

Reflex Stimulation of Continuously Oscillatory Firing α and γ -Motoneurons in Patients with Spinal Cord Lesion

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Abstract. Single nerve-fibre action potentials (APs) were recorded extracellularly from lower human sacral nerve roots, and simultaneous single-fibre impulse patterns of α and γ -motoneurons and secondary muscle spindle afferents were analysed

Identified α and γ -motoneurons fired oscillatory, due to the sustained stretch reflex of the external sphincters induced by an anal catheter (and, possibly, the bladder catheter) The motoneurons and the secondary muscle spindle afferents transiently synchronized their firing upon repetitive touch, pin-prick and dimpling stimulation of the perianal skin inside the anal reflex area, by reducing the duration of their oscillation period until resetting of the oscillation cycle In one case, the anal reflex area extended approximately 6 cm laterally from the anus

The responses to pin-prick stimulation were different from those to touch stimulation in three aspects Firstly, the response time till the shortening of the oscillation period was longer than the oscillation period (~ 100 ms) for pin-prick, and it was shorter for touch Second, the response to pain stimulus was longer (shortening of several oscillation periods) and stronger than for touch stimulation Pin-prick stimulation reduced the oscillation period to between 5 and 40 ms (mean = 18 ms), and touch stimulation to between 8 and 28 ms (mean = 15 ms) Third, transient synchronization of afferents and efferents was most pronounced for pin-prick stimulation

The shortest latency following touch was approx 10 ms when measuring from the afferent volley running in the direction of the spinal cord, and 30 ms when measuring from the beginning of the skin touch It is discussed that repetitive touch stimulation reinforced the sustained stretch reflex of the anal sphincter which is possible with no network reorganization (variation of the same network state) and therefore fast, whereas repetitive pin-prick stimulation replaced the sustained stretch reflex by the protection reaction of the anal sphincter (change from one network state to a different one) which made time consuming network reorganization necessary

Different sacral reflexes were analysed by studying time related activation changes of group conduction velocities in velocity distributions During the reflex response to stretch of the external anal sphincter, the α_2 -motoneurons (FR) (and the secondary muscle spindle af-

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ferents) were strongly activated whereas upon eliciting the bulbocavernosus reflex (squeezing of the glans penis) the α_3 -motoneurons (S) were mainly activated

Sacral reflexes are discussed with respect to the organization and reorganization of preformed neuronal networks, and the synchronization of oscillatory firing networks is discussed with respect to the overlapping of synfire chains

Key-words: Paraplegia – Nerve root – Single nerve-fibre action potential – Premotor neuronal network – Oscillatory firing – Sacral reflexes – Synchronization

Introduction

Two concepts have been developed to interpret central nervous system (CNS) functions of the human spinal cord. One, supported by the Sherrington school [4], rests upon the observation of the monosynaptic stretch reflex and explains human CNS functions through reflexes: all reflectory, excitatory and inhibitory actions take place via a direct action onto the motoneuron pool itself (reflex theory). The other concept, supported by v. Holst [12] and Jung [13], rests upon the basic observation of rhythmic movements, occurring in physiologic tremor: the most basic mechanism for coordinated movements is the „Schaltzellenapparat“ (neuronal network) of the spinal cord, onto which all impulses converge (oscillator theory); this concept also admits that there are certain spinal pathways which bypass the „Schaltzellenapparat“ and synapse directly onto the motoneurons. This recent, completely new development [17-27] in human neurophysiology supports the „oscillator theory“, brings further insight into the oscillator theory, and derives new knowledge from analyses of simultaneous natural impulse patterns of single afferent and efferent human nerve fibres. Upon receiving an afferent input in the spinal cord, preformed neuronal networks are getting self-organized and reorganized into spinal oscillators which in turn undergo relative coordination upon inputs from receptors of the skin, joints and muscles and supraspinal centres; this spinal processing bears some similarity with what has been a new understanding of how brain functions.

It was reported in the first paper of this series that α_1 (FF) and α_2 -motoneuronal networks (FR) fired oscillatory with alternating long and short oscillation periods [24], which resembles the firing of coupled half-centre oscillators found in the lamprey spinal cord [8], which inhibit each other reciprocally. But since motor units can change their firing from alternating to symmetrical oscillatory firing [27], alternating oscillatory firing may indicate coupling of non-equal oscillators especially those which activate motor units of antagonistic muscles, which must also be able to inhibit each other. Also, it has been stated in the second paper that α_1 -motoneurons fired oscillatory at approx. 10 Hz [25] as predicted earlier [20]. However, primary muscle spindle afferents were found to synapse directly (monosynaptically) onto the α_1 -motoneurons, in accordance with the monosynaptic stretch reflex connection. Secondary muscle spindle afferents, on the other hand, synapsed polysynaptically onto

α_1 and α_2 -motoneurons, suggesting that secondary spindle afferents project into the oscillatory firing networks of α_1 and α_2 -motoneurons (Fig.1).

In the present paper we shall describe the application of reflex stimulations during the motoneurons already firing in the oscillatory firing mode, to explore the relationship between reflex responses and oscillatory firing. The important question is whether the reflex or response times can be shorter than the duration of the oscillation period, since we want to see whether the afferent input can interact with the ongoing oscillation cycle and if yes, until what loop piece, and how strongly the oscillation loop is organized. Already P. Hoffmann [11] mentioned that the response subsequent to the reflex came after 100 ms (he measured on α_1 -motoneurons; silent period \approx 100 ms \approx oscillation period). Hoffmann and Delius [5,11] reported that a second reflex response (Archilles tendon stretch reflex) of reduced amplitude could be elicited as early as after 25 ms (Fig.15 of [11]). No reflexes could be elicited below 20 ms (absolute refractory period, as designated by Hoffmann). It will be shown in this paper that the reflex response time can be shorter than the oscillation period, and that the reflex response times depend on the organizational state of the motoneuronal networks. We shall demonstrate that touching the perianal skin reinforced the sustained stretch reflex of the anal sphincter and therefore resulted in a reflex time shorter than the oscillation period (30 ms), because no reorganization of the neuronal network state was necessary; whereas upon pin-prick stimulation of the perianal skin, the neuronal networks had to reorganize themselves from sustained stretch reflex to protection reaction, so that the response time was longer than the oscillation period.

The term „reflex“ is used here in the following sense. A reflex can be a special connection, which is activated by adequate stimulus (e.g., monosynaptic stretch reflex); it can be a special preformed neuronal network organization (serving certain functions, such as protection reaction) which is activated by adequate natural afferent input patterns from a certain area (e.g., the anal reflex, elicited by dimpling of the perianal skin) or intermediate cases. According to W.R. Hess [10] a reflex represents a response to a sensible stimulus in the form of a facilitated involuntary successful action of a certain organ. The reflex is called by its fulfilled goal.

Materials and Methods

Single-nerve fibre action potentials were recorded extracellularly from undissected nerve roots with two pairs of platinum wire electrodes (electrode pair distance 10 mm; electrode distance in each pair 4 mm) at two sites, preamplified (x 1,000), filtered (RC-filter, passing frequency 100 Hz - 10 kHz), and displayed on a digital storage oscilloscope (Vuko Vks 22-16), and also stored using a PCM-processor (Digital Audio Processor PCM-501ES) and a video recorder. Conduction velocity distributions of afferents and efferents were constructed, calibrated, group conduction velocities were identified; and multi-unit impulse patterns were split into simultaneous patterns of several single afferent and efferent nerve fibres. The intraoperative recordings were performed in patients with a complete spinal cord lesion du-

ring the implantation of an electrical anterior root stimulator for urinary bladder control. Details of the method are given elsewhere [17,21-24]. Bladder ($\varnothing = 6$ mm) and anal (8 to 20 mm) catheters were positioned. Further details of paraplegics 9 and 10 (patients with complete spinal cord lesion) are given in [24].

Results

Functional state at measurements

Single-nerve fibre action potentials (APs) were recorded extracellularly from lower sacral nerve roots. APs of certain nerve fibre groups were identified by the conduction velocity and AP waveform, and simultaneous single-fibre impulse patterns of α and γ -motoneurons and secondary muscle spindle afferents were analysed. Fig. 1 illustrates the basic assumptions underlying the measurements. Due to catheters positioned in the anal canal and the urethra (approximately isometric stretch), α and γ -motoneurons fired oscillatory (Fig. 2) as a result of the sustained stretch reflex of the external sphincters (not clear for the urethra). Natural stimulations, like touch, pin-prick, anal and bladder catheter pulling and eliciting of

Reflex-stimulation of oscillatory firing α and γ -motoneurons

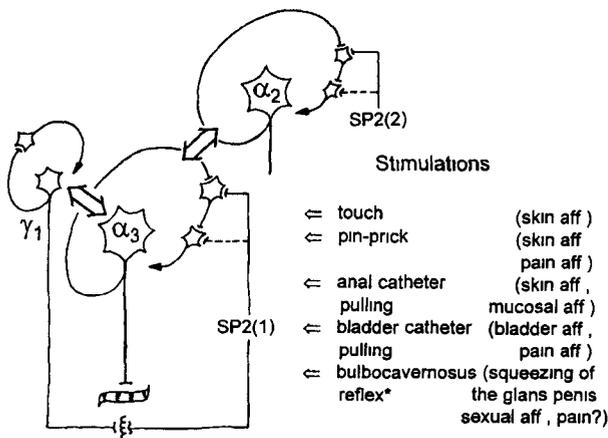


Figure 1. Schematic drawing of the probable state of the neuronal network organization of the sacral spinal cord upon the application of different sacral reflex stimulations. aff = afferents, * = not elicited during the first measurement. α -Motoneurons fired oscillatory, γ -motoneuron fired oscillatory or almost oscillatory. „ \leftrightarrow “ indicates interactions (transient synchronization) of motoneuronal networks. Inhibitory interneurons are not drawn because of lacking knowledge.

the bulbocavernosus reflex, were applied, to measure changes in the oscillatory firing. Since in the first measurement (Figs 2-5) all motoneurons fired oscillatory with impulse trains consisting of one AP (pathologic), the shortening of the oscillation period was related to the time of reflex eliciting. Synchronization between afferents and efferents will be mentioned and is discussed in detail in a following paper [26]. In the second measurement (Figs 6,7), sacral reflexes were analysed with quantified changes of motoneuron peaks in distribution histograms of conduction velocities.

Response of oscillatory firing to touch stimulation

Ten schematically drawn sweep pieces of simultaneous impulse patterns, of the α_2 , α_3 and γ_1 -motoneurons and the secondary muscle spindle afferent fibres SP2(1) and SP2(2) are shown in Fig 2. Following a sequence of 10 touch stimulations (Fig 2, upper right insert), the rhythmically firing motoneurons responded by a change in the duration of the oscillation period. Of interest is here how fast the α_3 -motoneuron reduced its oscillation period following the start of the touch stimulation or following the volley of skin-afferent APs running through the ventral root skin afferent fibres. The delay of the first reduction of the oscillation period is defined in Fig 2 following touch 7. The begin and the end of the stimulation are marked. There is a possibility that the α_3 -motoneuron (S) is actually an α_2 -motoneuron (FR), and the α_2 is an α_3 -motoneuron. Because of the pathologic oscillatory firing, the type of the motoneuron cannot be safely identified from the firing pattern any more, and identification on the basis of conduction velocity is not safe as the distributions of conduction velocities of α_2 and α_3 -motoneurons (and of other nerve fibre groups) overlap.

It can be seen in Fig 2 that the α_3 -motoneuron mostly reduced its oscillation period after a delay (measured from the beginning of the afferent volley) shorter than the duration of the oscillation period. The first reduction of the oscillation period is marked in the Figure by the small arrow. The response times are analysed quantitatively in Fig 4. Following touches 6 and 7 there occurred a partial transient synchronization of afferents and efferents, as can be seen by the similar occurrence times of the impulses. Also, a slight partial synchronization followed touches 2 and 3.

Since on the average, the delay in the shortening of the oscillation period occurred after a time interval shorter than the oscillation period, it was of interest to see whether the response times were similar to those for pin-pricking. It has been established in man that the difference between touch and pin-prick stimulation is that for pin-pricking, additionally pain fibres are activated [17], and pain fibre activity may facilitate different pathways to the motoneuronal networks (Fig 4).

As will be detailed in Discussion, the touch sites 1,2,6 and 7 were inside the anal reflex area, and the sites 4,5,9 and 10 were outside of it. The anal reflex area extended approx 6 cm laterally from the anus.

Response of an oscillatory firing α -motoneuron to painful pin-prick stimulation

After experiments with the touch stimulation at pen marked sites 1 to 10 close to the anus, the touching sites were now pin-pricked in a similar fashion approx every 0.8s. As can be seen from Fig 3, after a delay, there again was a reduction in the duration of the oscillation periods.

The responses to pin-pricking differed from those following touch stimulation in three aspects. Firstly, the response delay times were longer than the oscillation periods. Second, the response to pain stimulus application was of a longer duration and was stronger, mostly,

the duration of two oscillation periods was reduced following pin-prick stimulation and the reduction of the duration was greater. Following pin-pricks 3,7 and 8, the oscillation period was very short and resembled the resetting of the oscillation cycle. Third, the transient synchronizations of afferents and efferents following pin-pricks 6 and 7 were more pronounced.

Latency in the reduction of the duration of the oscillation period following touch and pin-prick stimulation

It can be seen from Fig. 4A that in 9 out of 10 cases, the latency of the oscillation period shortening following touch stimulation of the perianal skin (see inserts in Figs.2,3) was shorter in duration than the oscillation period (≈ 100 ms), represented by the dotted line. The shortest latency was approx. 10 ms, when measuring from the afferent volley running in direction

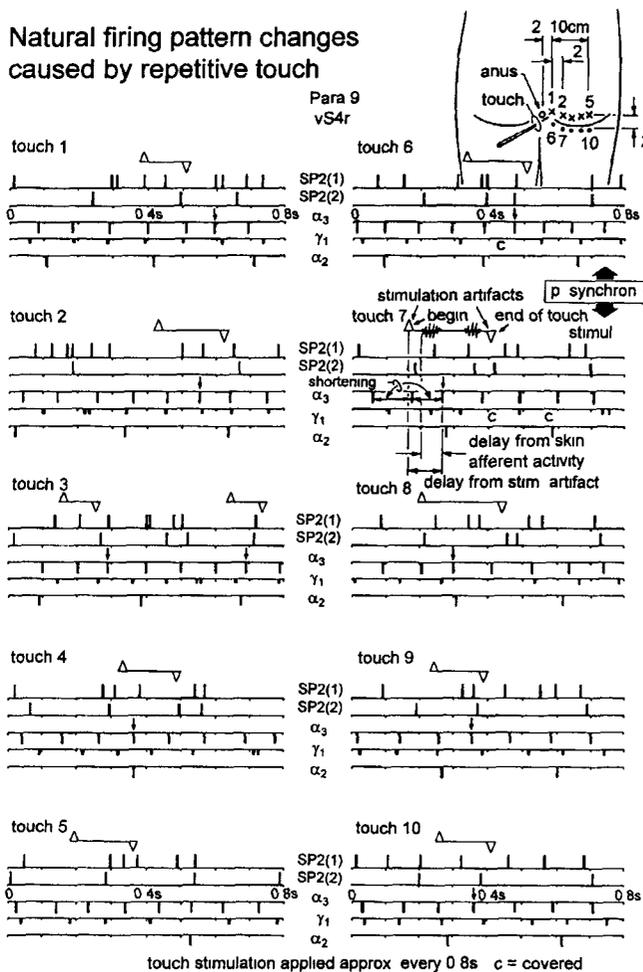


Figure 2. Changes of natural impulse patterns of α_2 , α_3 and γ -motoneurons and secondary muscle spindle afferents (SP2(1) and SP2(2)) in paraplegic patient 9 upon touching sites 1 to 5 (x) and 6 to 10 (\bullet) (insert) The small arrows indicate the first shortening of the oscillation period of the α_3 -motoneuron following the beginning of the touch stimulation (marked by an artificially generated artifact) Note that partial synchronization (p synchron) of the firing of the α_2 and α_3 -motoneurons and secondary muscle spindle afferents occurred upon touching sites 6,7 The α_2 and α_3 -motoneurons were only identified by their conduction velocities, it is therefore possible that the α_3 -motoneuron was actually an α_2 -motoneuron and the α_2 -motoneuron an α_3 -motoneuron (overlap of velocity distributions), the firing patterns were very pathologic, and could not be used for the motoneuron identification

of the spinal cord. The latency of the first reduction of the oscillation period, measured from the skin touch stimulation artifact, was longer or shorter than the duration of the oscillation period (Fig.4B). The shortest latency was approx. 30 ms. The difference in latency, i.e. the time from the stimulation artifact (touching of the skin) to the moment when the skin afferent volley passed the recording electrodes, was approx. 20 ms. According to the group conduction velocities of skin afferents (T1 skin afferents (PC) ≈ 44 m/s at 36 °C) [17,21], most of the time was lost in the touch receptors and the thin nerve fibres connected to them. With a conduction distance of 0.3 m, a conduction time of $t_{cond} = s/v = 300 \text{ mm}/44 \text{ mm}(ms)^{-1} = 7 \text{ ms}$ results.

The latency till the reduction of the first oscillation period duration following pin-pricking the sites 1 to 10 (Figs.2,3) was mostly longer than the oscillation period itself, independent of whether measured from the skin afferent volley (Fig.4E) or from the stimulation arti-

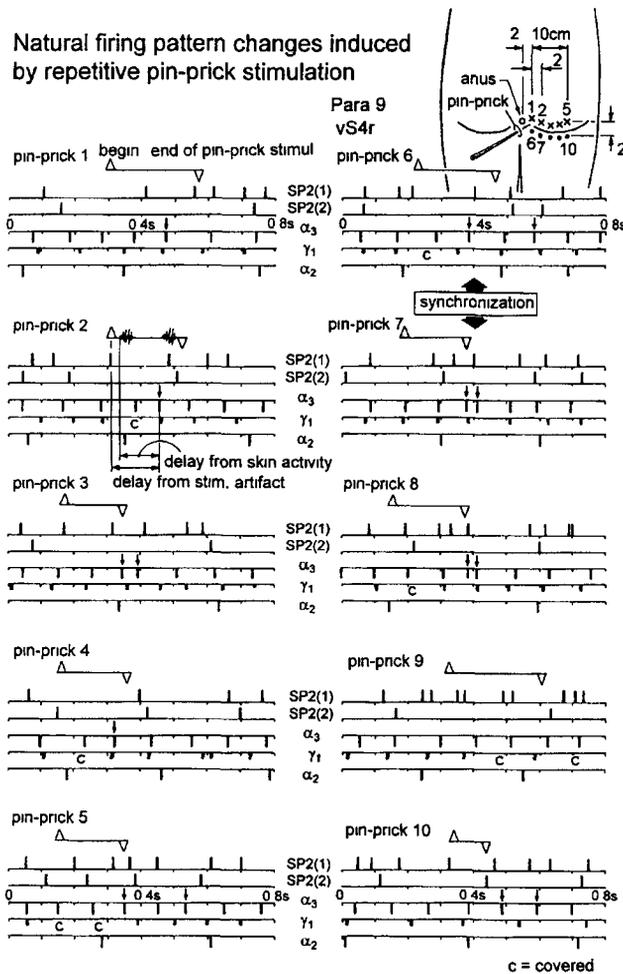


Figure 3. Changes of natural impulse patterns of α_2 , α_3 and γ -motoneurons and secondary muscle spindle afferents following repetitive pin-prick stimulation. For further details, see Fig. 2. Note that synchronization occurred at pin-pricking of sites 6,7. Note further that shortening of the oscillation period (indicated by the small arrows), often occurred 2 times following pin-pricking.

fact (Fig 4F) Since not every pin-prick was strong enough to generate pain, it is concluded that the latency from the pin-pricking to the first reduction of the oscillation period was longer than the oscillation period

By comparing the latencies to the first reduction of the oscillation period following repetitive touch and pin-prick stimulation of sites 1 to 10, it turns out that following touch stimulation the delay is shorter than the oscillation period, whereas it is longer following pin-prick stimulation It seems therefore that touching reinforced the sustained stretch reflex of the anal sphincter while pin-prick did not For further analysis see the Discussion section

Extent of oscillation period shortening following touch and pin-prick stimulation

The first shortening of the oscillation period (indicated by the small arrows in Figs 2,3) in comparison to two preceding periods is plotted in Fig 4D,C (touch) and in Fig 4H,G (pin-prick) The reduction of the oscillation period for touch stimulation was between 8 and 28 ms, and it was between 5 and 40 ms for pin-pricking The pin-prick stimulation generated a greater transient reduction of the oscillation period

When correlating the latency of shortening to the extent of shortening for pin-pricking (Fig 4H) it seems as if the shorter latency correlated with a slighter reduction of the oscillation period (more touch-like), and the long latencies correlated with the greater reduction of the oscillation period (more pain-like) A similar relation was not found following touch stimulation (Fig 4D) It will be discussed below that probably, the painful pin-prick stimulation transiently replaced the sustained stretch reflex of the anal sphincter by a protective reaction of the anal sphincter against pain application, the time needed for the reorganization of the oscillatory firing neuronal network was at least one oscillation period long

The relation between the sites of pin-prick (Fig 4G) or touch stimulation (Fig 4C) and the oscillation period shortening shows no clear correlation The dotted and the dashed lines may show similar latencies Perhaps the protective reaction against pin-pricking of the anal canal and the pelvic floor is highest at sites 3 and 8 at the border of the anal reflex region

Change of natural impulse patterns following anal reflex stimulation

Since repeated touching only partly elicited the anal reflex, the anal reflex could also be conveniently elicited by dimpling of the perianal skin The changes of the natural impulse patterns of motoneurons and secondary spindle afferents were measured and analysed (Fig 5)

Transient partial synchronization of secondary muscle spindle afferents and motoneurons occurred upon and following the anal reflex was elicited (10s to 14s in Fig 5) The distributions of interspike intervals and oscillation periods are given elsewhere [26]

Shortening of oscillation period (T) and latency upon touch and pin-prick stimul.

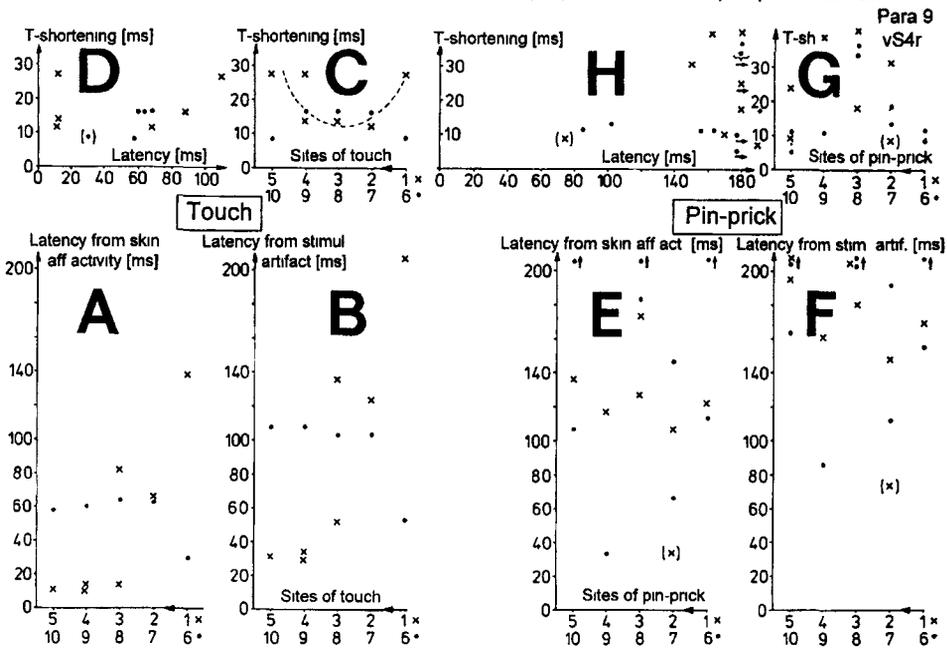


Figure 4. Shortening of the oscillation period T of the α_3 -motoneuron (perhaps an α_2 -motoneuron (see legend to Fig 2)) upon touch and pin-prick stimulation

A, B. Latency of the shortening of the oscillation period (for definition, see Fig 1) measured from the skin afferent activity (A) and from the stimulation artifact (B) with successive touching of sites 1 to 5 (x) and 6 to 10 (•) as indicated in Fig 2. Note that the delay is often shorter than the oscillation period

C,D. Shortening of the oscillation period (T-shortening), with respect to two preceding oscillation periods, in relation to the latency of shortening (D) and in relation to successive touching of sites 1 to 10 (C)

E-H. Same description as for A-D, only with respect to pin-pricking. Note that touch stimulation induced a shorter latency for the reduction of the oscillation period than did pin-pricking

Sacral reflex responses of motoneurons firing in the occasional firing mode, measured by velocity distributions

In paraplegic patient 10, sacral reflexes could partly be measured from motoneurons firing in the occasional firing mode. The analysis of the velocity distributions provided information on how certain groups of nerve fibres responded to the different stimulations.

Following pin-pricking at sites 3 and 8 (border of the anal reflex area (see Figs.2,3)), the α_2 -motoneurons, firing in the occasional firing mode, strongly increased their firing rate, whereas only few α_3 -motoneurons were activated (Fig.6A). Pin-pricking of the sacral der-

seen in Fig. 6D, the secondary muscle spindle afferent fibres strongly increased their firing rates as expected from the response of the stretch reflex. Primary spindle afferents were not activated, since they only are seldom present in the lower sacral range, and only sometimes seem to contribute to the regulation of the anal sphincter. Skin (T1 to T4) and mucosal afferents (M) were activated as expected. The activity of the α_2 , α_3 and γ -motoneurons increased, which means that slow (α_3) and moderately fast motoneurons (α_2) were activated along with the γ -loop. More details concerning the stretch reflex of the anal sphincter will be given below.

By squeezing the glans penis, the bulbocavernosus reflex was activated 2 times (Fig. 6E). Activity in the afferents of that particular S5 root increased only slightly. Afferents of the glans penis run through other roots (S1, S2?). Only the slow α -motoneurons (α_3) increased their activity in accordance with the slow muscle response of the bulbocavernosus reflex. γ -Motoneurons were activated, especially the static ones, since slow γ -motoneuron velocities were observed. The bulbocavernosus reflex will be analysed further below. No clear activation of nerve fibre groups was observed following pulling of the urinary bladder catheter (Fig. 6F).

Stretch reflex of the anal sphincter (reflex reinforcement)

The activation changes of motoneuron groups in velocity distributions (Fig. 6) seemed to suggest that the α_2 -motoneurons (FR) were strongly activated during the stretch reflex response of the external anal sphincter whereas with the bulbocavernosus reflex eliciting, the α_3 -motoneurons (S) were mainly activated. A more detailed analysis was therefore tried.

In Fig. 7A-D, the stretch reflex of the anal sphincter is analysed in more detail. Even though the exact timing of the intervals was not possible, the transient activity increase of α_2 and α_3 -motoneurons became evident.

The α_3 -motoneurons (S) increased their activity from before stimulation levels (A) of 3 APs / 0.2s to 6 APs (B) shortly after the stretch reflex, and decreased further their activity from 5 APs (C) to 4 APs (D). The α_2 -motoneurons (FR) responded more dynamically. They increased their activity from 2 APs / 0.2s (A) to 7 APs (B) and subsequently decreased their activity from 5 APs / 0.2s (C) to 1 AP (D). Continuously oscillatory firing motoneurons did only little or not at all affect the activity changes.

During the stretch response of the anal sphincter α_2 and α_3 -motoneurons increased their activity. The α_2 -motoneurons responded more dynamically in the reflex reinforcement of the sustained stretch reflex of the anal sphincter. We did not differentiate here between firing in the occasional and the oscillatory firing mode. It would also be difficult to do so, because activity increases in the occasional firing mode and in the transiently oscillatory firing mode are difficult to differentiate.

As expected, the secondary muscle spindle afferents increased their activity (B). Primaries are only sometimes present in the lower sacral range. The second response of the secondary muscle spindle afferents is difficult to discuss because of the timing of the anal catheter handlings. Afferents with similar group conduction velocities could contribute to

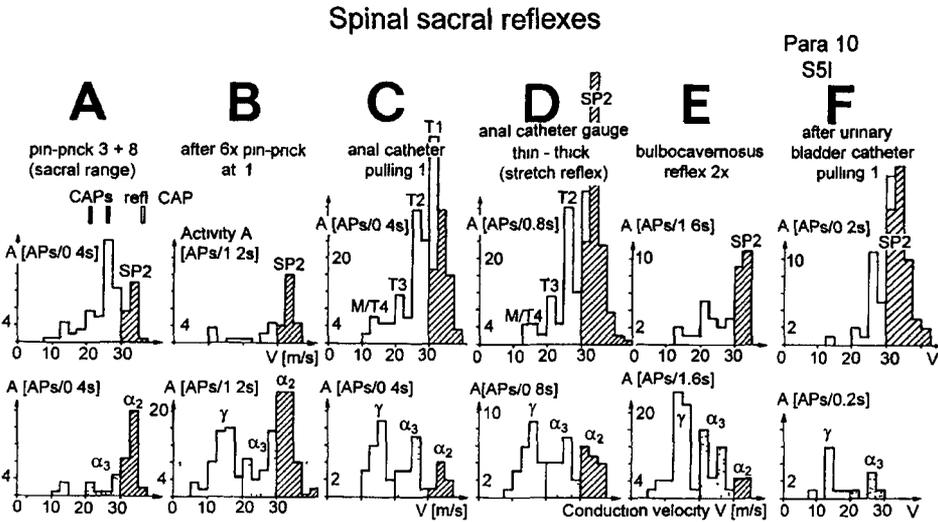


Figure 6. Conduction velocity distributions of afferents and efferents upon eliciting of sacral reflexes. Note that following changing the gauge of the anal catheter (8 mm to 20 mm), the secondary muscle spindle afferent activity (SP2) strongly increased. Note further that the bulbocavernosus reflex mainly activated the α_3 -motoneurons T1 (PC), T2, T3, T4 = skin afferents [14,18], M = mucosal afferents. CAPs = components of compound action potentials, refl CAP = reflected CAP. A = activity, measured in action potentials per time. Para 10, left root S5.

that second response. Golgi tendon organ afferents have not been identified so far in this research project; the external striated sphincters have no tendons.

Bulbocavernosus reflex

The bulbocavernosus reflex was elicited twice by squeezing the glans penis, and the two responses were added to see more clearly the changes in the activity patterns (Fig.7E-H).

The α_3 -motoneurons increased their activity from 8 APs / 0.4s (E) to 11 (E) upon reflex eliciting, and subsequently reduced their activity to 9 (G) and 7 APs (H). The α_2 -motoneurons did not increase their activity, which was an unexpected finding. Their activity changed from 4 APs / 0.4s (E) to 2 (F) and 3 (G) and 1 AP / 0.4s (H). The α_2 -motoneurons even seemed slightly inhibited following bulbocavernosus reflex eliciting.

Discussion

Anal reflexes

Anal reflexes were measured here with anal and bladder catheters positioned, i.e. under conditions of sustained stretch reflex of the anal sphincter. The responses of the motoneu-

rons innervating the external anal sphincter were different from those for touch and pin-prick stimulation. Since most likely, the anal reflex organization is designed to secure continence when material, fluid or gas is passing through the anal canal or when the anal mucosa is touched or pushed, the afferents stimulated in these ways are the adequate afferents of the anal reflex. It is therefore not surprising that the anal reflex responses were different from those for pin-prick stimulation. Since the response time was shorter for touch than for pin-prick stimulation, it is suggested that there is less reorganization necessary in the neuronal network of the sacral micturition and defecation centre to change the activation of sphincteric motoneurons in the case of touch stimulation. It is therefore likely that touching of the perianal skin reinforced the sustained stretch reflex which may be possible with little network changes. Since normally, pin-prick stimulation of the surface of the body is followed by a protective reaction of the body and or an avoidance reaction, it is likely that at least contraction of the muscles beneath the skin (protective reaction) also holds for the anal region. Probably, the protective reaction induces an organization of the neuronal network different from that necessary for the anal reflex. Probably, network reorganization (change from one network state to a subsequent one) needs more time than strengthening of a certain organization (variation of the same network state). It is therefore likely that the touch stimulation induced reinforcement of the anal reflex for which little time is needed, whereas pin-pricking

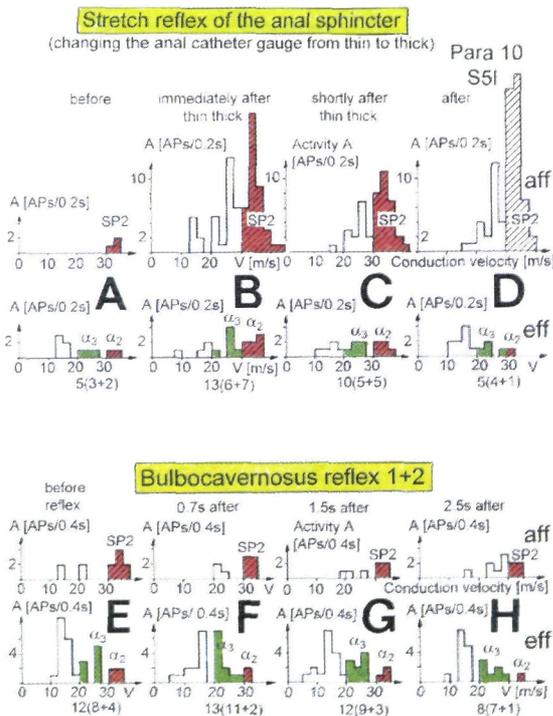


Figure 7. Conduction velocity distributions of afferents and efferents upon stretching of the anal sphincter (A-D) and squeezing of the glans penis (E-H). A, D. Stretch reflex of the anal sphincter. Note the strongly increased secondary spindle afferent activity (SP2) in B. Note further that the α_2 -motoneuron activity increased even more strongly (from 2 APs to 7) than did the α_3 -motoneuron activity (from 3 to 6). E-H. Bulbocavernosus reflex. Note that α_3 -motoneuron activity increased (8 APs to 11), whereas the α_2 -motoneuron activity decreased (4 APs to 2 APs).

elicited a protective reaction for which more time was needed because of the reorganization of the neuronal network.

Anal reflexes were measured using different kinds of electrical stimulation [1,2,6,9,14-16,28-32]. Since electrical stimulation (painful or not) is not an adequate stimulus, different response times have to be expected for different stimulations. Response times of approx. 50 [14] and 8 ms [9] were obtained. Even though electrically evoked responses of the anal sphincter cannot be compared with natural stimuli in which the afferent input patterns to the spinal cord have a natural composition, it is possible that the shorter latency (around 8 ms) was more adequate to elicit the anal reflex (shortest latency measured here was 10 ms) whereas the response with a latency around 50 ms was more adequate to elicit the protective reaction (latency measured here was in the range of 100 ms). Anyhow, these measurements indicate that electrically evoked responses of the anal sphincter are no real anal reflexes, since the sacral spinal cord is not getting the natural adequate afferent input composition for the network organization of the real anal reflex.

Stretch reflex of the anal sphincter

The stretch reflex of the anal sphincter has been measured here for the first time. The reflex was evoked by stretching of the anal sphincter by increasing the gauge of the anal catheter. In response to stretch, the activity of secondary muscle spindle afferents and α_2 -motoneurons increased. It has not been possible so far to measure the exact timing of the reflex. It would be of interest to compare, on one hand, the stretch reflex elicited through secondary muscle spindle afferent activity and acting on the α_2 -motoneurons, with the conventional stretch reflex, elicited through by primary spindle afferents and acting on α_1 -motoneurons. In the former case, the secondary muscle spindle afferents project into the interneuronal network; the activity runs a polysynaptic pathway, and stimulates the organization of oscillatory firing networks. In the latter case, the primary spindle afferents bypass the neuronal network of the CNS and synapse directly onto the α_1 -motoneurons. Secondary muscle spindle afferents stimulated simultaneously with the primaries will give rise to secondary effects on α_1 and α_2 -motoneurons, similarly (on α_2) to those of the former case.

Bulbocavernosus reflex

The bulbocavernosus reflex consists of the reflex contraction of the bulbocavernosus muscle elicited by squeezing of the glans penis. A simultaneous response can be recorded from the anal or urethral sphincters upon the stimulation of the glans or the clitoris. Its neurophysiological characteristics are supposed to be almost identical with those of the reflex recorded from the bulbocavernosus muscle itself (see page 321 of [28]), even though it seems as if the anal sphincter contracts faster than the bulbocavernosus muscle. Electrical stimulation of the glans or the clitoris will evoke a response from the bulbocavernosus and external sphincter muscles [6,28], but the responses may not be identical with the muscle

responses evoked by squeezing of the glans penis

The squeezing of the glans penis (Fig 7E,F,G,H) elicited an activity increase of the α_3 -motoneurons (S) only, which is in accordance with the slow contraction of the bulbocavernosus muscle observed when squeezing the glans penis. It would be interesting to know whether electrical eliciting of the bulbocavernosus response also selectively activates the fatigue resistant muscle fibres, innervated by the α_3 -motoneurons

Stimulation with respect to the phase of the oscillation cycle

When the afferent volley, induced by touch, pin-prick or dimpling stimulation of the perianal skin, runs into the neuronal network, the question arises whether the afferent impulses can interact with the ongoing oscillation cycle of oscillatory firing α -motoneurons or whether they can induce changes in the following cycle only

It is conceivable that if the composition of the afferent input is of the kind that the resulting network organization state is the same or very similar to the present one, then the response of the afferent volley would interfere with the present organization, and changes will directly be seen in the ongoing oscillation cycle. If however the afferent volley has a composition which will induce another network organization state, then a larger network reorganization has to take place. The response time to the α -motoneuron firing changes will then be longer.

The response time following touch-induced afferent volley was shorter than the oscillation period (Fig 4A,B). This may indicate that only little or no network reorganization took place. The ongoing oscillatory firing of the α -motoneuron, due to the sustained stretch reflex, was reinforced and this was possible with little network organization changes with the ongoing oscillation cycle.

Further, the response time upon pin-prick stimulation was observed to be mostly longer than the oscillation period (Fig 4E,F). It is therefore likely that the afferent volley following pin-prick stimulation organized another network state, and the network reorganization from one state to a subsequent one needed more time than reinforcement of the sustained anal stretch reflex. Since the pain afferents are the main difference in the composition between the afferent volleys following touch and pin-prick stimulation [17,19], the activity in the pain afferents is the cause for the reorganization. The pain afferents may therefore have an effective projection into the neuronal network for organizing certain network structures. Probably, the volley in the pain afferents formed a network structure to serve the protective reaction of the pin-pricked body part (muscles beneath the pin-pricked-stimulated skin) and/or an avoidance reaction in adjacent muscles, to „escape“ from the intruding needle.

Synchronization of spinal oscillators

According to the „oscillator theory“ of v. Holst and Jung [12,13], preformed neuronal networks are getting self-organized and reorganized into spinal oscillators, which in turn un-

dergo relative coordination upon inputs from receptors of the skin, joints and muscles and supraspinal centres. Movements and continence functions are achieved by relative coordination of rhythmically firing neuronal networks. The relative coordination is achieved by transient synchronization and desynchronization of rhythmically firing propriospinal subnetworks (probably subunits of pattern generators), and possibly partly also by spinal oscillators (premotor neuronal network) which are driven by the self-organized pattern generators (see Figs 19,20 of [27]). With the change of the state of the functional organization of the spinal cord neuronal network (from the anal reflex to the protection reaction), the premotor spinal oscillators did not stop to fire oscillatory. It seems therefore that spinal oscillators are building units for the functional organization of certain network states. In humans, synchronization can so far only be measured on the output mechanism, i.e. the motoneurons as a part of the premotor network.

It can be seen in Figs 2,3,5 that transient synchronization of oscillatory firing motoneurons occurred following repetitive touch and repetitive pin-prick stimulation, and upon eliciting true anal reflex (dimpling of the perianal skin inside the anal reflex area). The synchronization was strongest following pin-pricking of the perianal skin. The synchronization was partly achieved by a shortening of oscillation periods. The strong shortening following pin-pricks 7 and 8 (Fig 3) were more likely a resetting of the oscillation cycle than a shortening, and an indication of forced network reorganization. As will be shown in a following paper, synchronization is achieved by a transient adjusting of the oscillation periods and a transient adjusting of the firing patterns of the motoneurons [26]. Actually, the oscillation periods and the phases of the oscillatory firing motoneurons have to be similar for some time. It will be shown in a further paper that an oscillatory firing motoneuron first decreased its oscillation period to increase the activity output, and then increased the oscillation period again (decrease of activity) to adjust its oscillation period to that of another oscillatory firing motoneuron under the preservation of a certain phase of broad peak type [26].

If oscillatory firing neuronal networks synchronize, they also must desynchronize. Spinal oscillators can be approximated by premotor spinal oscillators (of which the motoneuron is a part) and the propriospinal oscillators. The activation of premotor spinal oscillators is independent of movements, since they are also activated for continence functions [23] and isometric contractions [27]. Propriospinal oscillators are mainly activated for movements, especially for rhythmic ones (see Figs 19,20 of [27]). Most of the time, the premotor oscillators fire not in a synchronized mode, but propriospinal oscillators may do. A reason for no synchronization of premotor oscillators could be the overlap in excitatory interneurons of oscillatory firing networks. If synfire chains are really the constituents of the oscillatory firing networks, then the sharing of interneurons of overlapping synfire chains could be the reason for strict synchronization over relative to no synchronization. For strict synchronization, oscillators with different frequencies may even synchronize according to multiple integers as was observed by E v Holst [12]. To date, the relationships of synchronization between premotor and propriospinal oscillators remain unclear. Nevertheless, for the case of no synchronization, the premotor oscillators fire nicely distributed over time. Further mea-

measurements on neuronal networks have to reveal how this distributed oscillatory firing is achieved. Random synchronization of oscillatory firing networks may give rise to tremor. Afferent input, especially of repetitive nature, will essentially contribute to transient synchronization of synfire chains of different oscillatory firing networks. The problem will be picked up in a following paper [26].

Animal research suggests that Ib afferents may provide crucial feedback to rhythm-generating circuits, as already postulated [7]. Experiments during fictive locomotion in cats pre-treated with DOPA have indicated that Ib afferents can indeed reset the cycle [3].

Reflexes and oscillatory firing networks

Reflexes and oscillatory firing networks are not mutually opposing phenomena. The monosynaptic reflexes are special connections, in which the afferent volleys bypass mainly the oscillatory firing networks, and synapse directly onto the motoneurons. In polysynaptic reflexes, the activated afferents project into the neuronal networks of the spinal cord and organize or reorganize the networks for motor output. If the afferent input only lasts for a shorter period of time, the self-organizing oscillators fire only transiently oscillatory. The shortest transient oscillation lasts for one oscillation cycle. The term „reflex“ may (depending on its definition) characterize the formation of a preformatted network to function in a certain way, if adequate afferent volleys enter the network from the periphery. Inputs from supraspinal centres, on the other hand, organize e.g. preformatted networks to perform volitional movements or muscle contractions (e.g., volitional contraction of the external anal sphincter).

Anal reflex area

The motoneurons in Figs. 2,3 synchronized their firing mainly following touching and pin-pricking of sites 1,2 and 6,7. The synchronization wore off while sites 4,5 and 9,10 were stimulated. Thus, the afferent input from the skin, 6 cm lateral to the anus (Figs. 2,3), elicited the anal reflex, while an input from outside of this perianal skin area did not. The anal reflex is thus elicited from the distal rectum, the anal canal mucosa and the perianal skin up to approx. 6 cm laterally (in this patient).

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