the afferent Ia volley in the test volley of the H than in the tendon reflex), which makes comparisons of the H and tendon reflexes not reliable as measures of γ activity [3].

Random alternance of control and conditioned reflexes

In most investigations, the MSR is used as a test reflex to assess the effect of conditioning volleys on the MN pool, and the size of the reflex is compared in the absence (control reflex) and in the presence (conditioned reflex) of the conditioning volley. Control and conditioned reflexes must be randomly alternated, since: i) this prevents the subject from knowing the reflex to come and to voluntarily alter it; ii) regular alternance produces erroneously larger results [16], likely due to post-activation depression (see below).

Any conditioning stimulation > 1 x MT producing a stretch of the tested muscle induces a post-activation depression of the test reflex (see below). When using a

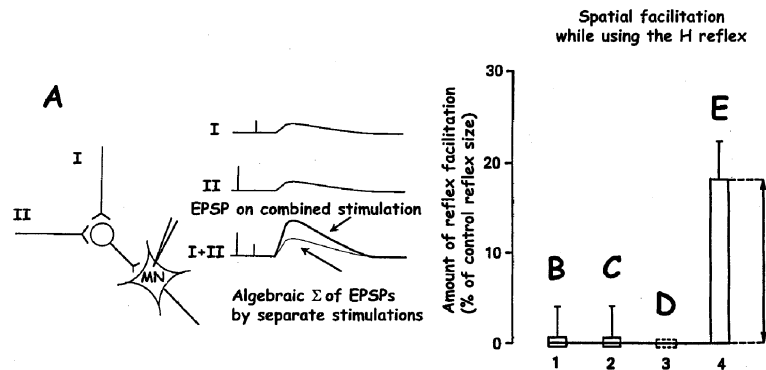


Figure 3. Spatial facilitation technique. **A:** sketch showing the principle of the technique when recording from a MN in animal experiments (adapted from [33]). **B-E:** the amount of facilitation of the FCR H reflex (difference between conditioned and control reflexes expressed as a percentage of the control reflex value) is compared in different situations: separate stimulation of the median nerve (**B**, 0.4 x MT, 6 ms conditioning-test interval), separate stimulation of the musculo-cutaneous nerve (**C**, 0.8 x MT, 5 ms conditioning-test interval) and combined stimulation (**E**). The column in **D** represents the algebraic sum of effects by separate stimuli. (From [6].)

regular stimulation at 0.3 Hz, this conditioning-induced depression will systematically reduce more the following control (3.3 s later) than the conditioned reflex (6.6 ms later). Thus, an excitatory effect evoked by the conditioning stimulation will appear larger because control reflexes will be smaller. In contrast, control and conditioned reflexes are similarly depressed by homosynaptic depression in the random alternance.

Spatial facilitation technique

Principle of the spatial facilitation technique

The spatial facilitation technique used to demonstrate convergence from two different fibre systems (I and II) onto common premotor interneurons while recording EPSPs in one MN in animals [33] rests on a comparison of effects of stimulation of these fibre systems when given separately and jointly. Spatial summation at a premotoneuronal level is inferred when the EPSP on combined stimulation (I + II) is larger than the algebraic sum of EPSPs evoked by separate stimulation of I and II systems (*figure 3A*).

Spatial facilitation judged from monosynaptic test reflexes

The principle of the spatial facilitation technique can also be applied while using a monosynaptic reflex to assess the MN pool excitability: the excitatory effects of two conditioning stimuli (I and II) are measured when applied separately and together and summation of excitatory effects elicited by I and II in common interneurons can be considered when facilitation of the reflex

on combined stimulation (I + II) is larger than the algebraic sum of the facilitations evoked by separate stimuli [17]. Thus, in the example illustrated in *figure 3B-E* [6], the H reflex recorded in the FCR was conditioned by two conditioning stimuli applied to the median (0.4 x MT) and to the musculoscutaneous nerves (0.8 x MT) (conditioning-test interval 6 and 5 ms, respectively). When applied separately, they did not modify the size of the test reflex (*figure 3B* and *C*), whereas, when applied together, they evoked a facilitation of the reflex (*figure 3E*), which was much larger than the algebraic sum of effects by separate stimuli (*figure 3D*). This extra facilitation on combined stimulation (double-headed arrow in *figure 3E*) indicates that volleys from median and musculoscutaneous converge onto excitatory premotoneurons.

Caveats

However, because the H reflex assesses the excitability of a MN pool, the extra facilitation on combined stimulation could also result from non-linearity or inhomogeneity within the pool, which have to be ruled out before inferring summation at a premotoneuronal level.

Non-linearity: at low reflex amplitudes the sensitivity of the H reflex to facilitation increases with increasing sizes of the control reflex (see below).

The resulting non-linear summation (within the pool) of the conditioning EPSP with the test EPSP could by itself be the cause of an extra facilitation evoked on combined stimulation: an excitatory

conditioning stimulus (I) increases the size of the test reflex and, if this reflex is small, this increases its susceptibility to facilitation by the second stimulus (II).

This drawback can be excluded by adjusting the strength of the conditioning stimuli so that at least one of them does not evoke any H reflex facilitation by itself [17].

Inhomogeneity would occur if the distribution of the conditioning EPSPs within the pool was different from that of the test Ia EPSPs (which excite preferentially slow MNs, see The orderly recruitment of MNs in the MSR).

The conditioning EPSPs might then excite preferentially fast MNs but insufficiently to allow them to be recruited by the test reflex, thus giving no demonstrable effect with separate stimuli. On combined stimulation, summation of conditioning EPSPs in these fast MNs would increase their excitability enough to fire them in the test reflex, producing an extra facilitation at MN level [17].

As discussed below (see Changes in the 'recruitment gain' in the MN pool), experiments in single MUs are required to eliminate this possibility.

A similar method is used to demonstrate convergence in inhibitory pathways (the reflex inhibition on combined stimulation is larger than the sum of inhibitions by separate stimuli).

CONTRIBUTION OF OLIGOSYNAPTIC PATHWAYS TO THE H REFLEX

Disynaptic inhibitory pathways may help limit the H reflex size

In some subjects, as shown by the dotted line in *figure 2G*, the stop in the increase in the H reflex size cannot be explained by the collision of the reflex discharge with the antidromic motor volley, since it occurs at intensities below $1 \times MT$. Thus, inhibitory pathways activated by the test volley help limit the H reflex size [5]. This might be a drawback of the method, since this implies that, while the first MNs participating in the H reflex are recruited at monosynaptic latency [35], the recruitment of higher threshold MNs may depend on pathways in which interneurons are interposed. Two disynaptic inhibitory pathways are good candidates (*figure 4A*): Ib inhibitory interneurons which are co-activated by Ia afferents, and Renshaw cells activated

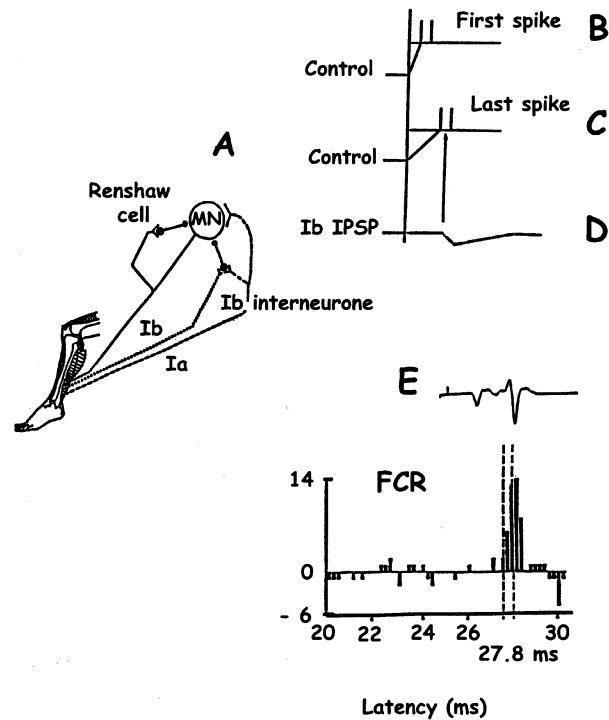


Figure 4. Disynaptic inhibitory pathways may help limit the size of the H reflex. **A:** the pathways of Ib inhibition (onto which Ia afferents converge, cf. [27]) and recurrent inhibition are sketched; bars and small filled circles indicate excitatory and inhibitory synapses respectively. **B-D:** because of the rise time of the test EPSP, the generation of the spike is delayed, and a disynaptic inhibitory volley entering the spinal cord synchronously with the monosynaptic test Ia volley may suppress the generation of the spike, at least in the last MNs recruited in the desynchronized reflex discharge (adapted from [52]). **E:** the amplitude of the H reflex in the FCR is compared to the initial part of the peak of homonymous Ia excitation in the PSTH of an individual FCR MU.

by the first MNs to discharge in the H reflex. *Figure 4B-D* explains how a disynaptic IPSP, which reaches MNs 0.8 ms later than monosynaptic Ia EPSPs [52], may derecruit MNs activated by the monosynaptic volley: because of the rise time of the test Ia EPSP, the generation of the spike is delayed, and there is time enough for the disynaptic IPSP to suppress the spike in the last motoneurons contributing to the test reflex discharge (there is at least 1 ms between the firing of the first and last individual motoneurons contributing to the H reflex, see [36]).

Do changes in disynaptic pathways contribute to changes in reflex size?

The question then to arise is the extent to which a conditioning stimulation is able to modify the H reflex size by changing the transmission in these inhibitory pathways. This may be approached by comparing the effects of a given conditioning stimulus on the H reflex and on the peak of homonymous Ia excitation in the PSTH of single units, in which it is possible to isolate the early, purely monosynaptic, part of the excitation. This is illustrated in *figure 4E*, showing the peak of homonymous monosynaptic Ia excitation in an FCR unit following median nerve stimulation (0.2 ms bin width). Since during its first 0.6 ms, the Ia excitation is not contaminated by any non-monosynaptic effect, the first three bins of the peak (between the two dashed lines) only depend on the size of the underlying monosynaptic Ia EPSP. If the contribution of Ib (or recurrent) pathways to changes induced by a given conditioning stimulation in the H reflex is not significant, this conditioning stimulation should evoke similar changes in the H reflex and in this initial part of the peak of excitation in single units. This has been proved to be the case with various conditioning stimuli so far explored and including vibratory inhibition [47], group II excitation [37], motor cortex stimulation [40] or in active maintenance of standing [28] or voluntary co-contraction of antagonists [46]. This suggests that the contribution of disynaptic pathways to the changes observed in the H reflex is not significant with respect to the changes in excitability of the MNs (and/or in presynaptic inhibition of Ia terminals, see below).

PRESYNAPTIC INHIBITION OF IA TERMINALS

This is a major drawback of the H reflex technique.

Gating of the afferent volley of the MSR

Frank and Fuortes [18] described a depression of monosynaptic Ia EPSPs which occurred without any observable change in MN membrane potential and conductance. This presynaptic inhibition, which is accompanied by primary afferent depolarization (PAD), is caused by axo-axonal GABA-ergic synapses (for references, see [55]) and transmitted by interneurons, referred to as PAD interneurons. In the cat, the resulting depression of the MSR lasts for several hundred ms and may be very dramatic [14]. In man, highly signifi-

cant changes in presynaptic inhibition of Ia terminals have been observed during voluntary movements [26] and after cortical stimulation [40]. A change in presynaptic inhibition of Ia terminals as well as in excitability of MNs must therefore be systematically considered when observing a change in the amplitude of the MSR.

Methods to assess presynaptic inhibition of Ia terminals in man

Different methods have been set up to assess presynaptic inhibition of Ia terminals in humans and to estimate the extent to which a change in H reflex amplitude reflects a change in this gating [51].

Assessing the efficiency of a conditioning stimulation in eliciting presynaptic inhibition of Ia terminals

Presynaptic inhibition of Ia terminals mediating the afferent volley of the test reflex is induced by a conditioning volley (vibration or electrical stimulation). The resulting reflex depression, the amount of which depends on the excitability of PAD interneurons, is then assessed: the larger this excitability, the larger the presynaptic inhibition of the test afferent volley and thus the reflex depression.

The vibratory paradox. Study of presynaptic inhibition in man has started with the vibratory paradox. Application of vibration to the Achilles tendon results in a depression of the soleus H reflex. Since the vibration-induced depression is seen along with a motor discharge (the tonic vibration reflex), reflecting an increased excitability of the MNs, the reflex depression must reflect a presynaptic mechanism. It has been postulated that this mechanism is presynaptic inhibition accompanying PAD [12]. However, when the conditioning vibration is applied on the homonymous tendon, the post-activation depression evoked by repetitive synaptic activation (see below) also contributes to the vibratory-induced depression of the reflex and makes the method invalid for investigating PAD of Ia terminals [44].

Short vibration of a heteronymous tendon. Another method has therefore been developed [43, 47] where the conditioning stimulation is a tap (or a brief train of three taps) applied to the tendon of a heteronymous flexor muscle (TA or biceps femoris). The resulting Ia volley from the flexor muscle is intended to produce activation of PAD interneurons and presynaptic inhibition of Ia afferents mediating the afferent volley of the

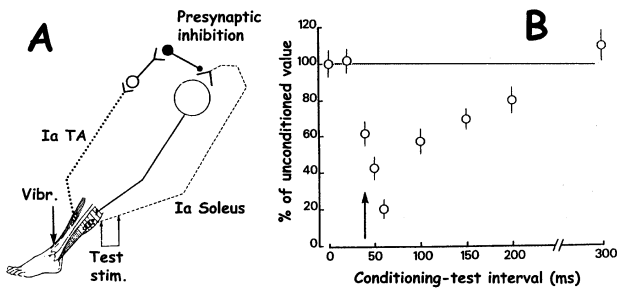


Figure 5. Changes in heteronymous vibratory inhibition of the soleus H reflex at the onset of soleus voluntary contraction. The experimental paradigm is sketched in **A**: the vibration-induced Ia discharge from tibialis anterior elicits presynaptic inhibition of soleus Ia terminals; bars and small filled circles indicate excitatory and inhibitory synapses respectively. **B**: time course of vibratory inhibition of the soleus H reflex at rest: the amplitude of the H reflex, expressed as a percentage of its unconditioned value, is plotted against the conditioning-test interval. (Modified from [51].)

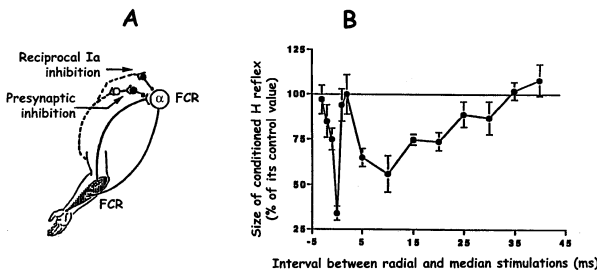


Figure 6. Radial-induced reciprocal Ia and D1 inhibition of the FCR H reflex. **A**: presumed pathways. **B**: the amplitude of the FCR H reflex (expressed as a percentage of its unconditioned value) is plotted against the conditioning-test interval. (Adapted from [40].)

test reflex (figure 5A). As shown in figure 5B, the conditioning vibration evokes a clear inhibition of the soleus H reflex, that has a long duration (200–300 ms), much as has been described for presynaptic inhibition of Ia afferents in the cat hind limb [14].

D1 inhibition. A variant of the method is the D1 inhibition in which PAD interneurons are activated by an electrically-induced conditioning volley to the radial nerve or to the common peroneal (CP) nerve which evokes in the H reflex of the antagonistic muscle (FCR [2] and Sol [42]) two phases of inhibition (figure 6): i) the early disynaptic reciprocal Ia inhibition followed by ii) a long lasting inhibition (5–30 ms), which has been called D1 and attributed to presynaptic inhibition of Ia

afferents mediating the test volley. The finding that, at conditioning-test interval corresponding to D1 inhibition of the H reflex, the same conditioning volley does not modify the cortical-evoked response in the FCR [2] and in the Sol [15] supports this presynaptic interpretation (a post-synaptic inhibition should suppress both H and cortical-evoked responses).

Assessing monosynaptic Ia facilitation of the H reflex

With this method, which relies on the existence of heteronymous monosynaptic Ia projections from Q to Sol MNs (figure 7A), the ongoing presynaptic inhibition exerted on Ia afferents mediating a heteronymous conditioning volley is assessed [25]. A conditioning volley is applied to the FN and produces a facilitation of the Sol H reflex, the time course of which is shown in figure 7B. Since during its first 0.6 ms the monosynaptic Ia excitation is not yet contaminated by any other effect (see above), the reflex facilitation then depends only on the size of the conditioning Ia EPSP. A constant conditioning stimulation should elicit an EPSP of constant size in MNs, and thus a constant reflex facilitation, unless presynaptic inhibition of Ia afferents mediating the conditioning volley is changing. The amount of heteronymous facilitation can therefore be used to assess ongoing presynaptic inhibition on these Ia fibres: the larger the reflex facilitation, the smaller the presynaptic inhibition (e.g., filled column in figure 7C shows the huge increase in this facilitation at the onset of Sol contraction). The validity of this method was established in animal experiments, but, as discussed below, a change in the recruitment gain of the reflex might also modify the amount of reflex facilitation, a possibility which can only be discarded by recording single MUs.

POST-ACTIVATION DEPRESSION

Another, and very different presynaptic mechanism, is the post-activation depression at the synapse Ia afferents-MNs, which is due to a reduced transmitter release from previously activated fibres. In figure 8 (from [9]), the time course of the recovery of the H reflex is shown after various conditioning stimuli: preceding H reflex (A, [34, 49]), subliminal tendon tap (B, [29]), voluntary contraction of ankle muscles (C-D, [9]). In all cases, the reflex depression is very dramatic at short intervals (1–2 s), and then progressively decreases.

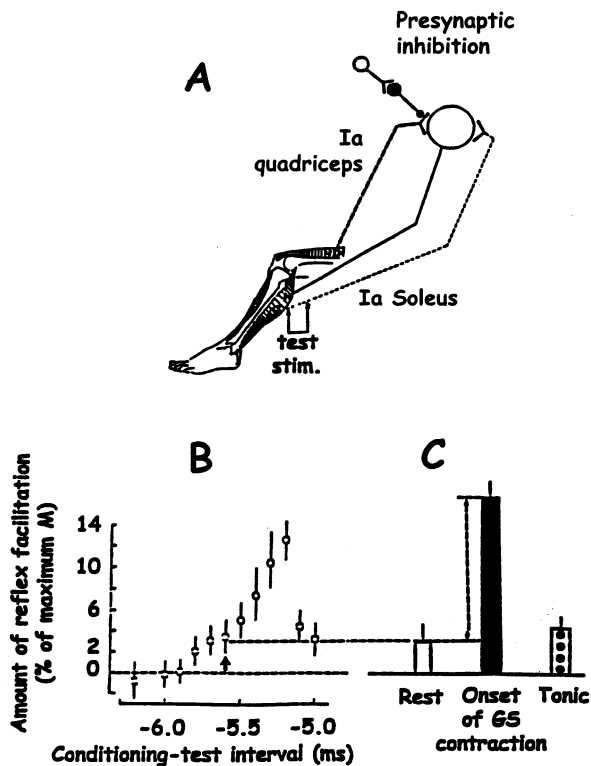


Figure 7. Changes in heteronymous Ia facilitation from quadriceps to soleus at rest and at the onset of soleus voluntary contraction. The experimental paradigm is sketched in **A**: the soleus H reflex is conditioned by a heteronymous Ia volley from quadriceps, whose efficiency to facilitate the reflex depends on presynaptic inhibition; bars and small filled circles indicate excitatory and inhibitory synapses respectively. **B**: time course of the early facilitation of the H reflex: the amount of reflex facilitation, i.e., the difference between the conditioned and control reflexes expressed as a percentage of M_{max} , is plotted against the conditioning-test interval. Owing to the more proximal position of the conditioning electrodes, the test shock has to be delivered before the conditioning one and the conditioning-test interval is said to be negative. The arrow indicates the conditioning-test interval (-5.4 ms) used in **C**. **C**: Amount of reflex facilitation at rest (open column), at the onset of GS contraction (filled column) and during tonic GS contraction with an equivalent level of EMG activity (column with dots). The test stimulus intensity was adjusted to obtain unconditioned reflexes of similar size at rest and during contraction. Each column represents the mean of 100 measurements. Vertical bars 1 standard error of the mean. Double headed arrow is the supplementary facilitation during contraction, i.e., the difference between the facilitation during contraction and that at rest. (From Pierrot-Deseilligny, [51].)

General frequency of stimulation

Figure 8A shows that, because of this depression, there is reflex attenuation as stimulus rate is increased above

0.1 Hz. Even though this attenuation requires at least 10 s to completely vanish, it is weakened enough after 3–4 s to allow explorations at 0.2–0.3 Hz. There is a compromise to find between this depression and the necessity to collect a large number of reflexes because of the reflex variability.

Post-activation depression from other origins

If effects of the stimulus rate on the reflex size have long been known and are generally taken into consideration, this is often not the case for the post-activation depressions from other origins.

Post-activation depression following the Ia discharge elicited by a passive stretch of the tested muscle is very dramatic [24]. Under these conditions any conditioning stimulation $> 1 \times MT$ producing a stretch of the tested muscle may induce a post-activation depression of the test reflex (when using the Sol H reflex this occurs with stimuli eliciting a TA contraction but can also occur after a contraction of thigh muscles, depending on the limb position).

Post-activation depression elicited by a voluntary contraction, which by itself generates Ia activity has also to be taken into account: this can be the Ia discharge due to co-activation of β -efferents during contraction of the tested muscle (figure 8D) or the Ia discharge elicited by the stretch of the tested muscle during a phasic contraction of its antagonist (figure 8C). Many misinterpretations have arisen when comparing changes in the test reflex observed at rest and during (or after) a voluntary contraction because this factor had been neglected. In order to be sure to eliminate the effects of movement-induced post-activation depression, test and conditioning stimuli have to be triggered at the very onset of the movement and at least 8 s after the end of the preceding movement [9].

Post-activation depression in conditioning pathways

In investigations where the involvement of a specific conditioning pathway is compared at rest and during contraction, a similar post-activation depression may alter the transmission in the conditioning pathway: e.g., the transmission of the Ia volley from the antagonistic muscle used to elicit reciprocal Ia inhibition of the tested motor nucleus is altered during voluntary contraction of the antagonistic muscle [24].

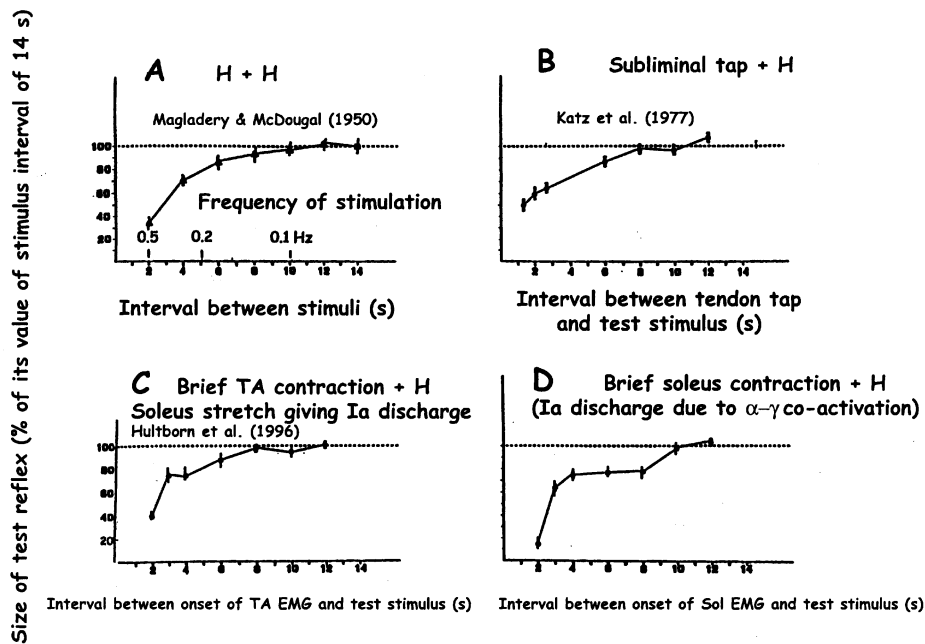


Figure 8. Post-activation depression. **A-D:** the size of the soleus H reflex (expressed as a percentage of its unconditioned value) is plotted against the conditioning-test interval. This shows the time course of the recovery of the H reflex after various 'conditioning' stimuli: **A:** a preceding H reflex (note that the abscissa is also graduated in Hz corresponding to the frequency of stimulation of the H reflex); **B:** a subthreshold tendon tap; **C:** a brief tibialis anterior voluntary contraction producing a Ia discharge due to soleus stretch; **D:** a brief soleus voluntary contraction producing a Ia discharge due to α - γ coactivation. (From [9].)

NON-LINEARITY WITHIN THE MN POOL

Different sensitivity of MSRs of different size

Another drawback of the method comes from the fact that the susceptibility of the H reflex to facilitation and inhibition varies with the size of the unconditioned reflex [8]. This is sketched in *figure 9*, where the amount of facilitation or inhibition elicited by a constant conditioning facilitatory (or inhibitory) input is plotted against the size of the control reflex. When the conditioning input is strong (continuous line), with increasing size of the control test reflex, the number of additionally recruited (or derecruited) MNs first increases, and then decreases. When the effect of the conditioning input is moderate (dotted line), there is a plateau between the two phases of increase and decrease. Several factors, including the intrinsic properties of the motoneurons and the distribution of test EPSPs and conditioning inputs within the motoneurone pool contribute to this effect.

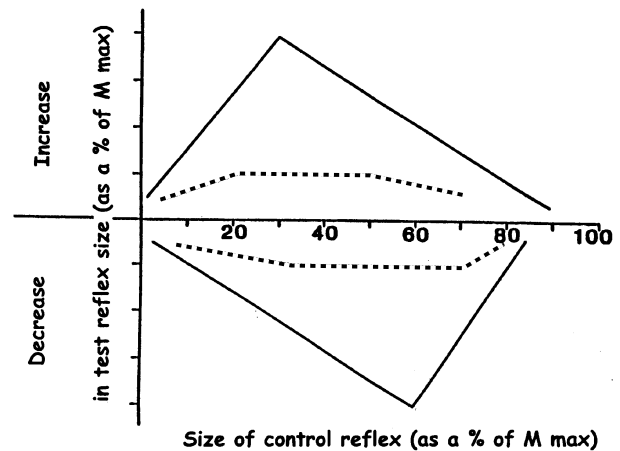


Figure 9. Diagram showing the sensitivity of monosynaptic reflexes to facilitation (upper part; strong facilitation, continuous line; weak facilitation, dashed line) and inhibition (lower part; strong inhibition, continuous line; weak inhibition, dashed line), as a function of the control reflex size. (From [8].)

Consequences when using the MSR

This factor has to be taken into account when using the spatial facilitation technique (see above) and when comparing the effects of a conditioning input in two situations (e.g., rest and contraction), where the size of the control H reflex evoked by the same test stimulation is different. In the latter case, ‘adjusting’ the test stimulus intensity so that the size of the unconditioned reflex is the same may seem to obviate the problem. However, changing the test stimulus intensity has two drawbacks: i) this changes the Ib volley which may help determine the size of the reflex (see above); ii) if the test reflex is applied to a voluntarily activated muscle, the weak test stimulus will overcome less easily the refractoriness of Ia afferents activated by the β - γ drive.

CHANGES IN THE ‘RECRUITMENT GAIN’ IN THE MN POOL

This concept, introduced by Kernell and Hultborn [31], is sketched in *figure 10*, which represents the input-output relation within a MN pool in two situations (rest and soleus voluntary contraction). Although the problem is very general, it is discussed below with respect to the enhanced femoral-induced facilitation of the soleus H reflex observed at the onset of soleus contraction (see *figure 7C*). The output (number of MNs recruited by the reflex discharge) is plotted against the ‘pool drive’, which implies three factors: i) the test Ia volley; ii) the conditioning effect (the monosynaptic femoral-induced EPSP in the example chosen); and iii) the ‘recruitment gain’, which is the slope of the input-output relation (which, for simplicity’s sake, is supposed to be linear). Vertical arrows on the left show the size of the control test reflex (continuous line), of the amount of reflex facilitation by the conditioning femoral EPSP at rest (dotted line), and of the increased facilitation of the reflex at the onset of contraction (dashed line). Assuming that the slope of the input-output relation is not modified during contraction, the increased facilitation of the reflex at the onset of contraction must reflect an increase in the conditioning EPSP (dashed horizontal arrow), attributable to a decrease in presynaptic inhibition of Ia afferents. However, this increased reflex facilitation could also be observed without increase in the conditioning EPSP, if there was during contraction a compression of the functional thresholds in the motoneurone pool (like in an accordion) and thereby an increase in the slope of

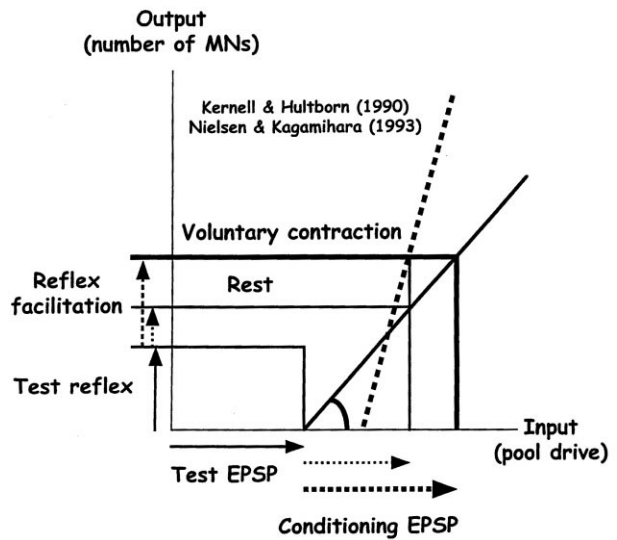


Figure 10. The input-output relation in the MN pool is represented at rest (continuous oblique line) and during a possible change in the recruitment gain occurring during contraction (interrupted oblique line). Vertical arrows represent the size of the control test reflex (continuous line) and the amount of femoral-induced facilitation of the reflex at rest (dotted line) and at the onset of Sol voluntary contraction (dashed line). (Adapted from Kernell and Hultborn [31].)

the input-output relation, sketched by the dashed thick oblique line.

This possibility has been observed by Nielsen and Kagamihara [45] in the tibialis anterior after stimulation of the sural nerve, where it results from a skewed distribution of cutaneous inputs within the MN pool (with inhibition of slow and facilitation of fast MNs). The only way to discard it with certitude is to record in parallel PSTHs of single units in order to detect whether the conditioning heteronymous Ia EPSP is changed or not in individual units. However, it is somewhat reassuring that changes in the recruitment gain have so far only been observed in heterogeneous muscles with fast and slow units, like the tibialis anterior, but not in the more homogeneous Sol.

TIME RESOLUTION OF THE MSR METHOD

Estimation of the central delay

In order to characterize the explored pathway (mono-, di-, or polysynaptic), it is essential to estimate its central delay. This can be made by comparing the earliest conditioning-test interval at which the test reflex is modified with the interval corresponding to a

synchronous arrival of the two volleys at spinal level: the longer the difference between these two values the more synapses are involved. However, the time resolution of the H reflex method is poor and leads to an underestimation of this central delay: for example, despite the extra 0.8 ms due to the interneurone interposed in the pathway of disynaptic reciprocal Ia inhibition, the earliest conditioning-test interval with inhibition corresponds to a simultaneous arrival of the two volleys at spinal level [11]. Already, the same finding in animal experiments had led Lloyd [32] to conclude (erroneously) that the pathway of this inhibition was monosynaptic. In fact, as shown in *figure 4B-D* (inspired by [1]), because of the rise time of the test Ia EPSP, the generation of the spike is delayed and the disynaptic IPSP may suppress the spike in the last MNs contributing to the test reflex discharge. Thus, the MSR method, because it explores a pool of MNs, does not give an accurate estimate of the central delays of the explored effects. To that end, investigations on single MUs are necessary.

Estimation of the duration of PSPs in MNs

The duration of the disynaptic reciprocal Ia inhibition from TA to Sol in man is much shorter when assessed with the synchronous H reflex (2–3 ms) than in the ongoing rectified voluntary EMG (15 ms) [50]. This probably reflects that the hyperpolarization of the MNs during the decay phase of the IPSP may prevent the asynchronous firing of the MNs in the EMG but not their synchronous response in the reflex. Accordingly, in animal experiments, it has been shown that the synchronous response characterizing the MSR is only significantly depressed during the rising phase of the underlying IPSP (i.e., when the hyperpolarization is accompanied by changes in the membrane conductance of the MNs) and hardly in the following decay phase [1].

EXPLORATION OF SPECIFIC PATHWAYS

This review focused on the validity of the H reflex as a tool to explore the excitability of the MNs. Specific methods are of course required to assess the response of MNs following the activation of a given spinal pathway, and reliable methods are now available to investigate several spinal pathways in humans: recurrent inhibition of homonymous [7] and heteronymous MNs [41], heteronymous monosynaptic Ia excitation [39],

reciprocal Ia inhibition [10, 11, 59], non-monosynaptic Ia excitation [17, 36], cutaneous depression of non-monosynaptic Ia excitation [48], presynaptic inhibition of Ia terminals [2, 25], post-activation depression [9], Ib inhibition [52], group II excitation [58], and polysynaptic pathways activated by flexion reflex afferents [23, 54].

CONCLUSION

The technique of the H reflex is simple, but a strict methodology is required to be able to validly interpret the results (e.g., it is necessary to take into account the post-activation depression and to randomly alternate control and conditioned reflexes). The reflex pathway is not quite as simple as it first seems. Most of the drawbacks related to this complexity of the MSR pathway may be tested by a parallel investigation of single MUs, with the PSTH technique or with the unitary H reflex [57], which should be therefore systematic.

When taking the precautions described above, the MSR remains one of the most important techniques presently available to investigate synaptic actions on human spinal MNs. Because it enables one to compare the results obtained at rest and during movement, it is the only available method with which it is possible to investigate in man how spinal pathways are used in motor control. This is of general interest, given that investigations concerning such changes cannot be done on 'reduced' animal preparations but require experiments performed during natural movement, as it can easily be performed in humans.

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