Phase correlated adequate afferent action potentials as a drive of human spinal oscillators

Giselher Schalow[1]

Abstract

1. *By recording, with 2 pairs of wire electrodes, single-fibre action potentials (APs) from lower sacral nerve roots of a brain-dead human and a patient with spinal cord lesion, impulse patterns of afferent APs and impulse trains of oscillatory firing motoneurons could be identified and correlated.*
2. *Two highly activated secondary muscle spindle afferents increased and decreased their activity at about 0.3 Hz. The duration of the doublet interspike interval of a secondary spindle afferent fibre showed no correlation to the oscillation period of the motoneuron.*
3. *A continuously oscillatory firing motoneuron innervating the external anal sphincter showed more transient breaks with the reduction of the number of phase correlated APs from 2 spindle afferents, indicating a looser oscillation. A transient brake of a 157 msec period α_2-oscillation could be correlated to the shift of a interspike interval distribution peak from 150 to 180 msec of the adequate afferent input, which suggests a transient loss of the necessary phase relation.*
4. *Oscillatory firing α_2-motoneurons innervating the external bladder and anal sphincters fired independently according to their phase correlated APs from the urinary bladder stretch receptor and muscle spindle afferents respectively; the bladder motoneuron slightly inhibited the anal motoneuron.*
5. *Receptors of the afferents and innervation sites of oscillatory firing motoneurons could be located within the urinary tract and the anal canal.*

Key-words: Man — Spinal oscillators — Adequate afferent input — Phase relation — Sphincteric motoneurons — continence.

Introduction

After having analysed in previous papers the impulse patterns of oscillatory firing motoneurons (13) and the impulse pattern of parent secondary spindle afferent fibres and their probable encoder sites at the heminodes or penultimate nodes (7) of the myelinated branches (1, 14), in this paper it will be compared the afferent activity, most likely driving the oscillatory system, with the motoneuron activity; this will continue the analysis of the previous paper (14).

Only the oscillatory system with its secondary muscle spindle afferent input, driving the anal sphincter, has been analysed so far. In this paper, also an oscillator, driving external bladder sphincter muscle fibres is reconsidered with its stretch receptor associated afferent input from the bladder. It will be shown that both oscillatory systems are firing simultaneously, but independent of each other, even though small interactions exist.

[1] Institute of Pathology, University of Greifswald and Institute of Neuropathology, Free University of Berlin, Germany. Swiss Paraplegic – Centre Nottwil

Materials and methods

Recordings were performed with 2 pairs of wire electrodes from sacral roots of a brain dead human (HT6) and a patient with a spinal cord lesion (paraplegic 1 = Para 1). For further details see Refs. 11, 12.

Results

Simultaneous recordings from oscillatory firing motoneurons and the afferents driving them

Figure 1 shows impulse trains of oscillatory firing α_2-motoneurons innervating the anal sphincter of HT6 and Para 1. Sweep pieces were selected to present afferent (upwards) and efferent (downwards) action potentials under consideration. Traces a and b are from the proximal and distal electrode pairs respectively. Usually, there was more spacing between the impulse trains of the motoneurons and the afferent action potentials (APs). In figure 1A an impulse train of α_2-motoneuron O2 is shown together with those of the secondary muscle spindle afferent fibres SP2(1), SP2(2) and SP2(5). Afferents SP2(2) and SP2(5) fired with doublets of 12 and 10 msec. SP2(2) AP is merged on trace b with SP2(5.2) AP. APs of SP2(5.1) and SP2(5.2) (trace b) were not conducted across the second electrode pair (trace a) or were strongly weakened. In figure 1B another impulse train of oscillatory firing α_2-motoneuron O2 is shown together with APs of afferents SP2(1) and SP2(3). It can be seen in figure 1A, B that the impulse trains could be identified by the interspike intervals (4.7 and 7.3 msec in A) and by the oscillation period (not shown); identification of the secondary muscle spindle afferent APs was by the wave forms. Time expanded wave forms of the afferents under consideration were shown in a previous paper (14). Approximately 3 other activated but unidentified spindle afferents of the same dS4 root had low activity and

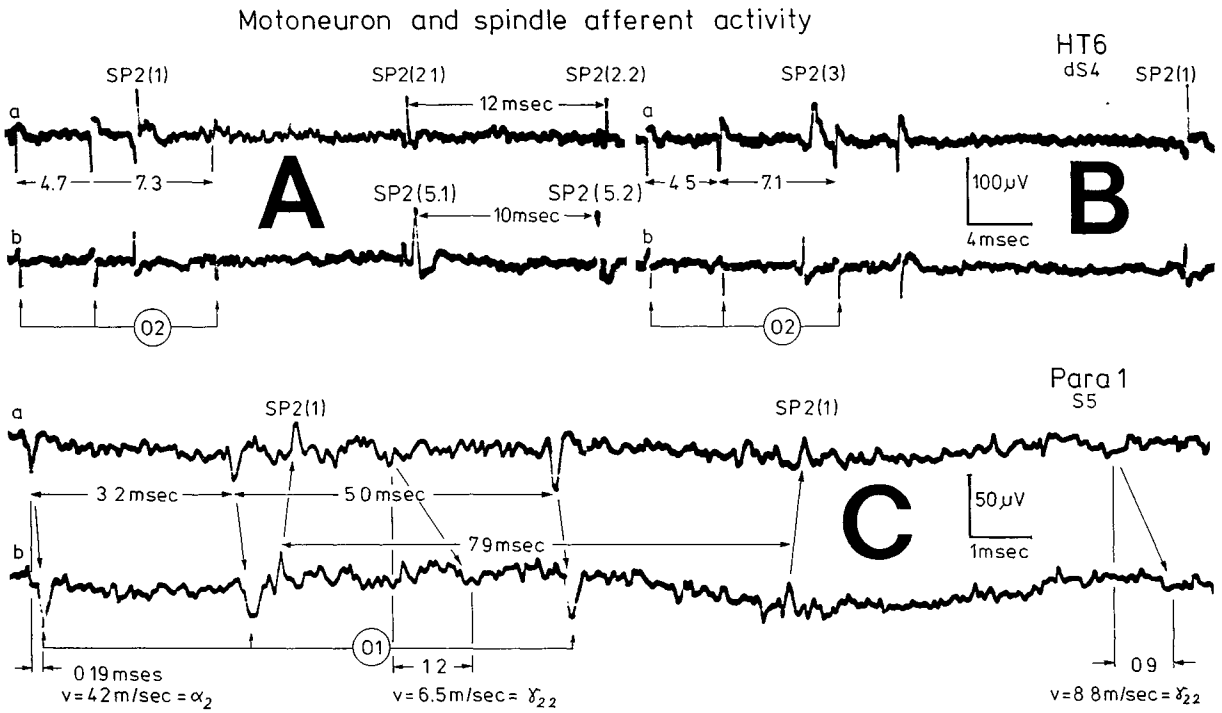

Fig. 1. — Recordings of the activity of α_2-motoneuron O2 and secondary muscle spindle afferents SP2(1), SP2(2), SP2(3) and SP2(5) (A, B) in HT6, and of α_2-motoneuron O1 and secondary muscle spindle afferent fibre SP2(1) in paraplegic 1. In A, trace b, the AP of SP2(2.2) is merged with that of SP2(5.2). APs of SP2(5), trace b, do not appear on trace a, being partly blocked.

therefore did not contribute to the strong excitation of the motoneuron. Figure 1C shows an impulse train of oscillatory firing α_2-motoneuron O1 of Para 1 together with APs of the secondary muscle spindle afferent fibre SP2(1). Some of the interspike intervals, conduction times and conduction velocities are indicated. Even though the quality of the recordings from the Para 1 was not as good as that from the HT6, it was also possible to identify the motoneuron and the SP2(1) APs after some training. Even the marked γ_{22} AP could be identified.

Stability of oscillation in dependence on the number of adequate afferent APs within a certain phase range

Figure 2A shows the activity levels of the afferents at least partly driving the oscillatory firing α_2-motoneuron O2 in HT6. Low activity of afferent fibres is not always plotted. It can be seen that throughout the activities of the different afferents are increasing and decreasing at a mean frequency of about 0.3 Hz. Even during no stimulation, between anal catheter pulling 4 and bladder catheter pulling 1, the increasing and decreasing continued on a reduced activity level. This finding is in accordance with the coordination of the impulse patterns of several spindle afferents (sharing activity) discussed in the previous paper (14). The summed activity of all afferents is smooth, as was shown previously for the same case (10). Following stimulation the single spindle afferent fibres responded differently. Fibre SP2(2) responded strongly to bladder catheter pulling (bladder 1), but not always in the way shown in figure 2. Thus, the firing of the spindle afferents was at least partly regulated by the efferent innervation, since the length of

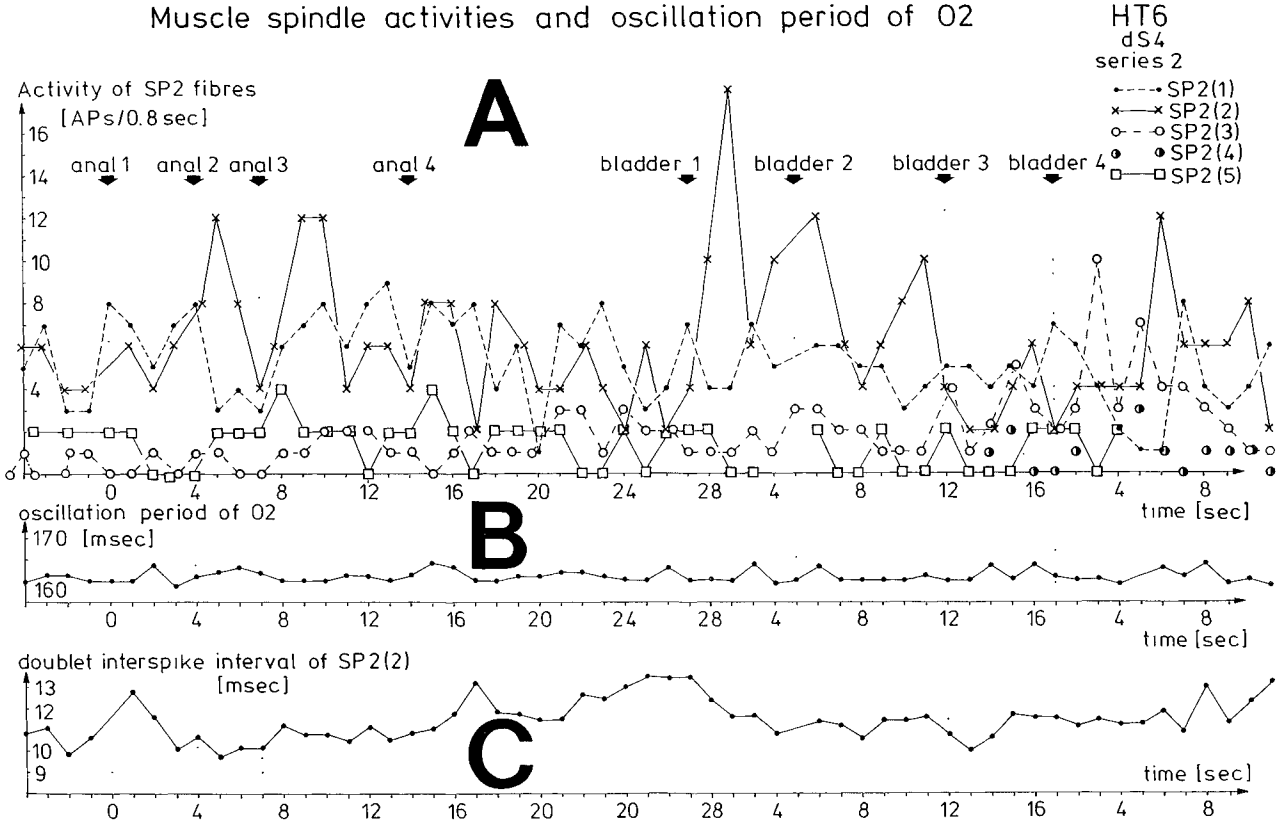

Fig. 2. — Activity of 5 secondary muscle spindle afferents (SP2(1 to 5)) (A) in relation to oscillation period of continuously oscillatory firing α_2-motoneuron O2 (B), and in relation to the doublet interspike interval of afferent fibre SP2(2) (C) following anal and bladder catheter pulling. All values measured simultaneously. HT6.

the anal sphincter muscle and of the functionally associated muscles of the pelvic floor (Fig. 7) probably remained rather constant.

In the second series of measurements (Fig. 2) the activity levels of the spindle afferents were higher in comparison to those of the first series (Fig. 3). There was an activation of the parasympathetic nervous system in between, which innervated the SP2(2)-fibre spindle, and maybe also some other spindles (15). With these high afferent activity levels (Fig. 2A) α_2-motoneuron O2 (Fig. 2B) fired continuously in the oscillatory mode with no breaks. It was shown in the previous paper (14) that many afferent APs were contributing, with a mean phase of 50 msec between the afferent APs and the first AP of the impulse train of the oscillatory firing α_2-motoneuron (50 msec/160 msec = 0.3, cycle phase 112.5°). In the first series of measurements (before the activation of the parasympathetic fibres) the situation was different (Fig. 3). The activity levels of the different spindle afferents were lower (Fig. 3A) and fewer APs were contributing to the oscillation, with a mean phase of 50 msec prior to the impulse train (14). Several times the continuous oscillation broke transiently (Fig. 3B). It is concluded that the lower activity levels with less contributing spindle afferent APs in phase drove the oscillator O2 less strongly, so that more breaks could easily occur.

Figure 2C shows the development of the mean doublet interspike interval of the SP2(2)-fibre with time and in dependence on its own activity level (Fig. 2A). No direct dynamic correlation between the activity of the SP2(2)-fibre and the duration of the doublet II can be seen. Following bladder catheter pulling 1 e.g. the activity first increased (Fig. 2A) and the doublet II decreased; however, when the activity quickly decreased, the doublet II did not increase as quickly. Doublet II decreased slowly with the increasing activity and increased slowly with the decreasing activity. This slowly change could come from the more static behaviour of the second encoder site generating the second AP (of intrafusal muscle fibre origin); could be due to slow and fast activity changes of the somatic intrafusal innervation; or could be due to the slowlier changes of the parasympathetic nervous system (15). The doublet II duration changes (Fig. 2C) showed no direct correlation to the duration of the oscillation period of the oscillatory firing α_2-motoneuron O2 (Fig. 2B).

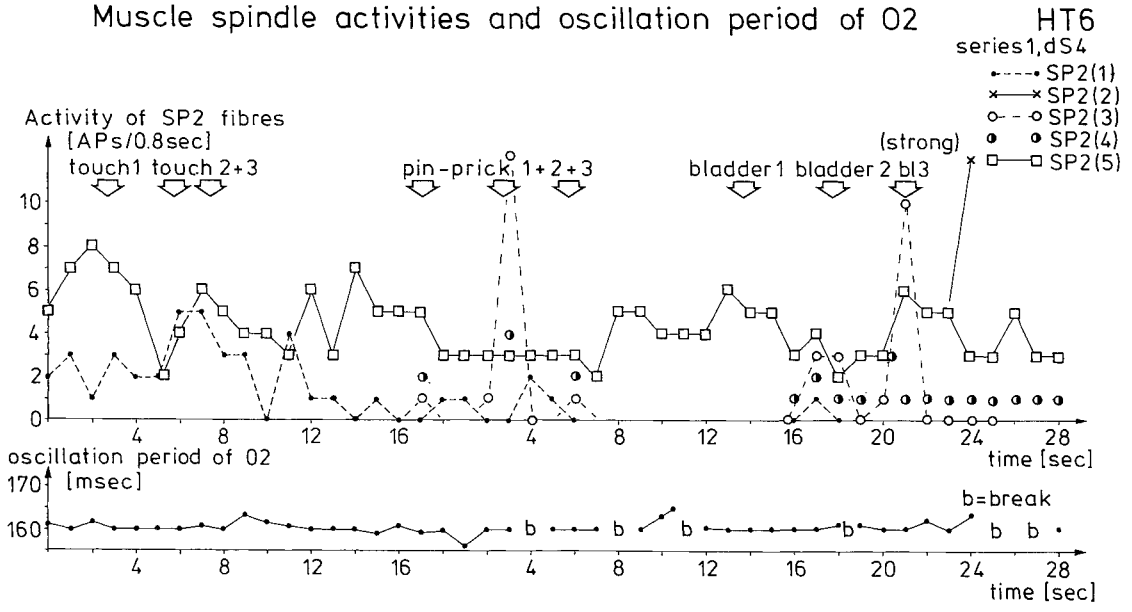

Fig. 3. — Activity changes of 5 secondary muscle spindle afferents SP2(1 to 5) in relation to oscillation period of continuous oscillatory firing α_2-motoneuron O2. Note that oscillation breaks occur more easily than in the case illustrated in figure 2. The activity of fibre SP2(2) is only suggested. Low activity is often omitted.

Break of α_2-oscillation in paraplegic 1 secondary to SP2(1)-fibre associated changes following anal catheter pulling

Probably the transient break of continuous oscillation is functionally unimportant. Nevertheless, it is of high interest here, because it may throw light on the mechanism which drives the oscillator. The drive of the oscillator includes adequate afferent input, certain activity levels of the afferent inputs and certain phases between the afferent impulse patterns and the oscillation cycle. The phases between the afferent APs and the first AP of the motoneuron impulse trains can be directly measured as the time difference between them. An indication for the existence of a necessary phase relation is a rather fixed relation of the respective afferent II distributions to the oscillation period. In Para 1, it could be shown that a break in continuous oscillation correlated with a strong shift of the afferent II distribution peak at about 150 msec in relation to the oscillation period.

Figure 4A shows the activity of the secondary muscle spindle afferent fibre SP2(1) in Para 1 before stimulation (a), upon anal catheter pulling (b), shortly thereafter (c), at a later interval (d) and after a longer interval following catheter pulling (e). After stimulation only the activity actually increased in response to catheter pulling (c). The light activity increase before catheter pulling, between 4 and 14 sec, was due to the light stimulation caused by the handling of the connection to the catheter. Long after stimulaiton (38 sec, d) the activity only returned to the pre-stimulation level. A transient break of the continuously oscillatory firing α_2-motoneuron O1 occurred only long after stimulation and afferent activity increase. In figure 4C the break in oscillation is correlated to the distributions of interspike intervals (IIs) at different time periods. Figure 4B shows the approximate intervals when oscillation occurred. The dashed line indicates transient oscillatory firing and the solid line continuous oscillatory firing. Numerous motoneurons were identified in the same S4 root of Para 1, which fired in the occasional firing mode (12), and 4 motoneurons were identified which fired in the oscillatory firing mode (13).

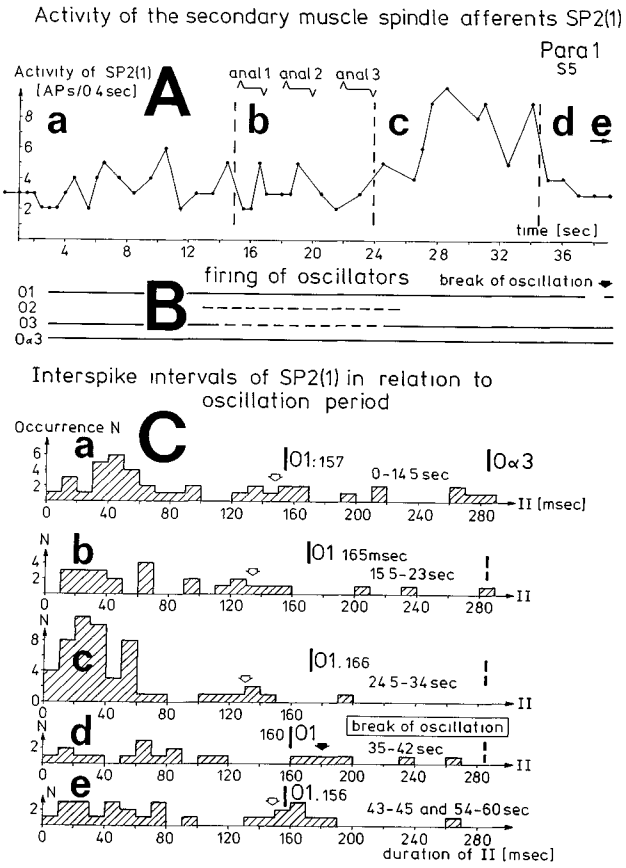

Fig. 4. — Activity and interspike interval changes of the secondary muscle spindle afferent fibre SP2(1) in paraplegic 1 before and following stimulation. A.a. Activity changes before anal-catheter pulling. Some stimulation appears between 4 and 15 sec due to catheter handling. b. Anal catheter pulling period. c. Immediate post-stimulation interval. d. and e. Later post-stimulation intervals. Intervals a to e same as in C. B. Oscillatory firing α_2-motoneurons O1, O2 and O3 and α_2-motoneuron Oα3. Full line = continuous oscillatory firing, dashed line = transient oscillatory, no line = no oscillatory firing. C. Interspike interval frequency distribution histogram of fibre SP2(1) before (a), upon (b), and after stimulaton (c, d, e). The time intervals used are indicated at each histogram. Exact mean oscillation periods of O1 at the same intervals are shown. Note that in d the 150 msec peak is shifted to 180 msec (filled arrow) (hysteresis-effect), at a time when oscillation broke. The oscillation period of the oscillatory firing α_3-motoneuron Oα3 is given.

Three of the 4 motoneurons were mainly continuously oscillatory firing, and one motoneuron was transiently oscillatory firing (O2). Most likely all the 4 oscillatory firing motoneurons contributed to the continence of the rectum.

The II distributions shown in figure 4C are those of the parent fibre SP2(1). It was not tried to split the activity into those of single encoder sites. As shown previously however (14), fibre SP2(1) in paraplegic 1 fired with bursts. It seemed therefore that the fibre was overactivated in relation to the activity of a comparable fibre in HT6 (SP2(3)) (14). Before anal catheter pulling, the distribution peak of fibre SP2(1) at 150 msec, (Fig. 4Ca) had a similar duration as the oscillation period of the oscillatory firing α_2-motoneuron O1 (157 msec). Upon anal catheter pullings (b) this peak slightly shifted towards shorter II durations and the oscillation period was prolonged (165 msec); this may be an indication for a less effective drive, nevertheless oscillation continued. With the activity increase in c the driving peak shifted to even shorter durations (130 msec), the oscillation period showed a further increase to 166 msec, but still, the oscillation holded. Then, with a drop of the activity of fibre SP2(1) (d), this peak shifted drastically to longer durations (180 msec) (filled arrow), and the oscillation broke. With a backward shift of the SP2(1) fibre distribution peak, the oscillation started again with a period of 160 msec. Later on (e), the former distribution peak of fibre SP2(1) shifted further backwards to shorter values closer to those of before stimulation (150 msec), and the oscillation period returned to the pre-pulling value (156 msec). This series of correlations indicate that the transient break in oscillation was related to the shift of the SP2(1)-fibre II distribution peak at about 150 msec (arrow). However, as seen from II distributions shown in figure 4C, not only the peak at 150 msec shifted with the break in oscillation (d): also, the peak between 40 and 80 msec moved to longer times and the whole activity was reduced. Thus, the break in oscillation was probably due to the change of the entire impulse pattern of fibre SP2(1), and this change could be made visible by the shift of the 150 msec peak. Several spindles must have contributed to the afferent drive of oscillation. Probably, the other spindle afferents showed a similar behaviour. Fibre SP2(2) in paraplegic 1 showed a similar distribution as that, shown in figure 4Ca. However, the wave form identification was not safe enough to allow considerations concerning longer intervals. That not only the afferent distribution peak at about 150 msec contributed to oscillation can be understood owing to a rather constant phase which must occur quite often between afferent APs and oscillation cycle, as determined by the first AP of an impulse train. If the oscillation period is of a duration of 157 msec and the driving peak of 150 msec, then after a couple of 150 msec intervals the necessary range for the drive of oscillation will be lost. Therefore, some IIs of other durations have to be interposed to regulate the phase. This can best be seen with the IIs of fibre SP2(1) in HT6 (Fig. 2A Ref. 14). A combination only of at least 145 and 85 msec IIs ($2 \times 85 = 170$ msec) can yield a mean II of about 160 msec, which is the interval required for the oscillation period to keep a constant phase.

Figure 2A of Ref. 14 suggested that the splitting of the II distribution peak of fibre SP2(1) in HT6 had been due to a hysteresis effect of the muscle spindle; namely, with further contraction the afferent IIs slightly differed from those for a decreased contraction of the same intrafusal muscle length (after effects and creep). Figure 4C supports this hypothesis, since the states shown in figures 4Ca and 4Cd had about the same activity levels (Fig. 4A, note the different time interval), but the II distributions were quite different.

Figure 4C also gives the oscillation period of the oscillatory firing α_3-motoneuron Oα3 (about 280 msec). Little is known about how α_3-motoneuron oscillators are driven. The distribution peaks at 280 msec and 140 msec, and also shorter ones, of fibre SP2(1) could also drive the oscillatory firing α_3-motoneuron.

Simultaneous oscillatory firing of α_2-motoneurons innervating the external sphincters of the bladder and the anal canal with their different adequate afferent inputs

Most measurements in the present work as reported in this series of papers were devoted to study the function of the external anal sphincter, even though a good function of the external

bladder sphincter is of considerably more importance for patients with spinal cord lesions (bladder infections). However, it is easier to measure anal sphincter functions. Nevertheless, some progress in the understanding of the external bladder sphincter function could also be achieved and will be reported here.

It was shown previously (9) that with the retrograde filling of the urinary bladder stretch (or tension) receptor activity activated an α_2-motoneuron to switch into the oscillatory firing mode for fillings larger than 600 ml. Considering information supplied by Refs. 13 and 14, more data could be extracted from the measurements.

Figure 5A shows 3 sets of successive interspike intervals (IIs) of stretch receptors (8). The indicated oscillation period of about 110 msec at the given stage of filling was similar to some IIs of the stretch receptors, at least those of fibre S1(1) (Fig. 5A). Since the number of APs per impulse train of this oscillatory firing α_2-motoneuron O1 in HT6 changed from 1.5 to 2 in different combinations with increasing filling of the bladder, the oscillation period changed (8). For stable oscillations, the theoretical value of the oscillation period for a 1 AP impulse train is 100 msec, and 130 msec for a 2 AP impulse train (13). Figure 5B shows an impulse train consisting of 2 APs. Since with this α_2-motoneuron O1 a recurrent fibre was identified, it was possible to identify each single AP of this motoneuron during all recordings. In figure 5B the conduction times and the conduction velocities of the oscillatory firing α_2-motoneuron O1 and of a mucosal afferent fibre (M) (8) are indicated.

With no bladder filling α_2-motoneuron O2 (HT6), most likely innervating the external anal sphincter, was oscillatory firing. With the filling of the bladder α_2-motoneuron O1, most likely innervating the external bladder sphincter, started additionally firing in the oscillatory firing mode for bladder fillings larger than 600 ml (Fig. 6B). With more than 600 ml volume in the bladder 2 oscillators oscillated simultaneously, but they were excited by their own different adequate afferent inputs. The oscillatory firing motoneuron O2 (Fig. 5C) received its adequate

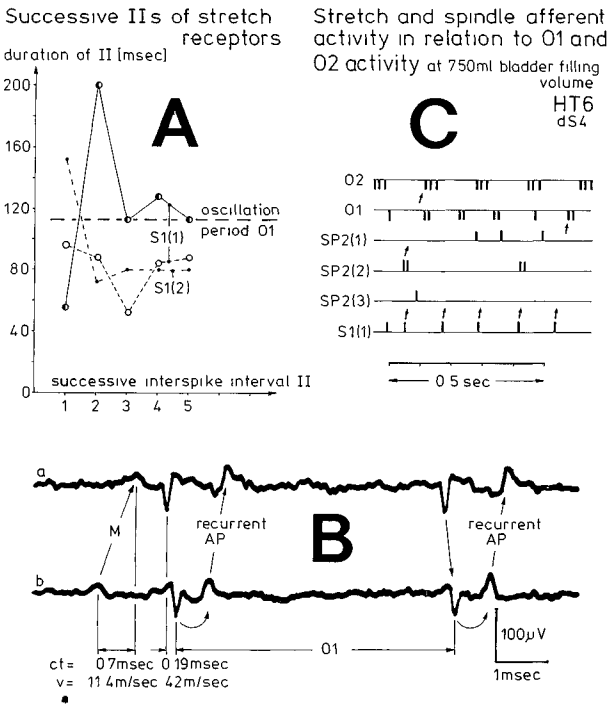

Fig. 5A. — Three series of successive interspike intervals of 2 stretch receptor afferent fibres (S1(1), S1(2)), activated by retrograde urinary bladder filling. Oscillation period is given of oscillatory firing α_2-motoneuron O1, activated only by bladder filling. B. Recording of α_2-motoneuron O1, which most likely innervated the external urethral sphincter. The motoneuron possessed a recurrent fibre (time-locked afferent-like action potential). ct = conduction time, v = conduction velocity, M = mucosal mechanoreceptor afferent AP. C. Impulse patterns of oscillatory firing α_2-motoneuron O2 innervating the external anal sphincter, in relation to the muscle spindle afferent activity SP2(1 to 3)), activated by the stretch of the anal sphincter by the anal catheter, and impulse patterns of oscillatory firing α_2-motoneuron O1 innervating the external urethral sphincter, in relation to the stretch receptor afferent activity (S1(1)) of the urinary bladder, activated by 750 ml bladder filling. Phase relations between APs of SP2(2) and O2 and between APs of S1(1) and O1 are indicated by small arrows.

afferent input from APs in phase of the secondary muscle spindle afferents SP2(1)and SP2(2) and partly SP2(3). An AP in phase from fibre SP2(2) is marked with the small arrow in figure 5C. The simultaneously oscillatory firing α_2-motoneuron O1 (Fig. 5C) received its adequate afferent input in phase from APs of the stretch receptor afferent fibre S1(1), and maybe other fibres. Its APs in phase are also labeled with the small arrows. The phase between these

5 APs and the AP of the O1 motoneuron impulse train was about 50 msec ± 6. As shown previously (14), the phase between APs of the SP2(1) and SP2(2)-fibres and the first AP of the impulse train of α_2-motoneuron O2 was also 50 msec. The similarity of the two phases is probably accidental. Each oscillatory firing α_2-motoneuron fired according to its own adequate afferent APs in phase. For longer periods of time it was difficult to identify single stretch receptor afferents by their wave form.

Since it is known that there are some interactions between the external anal and the external bladder sphincters in humans (16), the frequency and the activity of both oscillatory systems were plotted (Fig. 6B, C). The mean activity and the frequency of the bladder sphincter motoneuron O1 were taken from a previous work (9). As can be seen from figure 6C, the anal sphincter α_2-motoneuron O2 reduced its activity and mean frequency with the increasing activity and frequency of the bladder sphincter α_2-motoneuron O1. Partly antagonistic function of external anal and bladder sphincters are known for humans (16). With the beginning of the overflow mechanism of the bladder for bladder fillings larger than 800 ml the mean activity and the frequency of motoneuron O1 decreased, and the mean activity and frequency of motoneuron O2 increased again.

Function and location of receptors contributing to micturition and defecation

Further knowledge about the function and the anatomical location of the receptors of the secondary muscle spindle afferents SP2(1) to SP2(3) and the stretch receptor afferent fibre S1 could be obtained from their activity changes associated with the filling of the bladder (Fig. 6A). The single afferent fibre S1 of a urinary bladder stretch receptor increased its activity with the filling of the bladder. The other stretch receptor afferents in the same root showed similar activity changes (9). The single fibre S1 reduced its activity during a 10 to 20 min break in filling (Fig. 6A), most likely the bladder adapted to the filling (2) (smooth muscle fibre shift). With further filling, the activity of fibre S1 increased again, and decreased upon onset of the overflow mechanism of the bladder at filling volumes exceeding 800 ml. Fibre S1

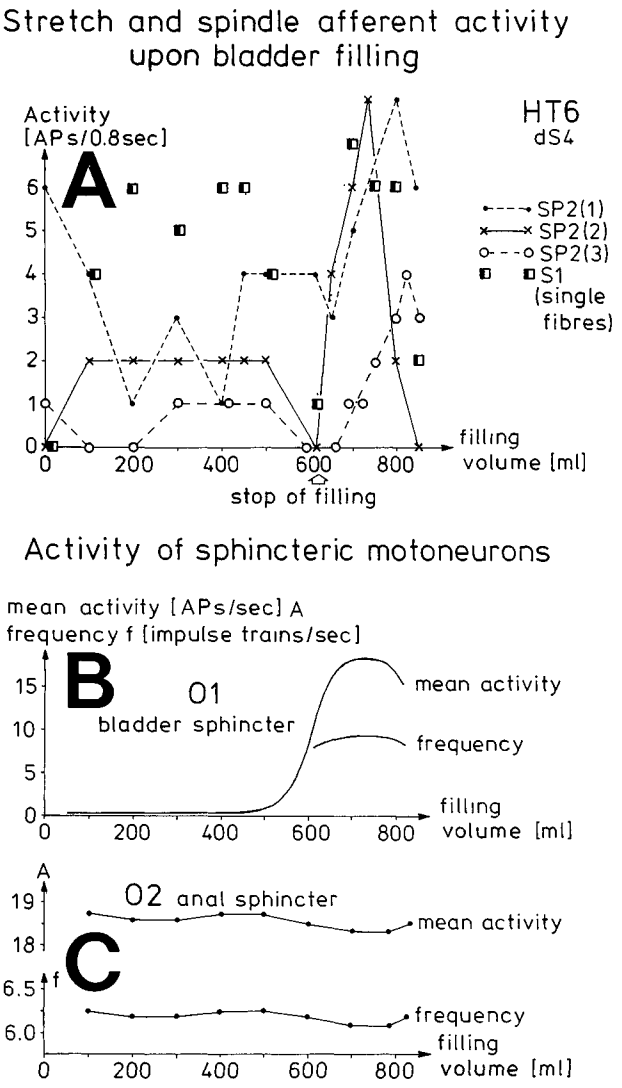

Fig. 6. — Activity changes of secondary muscle spindle (SP2) and urinary bladder stretch receptor (S1) afferents (A) in relation to activity changes of sphincteric α_2-motoneuron O1 of the external urethral sphincter (B), and in relation to the activity changes of sphincteric α_2-motoneuron O2 innervating the external anal sphincter; increasing filling volume of the bladder. Motoneuron O2 fired in the constant oscillatory firing mode, slightly affected by the filling of the bladder. Motoneuron O1 fired until approx. 550 ml filling volume in the occasional firing mode (very low activity), until 620 ml in the transient oscillatory firing mode (medium activity level), and until 820 ml in the constant oscillatory firing mode (high activity) (9).

indicated pressure in the bladder, and most likely monitored tension in the bladder wall. Most probably, its receptor was located in the bladder wall, as illustrated in figure 7 on the lower female pelvis. The secondary muscle spindle afferent fibre SP2(2), which was very sensitive to strong bladder catheter pullings (Fig. 2), increased its activity with the bladder filling and reduced it upon the filling stoppage (Fig. 6A). A strong increase in activity was again recorded upon further bladder filling, and a sudden decrease just before the onset of the overflow mechanism at 800 ml volume. Thus, the muscle spindle of this secondary afferent fibre must have been located in a muscle involved in performing of the continence function of the urinary bladder. Since most likely there are no muscle spindles in the external urinary bladder sphincter (9), the SP2(2) muscle spindle was probably located in the musculus pubococcygeus (Fig. 7), which contributes to the continence of the urinary bladder (3). Therefore, in figure 7 the SP2(2) spindle is sited into this muscle. The secondary muscle spindle afferent fibre SP2(3) responded strongly to painful pin-prick and painful (strong) bladder catheter pulling (Fig. 3, Figs. 7, 8 of Ref. 14). The activity of fibre SP2(3) increased slightly with the bladder filling, but increased most strongly upon reaching the highest pressure in the bladder or immediately after (Fig. 6A), as measured by the S1 fibre activity. Thus, fibre SP2(3) somehow monitored painful pressure in the bladder, which is the highest with the highest pressure in the bladder. Upon the application of painful stimuli, the sphincters and the pelvic floor will contruct. Since fibre SP2(3) did not respond strongly to bladder and anal catheter pullings of medium intensity, spindle SP2(3) was probably located in the pelvic floor (Fig. 7). The secondary muscle spindle afferent

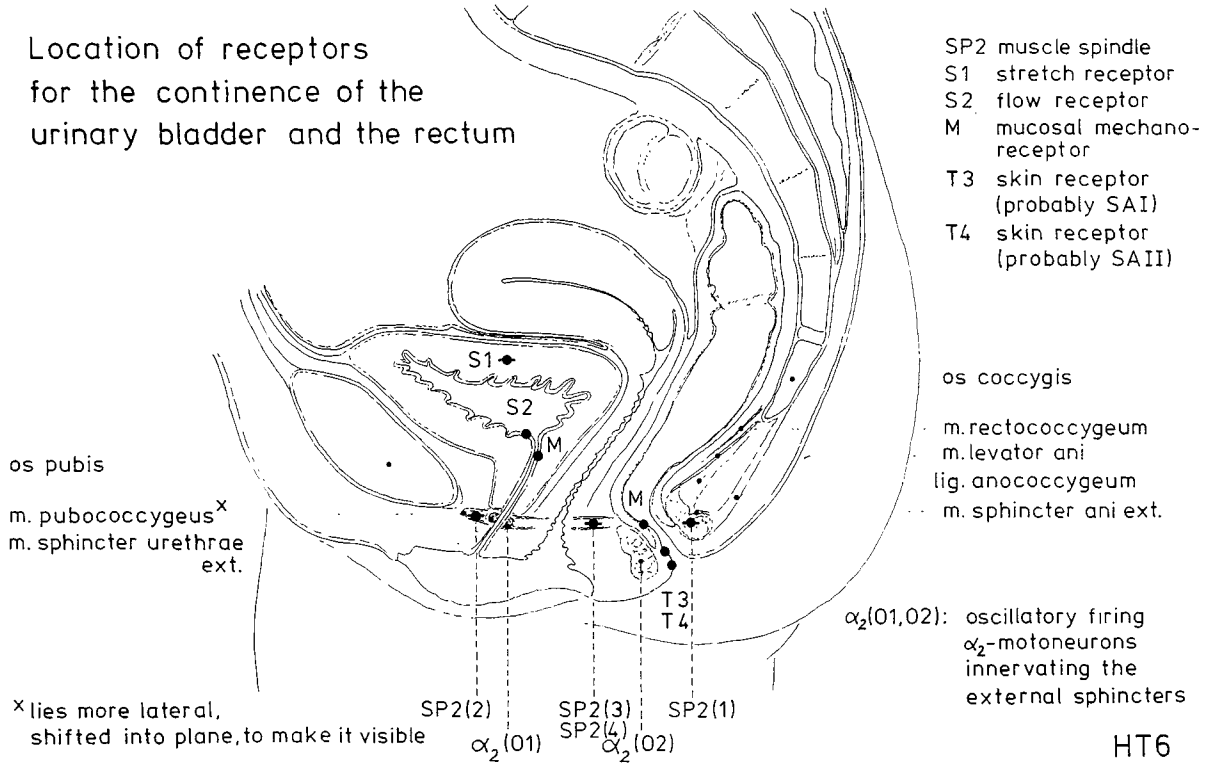

Fig. 7. — Location of the receptors for the continence of the urinary bladder and the rectum. Most likely the external anal sphincter is innervated by the pudendal nerve, whereas the external bladder sphincter via the pelvic nerves (3). It has been established with certainty that motoneurons innervating the external bladder and anal sphincters run through the lower sacral nerve roots.

fibre SP2(1) showed the highest activity before bladder filling and for the highest filling, and reduced its activity for medium bladder fillings (Fig. 6A). Stoppage of the bladder filling had little effect on this activity. Thus, fibre SP2(1) is not directly involved in the continence of the urinary bladder. The reduced activity upon medium-sized bladder fillings, and thus slightly antagonistic bladder function, indicates association to the continence of the rectum. Since fibre SP2(1) responded to anal catheter pulling (Fig. 2) and to touch (Fig. 3), and not to bladder catheter pulling (Fig. 3), spindle SP2(1) was probably situated in the superficial parts of the external anal sphincter (Fig. 7). The pain sensitive tertiary muscle spindle afferent fibre SP2(4) innervated the same muscle spindle as did fibre SP2(3) (14). It was not possible to locate spindle SP2(5) as it did not respond specifically.

Even with recording from a S4 dorsal root, and having no anatomical knowledge about which are the body parts certain fibres run to, the changes of impulse patterns and activity levels provide quite a lot information about which parts of the pelvis are innervated by the afferents and what functions they transmit. Figure 7 shows the female pelvis with the bladder and the rectum, and the muslces contributing to their continence. It was reasoned above to which muscles the muscle spindles and the stretch receptors have to be attributed to. Moreover, figure 7 shows the two sphincters which are innervated by the oscillatory firing α_2-motoneuron O1 and O2. Flow receptors, which were strongly activated with retrograde bladder filling (8) are sited to the trigonum vesicae, where the density of the flow receptors is probably the strongest. Mucosal afferents (M) were stimulated upon bladder and anal catheter pulling (8), and are thus sited into the urethra and the anal canal. Skin receptor afferents were stimulated upon anal catheter pulling, and almost not at all upon bladder catheter pulling (8). The low threshold T3 and T4 skin afferent receptors were sited into the anal canal. Their function is important, similarly as that of afferent skin receptors T1 and T2 (8) for the discrimination between gas, fluid and solid substances (6, 8, 16). Quite a lot of specific afferent and efferent nerve fibre functions can be measured with different stimulations necessary for micturition and defecation, by recording with 2 pairs of wire electrodes from a lower sacral dorsal nerve root.

Discussion

Phase relation between oscillation cycle and APs of the adequate afferent input

It was shown that α_2-motoneuron O2 fired in the oscillatory mode with no breaks (Fig. 2) when the activity of the secondary spindle afferents SP2(1) and SP2(2) was high. Breaks occurred (Fig. 3) when the activity of fibres SP2(1) and SP2(2) was low. Thus, the activity levels of the adequate spindle afferents were one factor for the excitation of the oscillators. The oscillatory systems consisted mainly of the motoneuron itself and of sets of coupled interneurons (13). Mechanical and electronic oscillators need rather continuous energy supply in phase for the oscillation, to overcome damping. As the phases in figure 5C indicate, not only the number of APs of the adequate afferent type is sufficient for continuous oscillation to occur, but also the impulse patterns must be in a way that the APs have a certain time correlation to oscillation cycle. From figure 4 it can be seen that oscillation of α_2-motoneuron O1 broke upon the anal catheter pullings, even though the activity level was the same as before (Fig. 4Aa (left part)). During the break of oscillation, the interspike interval distribution had completely changed (Fig. 4Cd) in comparison to the pre-stimulation pattern (Fig. 4C,a-c). In particular the peak at about 150 msec changed its position. Figures 7, 8 of Ref. 14 showed (small arrows) moments when SP2(1) and SP2(2) fibre APs were in phase, within a certain range (50 ± 20 msec), to the first AP of the impulse train of the oscillatory firing motoneuron. Also in the present recordings there was a phase relation of 50 ± 6 msec between S1(1) APs and motoneuron O1 impulse trains in a completely different oscillatory system. The identicity of phases is probably accidental. Probably the actual value of the phase (range) is not as important, as there could be time consuming

interneurons between the afferents and the oscillation loop to adjust the phase. In mechanical and electronical oscillators only energy in phase contributes to oscillation. In further studies, the distribution of phases of the afferent APs will have to be correlated to oscillation period and the stability of oscillation. Also, the possibility has to be excluded that the phases are distributed statistically.

The durations of the interspike intervals of the spindle afferents, which in different combinations were similar to that of oscillation period, could have been generated by the muscle spindle itself or together with the impulse patterns of the efferent muscle spindle innervation. At least to keep a constant phase however, the spindle has to be under a control system, which guards that the spindle activity is not drifting. In electronic oscillators the output is coupled back to the input to establish a constant phase. Since only efferent innervation can precisely control the muscle spindle, the intrafusal motoneurons (and maybe the autonomic system) need information on the phases of oscillation. It will be shown in the following paper (15) that there was a rather constant phase relation between the occurrences of γ-APs and the first AP of the oscillatory firing α_2-motoneuron.

The constant phase from the activity of the efferent spindle innervation, via that of the muscle spindle afferent fibre, to the oscillatory system, can be broken more directly by the γ-efferent activity, not under consideration here, and by intrafusal muscle fibres, coupling the activity of the afferent and efferent spindle innervation. The different properties of the bag 1, bag 2 and chain fibres (1) can change the phase relation. Following stimulation the summed or single (chain fibre) contributions from intrafusal muscle fibres can result in a hysteresis effect: too few APs of the adequate afferents in the necessary phase range will break oscillation. When the steady state is nearly achieved again, sufficient APs with the right phase occur again and the oscillator starts oscillating again. The steady state is given by the constant stretch of the anal sphincter maintained by the catheter. Since each spindle afferent fibre innervates with its branches several intrafusal muscle fibres (1), so that several encoding sites exist (14), and since also each motoneuron innervates different intrafusal fibres (4), there is a considerable complexity in the muscle spindle receptor.

A single encoding site can send unmyelinated branches to different intrafusal muscle fibres, so that a single encoder can obtain information from different intrafusal muscle fibres, and can therefore receive drive from different intrafusal motoneurons. Generator potentials may spread from one branch to an other, giving rise to interactions of different encoders belonging to the same parent fibre. However, using this method to determine the impulse patterns of the muscle spindle afferents, and being able to split them into impulse patterns of single encoders (probably, only 1 or 2 encoders are sometimes active of the several existing), and recording simultaneously the impulse patterns of single intrafusal motoneurons (15), the impulse pattern changes through the spindle can be measured.

Under constant stretch reflex of the anal sphincter the oscillatory system, consisting of the motoneuron and the interneurons, receives its afferent APs in phase from the stretched spindles. Since the spindle afferents fire in a certain phase, they are part of the loop, which excites the oscillatory system. The control of the external anal sphincter acts on the muscle spindles as the essential part of this excitation loop.

Concerning the continence of the bladder, the APs of one stretch receptor afferent fibre also very often were in phase with the impulse train of the oscillatory firing α_2-motoneuron, innervating the external bladder sphincter (Fig. 5C). The parasympathetic division might be a candidate for supplying certain phase or for stopping the receptor activity from drifting.

Different oscillatory systems

One kind of oscillators are here the α_2-motoneurons innervating the external anal sphincter, with its interneurons, excited by the afferents of muscle spindles of the anal sphincter or functionally associated muscles. Activity from mucosal and skin afferents (Fig. 7) may contribute to drive the oscillator. The other kind of

oscillators are α_2-motoneurons innervating the external urinary bladder sphincter with their interneurons, which are excited by the activity of the stretch receptor afferents of the bladder wall. Activity from mucosal and flow receptors (8) of the urethra and trigonum vesicae may contribute to the excitation or inhibition (9) of the oscillator. The interaction between the two kinds of oscillatory systems contribute to the agonistic and antagonistic functions of micturition and defecation. α_3-motoneuron oscillators have also been detected (9, 13). The irregularity in the interspike intervals of long α_3-motoneuron impulse trains (9, 13) may indicate coupling of the oscillators. In the occasional firing mode extrafusal and intrafusal motoneurons are recruited rhythmically (11, 12). Rhythmicity was observed in the activity changes of the oscillatory firing α_2-motoneuron O4 in Para 2 (13). Secondary spindle afferents increased and decreased their activity with a frequency of 0.3 Hz (Fig. 2). In the brain stem oscillators have been detected for breathing and the control of the heartbeat (5). Many kinds of oscillators and oscillator couplings probably exist in the human central nervous system.

References

1. BANKS, R.W., BARKER, D. and STACEY, M.J.: Form and distribution of sensory terminals in cat hindlimb muscle spindles. *Phil. Trans. R. Soc. Lond.*, B299: 329-364, 1982.
2. DENNY-BROWN, D. and ROBERTSON, E.G.: The state of the bladder and its sphincters in complete transverse lesions of the spinal cord and cauda equina. *Brain*, 56: 397-463, 1933.
3. GOSLING, J.A., DIXON, J.S. and HUMPHERSON, J.R.: *Functional anatomy of the urinary tract*, Livingstone, Gower Medical Publishing, London, 5-18, 1983.
4. KUCERA, J.: Reconstruction of the nerve supply to a human muscle spindle. *Neurosci. Lett.*, 63: 180-184, 1986.
5. LANGHORST, P., SCHULTZ, G. and LAMBERTZ, M.: Intergrative control mechanisms for cardiorespiratory and somatomotor functions in the reticular formation of the lower brain stem. In: Grossman, P., Janssen, K.H. and Vaitl, D. (Eds.), *Cardiorespiratory and Cardiosomatic Psychophysiology*, Plenum Publishing Corporation, 9-39, 1986.
6. PERCY, J.: The neural control of the bowel. In: Swash, M. and Kennard, C. (Eds.), *Scientific Basis of Clinical Neurology*, Livingston, Edinburgh, 503-510, 1985.
7. QUICK, D.C., KENNEDY, W.R. and POPPELE, R.E.: Anatomical evidence for multiple sources of action potentials in the afferent fibres of muscle spindles. *Neuroscience*, 5: 109-115, 1980.
8. SCHALOW, G.: Conduction velocities and nerve fibre diameters of touch, pain, urinary bladder and anal canal afferents and α and γ-motoneurons in human dorsal sacral roots. *Electromyogr. Clin. Neurophysiol.*, 31: 265-296; 1991.
9. SCHALOW, G.: Oscillatory firing of single human sphincteric α_2 and α_3-motoneurons reflexly activated for the continence of urinary bladder and rectum. Restoration of bladder function in paraplegia. *Electromyogr. clin. Neurophysiol.*, 31: 323-355, 1991.
10. SCHALOW, G.: Coactivity of secondary spindle afferents and α_2, α_3, γ and γ_2-motoneurons innervating anal and urinary bladder sphincters in humans. *Electromyogr. Clin. Neurophysiol.*, 31: 223-241, 1991.
11. SCHALOW, G. and WATTIG, B.: Recruitment of α and γ-motoneurons in rats, dogs and humans. *Electromyogr. Clin. Neurophysiol.*, 33: 387-400, 1993.
12. SCHALOW, G.: Recruitment of motoneurons in the occasional firing mode in paraplegics. *Electromyogr. Clin. Neurophysiol.*, 38: 401-408, 1993.
13. SCHALOW, G.: Spinal oscillators in man under normal and pathologic conditions. *Electromyogr. Clin. Neurophysiol.*, 33: 409-426, 1993.
14. SCHALOW, G.: Impulse patterns of single encoding sites of human secondary muscle spindle afferents. *Electromyogr. Clin. Neurophysiol.*, this volume, 451-464.
15. SCHALOW, G.: Action potential patterns of intrafusal γ and parasympathetic motoneurons, secondary muscle spindle afferents and an oscillatory firing α_2-motoneuron and the phase relations among them in humans. *Electromyogr. clin. Neurophysiol.*, this volume, 477-503.
16. SCHUSTER, M.M.: Motor action of rectum and anal sphincters in continence and defecation. In: Heidel, W. (Ed.), *Handbook of Physiology, Section 6, Alimentary Canal, Vol. IV, Motility*, American Physiolog. Society, Wash. DC., 2121-2146, 1968.

Address reprint requests to:
G. Schalow, M.D., Ph.D.
Schweizer Paraplegiker-Zentrum
6207 Nottwil
Switzerland