Mono- and Polysynaptic Drive of Oscillatory Firing α_1 (FF) and α_2-Motoneurons (FR) in a Patient with Spinal Cord Lesion

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Abstract. Single-nerve fibre action potentials (APs) were recorded extracellularly from lower sacral nerve roots of patients with spinal cord lesions (paraplegics), and simultaneous single-fibre impulse patterns of α_1 (FF) and α_2-motoneurons (FR) and primary and secondary muscle spindle afferents were analyzed.

An α_1-motoneuron was activated in a time-locked manner by a primary spindle afferent fibre to fire oscillatory with an oscillation period of 110 to 140 ms. The distribution width for the time-locking (phase) was approx. 3 ms, which is interpreted as monosynaptic activation.

A phase-correlated firing of a secondary muscle spindle afferent fibre gave rise to an additional oscillation period of the oscillatory firing α_1-motoneuron, when the primary fibre ceased firing. The phase distribution width was approx. 80 ms, and therefore indicates polysynaptic drive. The drive of the oscillatory firing α_1-motoneuron thus included a monosynaptic from a primary and a polysynaptic activation from a secondary muscle spindle afferent fibre.

An α_2-motoneuron was simultaneously activated to fire oscillatory by a different secondary spindle afferent fibre. The phase distribution width between them was approx. 120 ms, which indicates polysynaptic drive.

The α_1 and α_2-motoneurons fired in the occasional firing mode and in the transient and continuous oscillatory firing mode. Upon touch, pin-prick and bladder and anal catheter pulling, the α_1-motoneuron changed its firing rate more quickly than did the α_2-motoneuron. Thus, the α_1-motoneuron fired more dynamically than did the α_2-motoneuron.

Synchronous oscillatory firing of the α_1 and α_2-motoneurons occurred transiently during pin-pricking.

It is discussed that transient synchronization of oscillatory firing motoneurons points to relative coordination of self-organized oscillatory firing motoneuronal networks to generate locomotion and other intergrative functions. It is further discussed that loss of specific properties of spinal oscillators following spinal cord lesion may give rise to pathologic synchronization, and in this way to disorders in movement.

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Introduction

When recording single-fibre action potentials (APs) extracellularly from lower sacral nerve roots and analyzing simultaneously single-fibre impulse patterns, functions have mainly been explored of α_2 and α_3-motoneurons (contributing to continence), secondary muscle spindle afferents and afferents from the sacral skin, the urinary bladder and the anal canal Highly activated α_2 and α_3-motoneurons were found to fire oscillatory, and self-organizing motoneuronal networks were activated by the different afferents Monosynaptic projections of secondary muscle spindle afferents onto α_2 and α_3-motoneurons have not been found so far [20-22]

Neurologic research on the other hand is often concerned with reflex measurements of limb muscles The monosynaptic activation of unspecified α-motoneurons by primary spindle afferents following electrical stimulation or muscle stretch has been studied extensively So-called secondary effects and „rebound" phenomena have been discussed [7,12,30] In animal research, monosynaptic connectivity has been studied most extensive because it happens to be most easily accessible experimentally, it is not known which precise role specific oligo- and polysynaptic connectivity pattern play for example in tremor suppression

A gap seems to exist between the standard neurologic research and this new research in human neurophysiology Even though functions may differ in different parts of the body, a theory or concept should be able to explain functions of the whole body
Since foot muscles can often slightly be activated by electrical stimulation of lower sacral nerve roots during surgery, and α_1-motoneurons were sometimes identified electrophysiologically and morphometrically, a recording situation should sometime occur in lower sacral nerve roots, in which α_2 and α_1-motoneurons fire oscillatory driven by their respective afferents Then, it should be possible to analyze simultaneously the way of activation of α_1 and α_2-motoneurons and identify differences in the activation between both kinds of motoneurons

In this paper we report a measurement in which α_1 and α_2-motoneurons fired simultaneously oscillatory It was found that also α_1-motoneurons fired oscillatory as predicted [19], and that the main drive came from a primary spindle afferent fibre synapsing monosynaptically onto the α_1-motoneuron The α_2-motoneuron was polysynaptically activated to fire oscillatory by secondary muscle spindle afferents (Fig 2)

Based on the method of single-nerve fibre action potential recording and on the classification scheme for the human peripheral nervous system [23-25], in which nerve fibre groups are characterized by group conduction velocities and group nerve fibre diameters, no contradiction has been found between the results of research in neurology and that of basic human neurophysiology, provided differentiation is made between α_1, α_2 and α_3-motoneurons α_1-Motoneurons are mainly activated monosynaptically by primary muscle spindle af-

ferents to fire oscillatory The response of an α_1-motoneuron to a single primary spindle afferent AP represents a special case of the oscillatory firing mode With the inclusion of the oligosynaptic drive from secondary muscle spindle afferents, the α_1-motoneuron started to fire transiently oscillatory, i e it responded with a second AP after 90 to 130 ms Muscle stretching may activate primary and secondary muscle spindle afferents and, in turn, α_1 and α_2-motoneurons In discussing the monosynaptic stretch reflex as early as in 1934, P Hoffmann spoke of rhythms of approx 100 ms and of refractory periods, a silent period and a rebound (second impulse train when starting to fire transiently oscillatory) [7] Antidromic motoneuron activation gave similar excitation patterns as those of spindle afferents [7] Synchronized activation of different motoneurons to fire transiently oscillatory can explain all effects observed in so-called reflex measurements (not defined exactly as yet)

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 (x1,000), 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 complete spinal cord lesions during the implantation of an electrical anterior root stimulator for urinary bladder control Details of the method are given elsewere [15,23-26] For further data of the patient, see [26]

Results

Single-fibre action potentials (APs) were recorded extracellularly from lower sacral nerve roots, nerve fibre groups identified based on conduction velocity distribution histograms (Fig 1 of [23]), and impulse patterns of single α_1 (FF) and α_2-motoneurons (FR) and primary (SP1) and secondary muscle spindle afferents (SP2) were analyzed

Time-locked (temporally strict correlation) activation of an α_1-motoneuron by a primary spindle afferent fibre

In Fig 1A a sweep piece is shown with APs of an α_1-motoneuron (FF) and a primary spindle afferent fibre (SP1) The time difference between the α_1-motoneuron AP and the primary spindle afferent AP is marked with 13 6 ms The rhythmic firing pattern of the α_1-motoneuron and the primary spindle afferent fibre is drawn schematically in Fig 1B The time interval between consecutive APs of the α_1-motoneuron (oscillation period $T\alpha_1$) is marked

In Fig. 1C,E,G the duration is shown of the oscillation period of the α_1-motoneuron, and in Fig. 1D,F,G distributions of the phase between the responses of the α_1-motoneuron and the primary spindle afferent fibre are shown for different stimulations. The phase between the α_1-motoneuron and the primary spindle afferent fibre firing varied with the difference being approx. 3 ms (Fig.1D,F,H), and the oscillation period showed differences of approx. 30 ms (Fig.1C,E,G). The narrower distribution (by a factor of 10) of the phase between the α_1-motoneuron and the SP1 fibre firing as compared to the oscillation period justifies the term time-locked firing and indicates monosynaptic activation of the α_1-motoneuron by the SP1 fibre (see Discussion).

Since there was no time-locked firing found between secondary muscle spindle afferents and α_2-motoneurons (FR), it is of interest to know whether each α_1-motoneuron AP
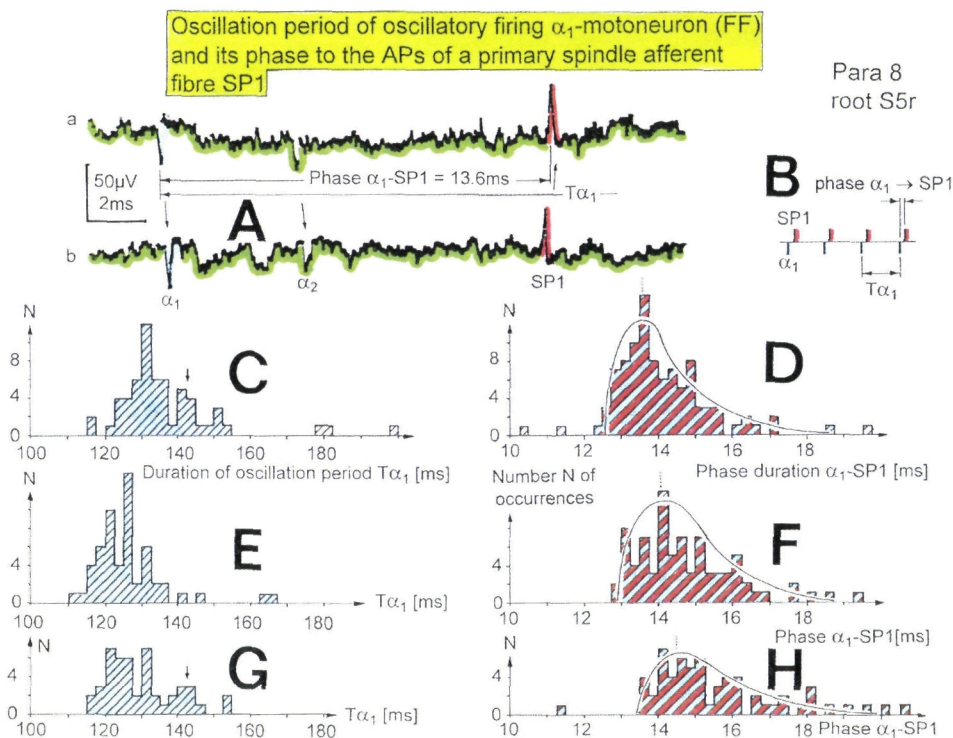

Figure 1. Distributions of the oscillation period of an oscillatory firing α_1-motoneuron (FF) and the phase to its driving primary spindle afferent fibre SP1.

A: Original recording of APs of the α_1-motoneuron and the SP1 fibre.

B: Definition of oscillation period $T\alpha_1$ and phase $\alpha_1 \to$ SP1.

C.-H: Oscillation periods and the corresponding phases following different stimulations (C;D, oscillation period and phase distributions for the time interval 65-82s; Fig.4A (strongest afferent drive). E; F, distribution for the time interval 1-30s; Fig.4B. G;H, for 31-66s, Fig.4B). In „C" and „G", the small arrows mark subpeaks in the oscillation period distributions. Para 8, right root S5.

was a response to an AP of this particular SP1 fibre, and how the differences in oscillatory firing are between the α_1-motoneurons and the primary spindle afferents on one hand, and the α_2-motoneurons and the secondary spindle afferents on the other hand.

Different drive of α_1 and α_2-motoneurons by spindle afferents

Fig. 2 shows the differences in firing between an α_1-motoneuron and a primary spindle afferent fibre on one hand, and an α_2-motoneuron and a secondary spindle afferent fibre on the other hand. The phase relations are defined in Fig. 2A,B.
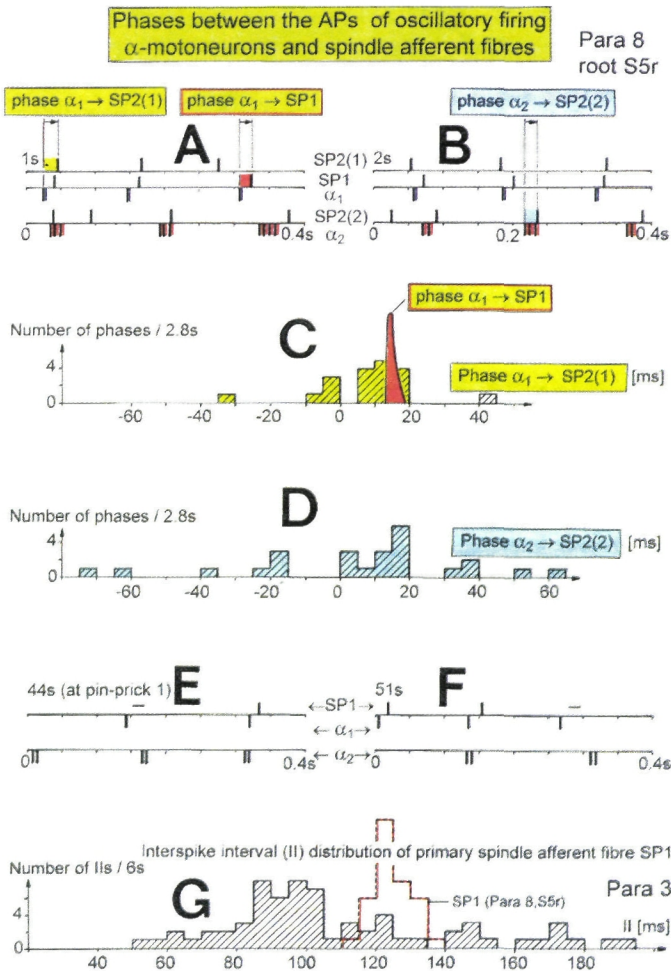

Figure 2. Phase relations between the α_1 (FF) and α_2-motoneurons (FR) and its driving primary (SP1) and secondary (SP2) muscle spindle afferent fibres.

A., B: Definition of the different phases.

C: Distribution of the phases between the α_1-motoneuron and the secondary muscle spindle afferent fibre SP2(1). Note that the phase distribution $\alpha1 \rightarrow$ SP2(1) is approx. 40 times broader than that of the $\alpha_1\rightarrow$ SP1 distribution (phase $\alpha_1\rightarrow$ SP1 redrawn from Fig.1).

D: Distribution of the phases between the α_2-motoneuron and the secondary muscle spindle afferent fibre SP2(2). Note that the phase distribution $\alpha_2 \rightarrow$ SP2(2) is similar to that of the $\alpha_1 \rightarrow$SP2(1) (approx. 4 times broader).

E., F: Note that every α_1-AP of the oscillatory firing α_1-motoneuron is accompanied by a time-locked SP1-AP. „A"-"F" = para 8.

G: Interspike interval (II) distribution for a primary spindle afferent fibre of paraplegic 3. Note that the distribution peak lies approx. at 95 ms; probably, this fibre was driving an α_1-motoneuron with an average oscillation period of 95 ms. The SP1 fibre distribution for paraplegic 8 is included for comparison.

Fig 2C shows the phase distribution $\alpha_1 \rightarrow$ SP1 (redrawn from Fig 1), and Fig 2D shows that of $\alpha_2 \rightarrow$ SP2(2) The phase distribution between the firing of the α_2-motoneuron and of the secondary spindle afferent fibre SP2(2) (120 ms) is broader by a factor of 40 than that between the α_1-motoneuron and its monosynaptically driving primary spindle afferent fibre SP1 It is obvious that there was a polysynaptic drive of the oscillatory firing α_2-motoneuron by the secondary spindle afferent fibre SP2(2)

The question arises whether the oscillatory firing α_1-motoneuron is only driven by a primary spindle afferent fibre or also additionally by secondary spindle afferents It can be seen in Fig 2E,F that every SP1 fibre AP locked an α_1-motoneuron AP but not every α_1-motoneuron AP was a response to an AP of that particular primary spindle afferent fibre SP1 A secondary muscle spindle afferent fibre (SP2(1)) could be found which fired phase-correlated to the α_1-motoneuron (Fig 2C) The phase distribution (approx 80 ms), was broader by a factor of 30 than those of the SP1 fibre and the α_1-motoneuron (Fig 2C), and slightly narrower than the phase distributions of the α_2-motoneuron and the secondary spindle afferent fibre SP2(2) (Fig 2D)

Thus this measurement suggests that the α_1-motoneuron was primarily driven by its primary spindle afferent fibre SP1, but got additionally some drive in phase from the secondary spindle afferent fibre SP2(1) The drive from the SP2(1) fibre, and perhaps some other afferents, made it possible for the α_1-motoneuron to fire one AP without the drive from its primary spindle afferent fibre This additional AP which did not result from an SP1 AP, may explain the so-called rebound phenomenon, observed in „reflex measurements"

In paraplegic 3 (Fig 2G), a primary spindle afferent fibre could be detected, with an interspike interval of mostly between 85 and 105 ms, probably driving an α_1-motoneuron with an oscillation period in that time range The interspike interval distribution of the SP1 fibre for para 8 is indicated in Fig 2G by the dashed line The two rhythmically firing primary spindle afferent fibres had a broad distribution, similar to the distributions of secondary spindle afferents The main difference between the paired α_1-motoneuron with its driving primary spindle afferent fibre and the paired α_2-motoneuron with its driving secondary spindle afferent fibres is the temporally strict coordination (time-locking) between the firings of the α_1-motoneuron and the primary spindle afferent fibre (phase distribution width $\approx$3 ms), i e the monosynaptic drive of the α_1-motoneuron by the primary spindle afferent fibre

Synchronization in firing between the α_1 and the α_2-motoneuron

The question arises whether α_1 and α_2-motoneurons (distinguished by the velocity of conduction, the firing pattern (including the distributions of the interspike intervals of the impulse train) and mostly the AP amplitude) interact with each other when firing oscillatory Extracellular APs of α_1 and α_2-motoneurons are shown in Fig 3A, and sets of schematically drawn impulse patterns are given in Fig 3B,C,D,E

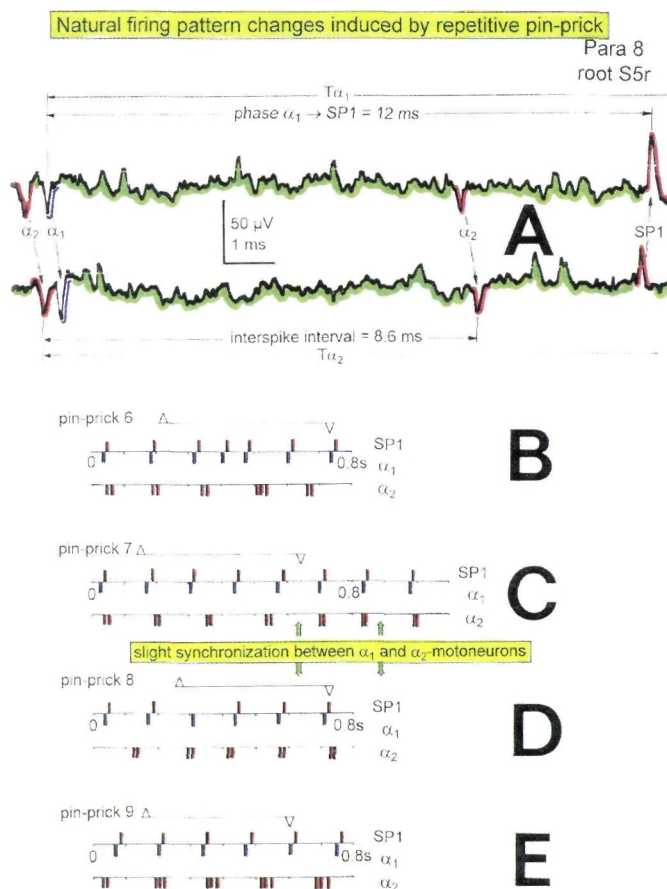By comparing the occurrences of the impulse trains of the α_1-motoneuron (AP impulse

Figure 3. Natural impulse patterns of α_1 (FF) and α_2-motoneurons (FR) and of a primary muscle spindle afferent fibre (SP1) upon repetitive pin-prick. A: Original recording of APs of the α_1 and α_2-motoneurons and the SP1 fibre.
B - E: Firing patterns upon pin-pricking sites 6,7,8,9 (sacral dermatome, close to the anus [27]). Note that at pin-prick points 7 and 8 there was partial synchronization between the α_1 and the α_2-motoneurons. Note further the smaller amplitude and the larger conduction time of the α_2-motoneuron APs.

train length = 1 AP) and the α_2-motoneuron (impulse train length = 2 to 3 APs) in Fig. 3C,D with those in Fig. 3B,E, some synchronization can be seen between the firing of the α_1 and the α_2-motoneurons upon pin-prick stimulation 7 and 8 (for further details of the pin-prick stimulation, see [27]). This indicates that oscillatory firing α_1 and α_2-motoneuronal networks can transiently synchronize their firing upon pin-prick stimulation, which can also be seen in corresponding peaks in the oscillation period distributions (see Discussion).

More dynamic recruitment of the oscillatory firing α_1-motoneuron in comparison to the α_2-motoneuron

If α_1 and α_2-motoneurons fire oscillatory, what is then the difference between both self-organizing neuronal networks? The α_1-motoneurons, innervating fast fatigue muscle fibres, are mainly driven by the dynamic primary spindle afferents, whereas the α_2-motoneurons, innervating fast fatigue resistant muscle fibres, are activated by the less dynamic secondary
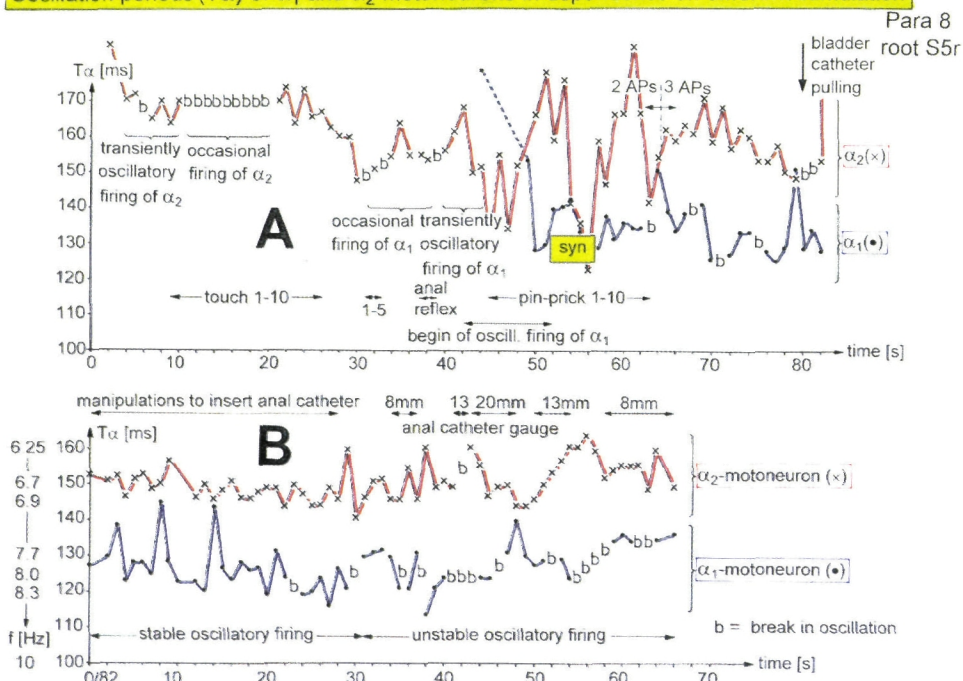
Figure 4. Oscillation periods (Tα) of an α_1 (FF) and an α_2-motoneuron (FR) in dependence on different stimulations; „B" is a continuation of „A". Touch 1 - 10 = Touching with a needle at points 1, 2,3,4,5 (upper row) and 6,7,8,9,10 (lower row) (see [27]). 1-5 = Touching from point 1 to point 5 (perpendicular to the direction of anal stimulation). 8,13,20,13,8 mm = changing the diameter of the anal catheter from 8 to 13 to 20 to 13 and back to 8 mm (3 gauges of anal catheter were used). syn = partial synchronization of the oscillatory firing patterns of the α_1 and the α_2-motoneurons. 2 APs / 3 APs = impulse train of the α_2-motoneuron mainly consisted of 2 or 3 APs respectively. Note that α_1 and α_2-motoneurons first fired transiently oscillatory before firing continuously oscillatory. Note further that the oscillatory firing was most regular upon manipulation at the anus (0-30s in „B", anal reflex stimulation to secure continence).

muscle spindle afferents. It is therefore conceivable that the α_1-motoneuronal network is recruited for oscillatory firing more dynamically. Actually, this is the case as can be seen from Fig. 4.

From Fig. 4A,B it can be seen that the α_2-motoneuron fired oscillatory during the time interval of 140 s, apart from the 20 s at the beginning of the measuring time where there was no or only little stimulation applied. During the first 30s the α_1-motoneuron (Fig.4A) was not firing at all, it then started firing occasionally and transiently oscillatory upon slight skin stimulation, and fired continuously oscillatory upon pin-prick stimulation of sacral dermato-

mes Breaks (b) in the oscillatory firing occurred more often in the oscillatory firing of the α_1-motoneuron than in the α_2-motoneuron The difference in oscillatory firing between the α_1 and the α_2-motoneuron (Fig 4) is the following First, the α_1-motoneuron was recruited for oscillatory firing more transiently (dynamically) In the time interval between 20s and 30s (Fig 4A) following touch stimulation, the α_2-motoneuron was already firing continuously oscillatory, whereas the α_1-motoneuron was not even firing occasionally Second, in this measurement the α_1-motoneuron had a higher skin stimulation threshold for the recruitment in the occasional and oscillatory firing modes Thirdly, the α_1-motoneuron fired with a higher frequency (≈ 8 Hz) than did the α_2-motoneuron ($\approx 6\ 7$ Hz)

When increasing the intensity of the skin stimulation, i e upon changing from touch (only touch afferents stimulated) to pin-prick (touch plus pain afferents stimulated [15]), both the α_1 and the α_2-motoneurons increased their firing rates Since the α_1-motoneurons can fire only with 1 AP impulse trains, the α_1-motoneuron could only increase its firing rate by increasing the oscillation frequency (decreasing the interspike intervals) The α_2-motoneuron increased its firing rate by increasing its oscillation frequency and by increasing the number of APs from 2 to 3 per impulse train (4 AP impulse trains occurred only occasionally)

Occasional, transient oscillatory and continuous oscillatory firing modes also for α_1-motoneurons

With the increasing stimulation intensity the α_1-motoneuron changed its firing mode from occasional firing via transient oscillatory firing to continuous oscillatory firing, similarly as shown earlier for an α_2-motoneuron [16] With little stimulation in the time period 0-30s (Fig 4A), the α_1-motoneuron did not fire at all With more intensive stimulation (30 to 48s), the α_1-motoneuron first fired occasionally and then transiently oscillatory With stronger stimulation (pin-pricking), the α_1-motoneuron fired continuously oscillatory, even though breaks (b) occurred in its continuous oscillatory firing (Fig 4A, 50-80s, Fig 4B) With a reduction in the strength of stimulation (Fig 4B, 40 to 66s), the oscillation periods increased and more breaks occurred in its oscillatory firing, the α_1-motoneuron turned back to the transient oscillatory firing mode

Upon inserting the anal catheter, the α_1 and α_2-motoneurons fired most stable and most frequently (Fig 4B, 0-30s) It therefore seems that the α_1-motoneuron was also recruited to fire oscillatory, to secure rectal continence It is likely that the α_1-motoneuron innervated pelvic floor muscles to secure continence It is also possible however that the α_1 motoneuron innervated a foot muscle and was activated by reflex (response) generalization

Discussion

More dynamic firing of the α_1-motoneuron as compared to the α_2-motoneuron

In analyzing Fig 4 it could be found that the α_1-motoneuron was more dynamically recruited to fire oscillatory than was the α_2-motoneuron This finding is in accordance with the innervation pattern according to the muscle fibre type, namely that α_1-motoneurons innervate fast fatigue (FF) and α_2-motoneurons fatigue resistant (FR) muscle fibres

An α_1-motoneuron was identified getting monosynaptic projection (see below) from a primary (dynamic) muscle spindle afferent fibre (Figs 1,2) Since the α_1-motoneuron is the motoneuron type which was most dynamically recruited for oscillatory firing, it is conceivable that during phylogenesis, the nature introduced an even faster dynamic recruitment for the α_1-motoneuron firing, namely monosynaptic activation by primary spindle afferents This monosynaptic projection of the primary spindle afferents onto the α_1-motoneurons bypassed the oscillatory firing network as proposed in 1941 by R Jung [9]

No monosynaptic connection could be found so far between α_2-motoneurons and secondary spindle afferents, and probably such connections do not even exist Phase relation consideration showed (Fig 2) that a secondary spindle afferent fibre did also project onto the α_1-motoneuron, but not monosynaptically The projection was only of small strength Probably, additional secondary spindle afferents of low synaptic strength contributed to the generation of the additional AP for the oscillatory firing when the primary spindle afferent fibre ceased firing (Fig 2E,F) It was found earlier that oscillatory firing α_3-motoneurons innervating fatigue resistant muscle fibres (S) show even less dynamic properties than the α_2-motoneurons, when changing the kind and strength of stimulation [16]

Fig 5 illustrates schematically how the α_1 and α_2-motoneurons may be „wired up" with the primary and the secondary muscle spindle afferents, and how the α_1 and α_2-motoneuronal networks could interact by overlapping of their synfire chains

Monosynaptic projection of the primary spindle afferent fibre onto the α_1-motoneuron

From the variation in phase of approx 3 ms (Fig 1) it was concluded that the primary spindle afferent fibre projected monosynaptically onto the α_1-motoneuron, because the polysynaptic projection of secondary muscle spindle afferents onto α_2-motoneurons had a phase variation of about 120 ms (Fig 2D), this means that the $\alpha_1 \rightarrow$ SP1 phase distribution was narrower by a factor of 40 The possibility that the SP1 AP was actually an α_1-motoneuron AP, because the α_1 motoneuron performed a loop and then used another root to emerge from the medulla, is unlikely since the variation in the occurrence would then be in the range of 0 1 ms (Fig 12A,C of [24]), i e narrower by a factor of 30 It is unlikely that the SP1 AP was a reflected α_1 motoneuron AP (primary spindle afferents and α_1-motoneurons have approx the same group conduction velocities [23,26]) because of the regularity of the firing pattern Such considerations are not subtlety, since the method of recording of single-fibre APs from undamaged roots is that specific that anomalies can easily be measured In the lower sacral

nerve roots, there are quite a lot of variations concerning the root, through which nerve fibres run. Ventral root afferents and dorsal root efferents of lower sacral nerve roots are the most obvious variation [15,33].

It is unclear why the SP1 AP occurred (Fig.1A) approx. 14 ms after the α_1-motoneuron AP. A loop performed by the primary spindle afferent fibre is one possibility. As stated above, there are many variations in the lower sacral nerve roots, and α_1-motoneuron and SP1 fibres only seldom run through S5 roots.

Relative synchronization (coordination) of oscillatory firing motoneurons

Some synchronization can directly be seen in Fig. 3C,D between the α_1 and the α_2-motoneuron APs. Such a transient partly synchronization means that the α_1 and α_2-motoneuronal oscillatory firing circuitries interact with each other and give rise to a relative coordination, as proposed in 1939 by E.v. Holst [8]. This relative coordination can also be seen in the distributions of the oscillation periods for the α_1 and α_2-motoneurons. The major peaks in the distributions of the oscillation periods for the α_2-motoneuron (Fig.8C of [26] (para 8)) are the subpeaks in the distribution of the oscillation periods for the α_1-motoneuron, at approximately 140 (marked by the arrow in Fig.1C,G) and 150 ms (para 8), and the main peak in the distribution of the oscillation periods for the α_1-motoneuron (130 ms in Fig.1C) also occurred as a subpeak in the distribution of the oscillation periods for the α_2-motoneuron (Fig.8E of [26]). This means that the self-organized oscillatory firing α_1-motoneuronal circuitry occasionally synchronized itself with the self-organized oscillatory firing α_2-motoneuronal circuitry, and somethimes, the α_2-motoneuronal circuitry synchronized itself with the α_1-motoneuronal circuitry. When analyzing tremor, R. Jung [9] and E.v. Holst [8] called this change in the leading of the dominating rhythm „the change of the focus". E.v. Holst proposed that locomotion is generated by relative coordination (synchronization) of spinal oscillators [8]. A change in the leading of the dominating rhythm seems also to occur in alternating oscillatory firing, which is probably generated by coupling of oscillatory firing subnetworks including inhibitory coupling [26,28].

Relative synchronization of different rhythms was recently observed in the brainstem of dogs [10,14,29]. The coordination of various functional systems of the organism in the course of behavior is realized via temporal interlacing of different rhythmical patterns. Different types of temporal coordination of functional systems are associated with different pattern components in the post-event-time histograms (PETHs). This means that narrow peaks and troughs in the PETHs indicate a temporally strict coordination, whereas wide peaks and troughs reflect coordination of lesser strictness. The pattern components and their transmission depend on the activity level and state of functional organization of the neurons. Therefore, activity level, phase and functional organization influence the momentarily occurring kind of coordination. This means that, for the integration of the various subsystems in the sense of regulation, an adequate spatio-temporal distribution of the degree of central nervous activity is a prerequisite [11].

The synchronization of premotor oscillatory firing motoneuronal networks and the inclusion of the γ-loop into the oscillatory firing will further be analyzed elsewere [27], it will provide a therapy for incomplete spinal cord lesions, namely that patients with incomplete cord lesions will be able to re-learn running, even though their walking is not fully controlled [28]

Interaction between spinal oscillators and synfire chains

The question is now, how self-organizing oscillatory firing cicuitries can interact with each other As a working hypothesis, the oscillatory firing circuitries are self-excitatory reverberatory circuits [30] in which the dedicated lines are replaced by „synfire chains" [1] (Fig 3 of [26]), and the oscillatory firing circuitries interact by overlapping of synfire chains

A „synfire chain" consists of a set of neurons that converge on a subsequent set, which in turn converges on another set etc (see Fig 3 of [26] and Fig 5) When the neurons in the first set fire in near-synchrony, each of the cells in the second set receives near-synchronous synaptic input which synchronously excite the subsequent next set etc Synchronous presynaptic cell discharges are so important because coincident firing seems to be about 10 times more efficient than asynchronous integrated activity [1] The transmission along a chain is secured by the synchronous firing of sets of cells The synfire chains are very flexible dynamic functional entities, because very probably, such a chain of synchronously firing neurons is activated only occasionally Therefore, a chain is not a rigid structure always traversed by a fixed pattern of activity, but a rather dynamic entity that may be turned on or off according to the spatio-temporal pattern of activity in the neuronal network of the spinal cord

Probably, the neuronal networks of the sacral spinal oscillators are mainly located in the spinal cord segments S1 to S5, as follows from spinal cord lesion levels The neurons of the sets of neurons in a synfire chain of the self-excitatory reverberatory circuit may not be localized close to its motoneuron, but may be distributed [5] One possibility how self-organizing oscillatory firing circuits interact, is overlapping of synfire chains (Fig 5) This means that the same interneuron may participate in many different synfire chains according to whether it fires synchronously with one set of neurons or with another According to Abeles, an interneuron cannot participate at exactly the same time in two different synfire chains (see crossing of synfire chains in [1]) On the basis of the synfire chain working hypothesis, an overexcitation of the central nervous system may therefore lead to a disorder of the spinal cord which may result in spasticity (see discussion in [24]) It may however be that overlapping of synfire chains (Fig 5), namely that at the same time some interneurons participate in different synfire chains of oscillatory firing motoneuronal networks, gives raise to transient synchronization and relative coordination of spinal oscillators

Precise measurements using basic electrophysiologic methods are needed to identify how oscillatory firing circuitries interact with each other The dynamic formation and dissolution of versatile functional oscillators and their interactions with each other are defined

functionally through their spatio-temporal activity patterns. These dynamically changing oscillators are connected by synaptic contacts, but these connections are thought to be modifiable through processes of synaptic learning (for example, reinforcement learning [2] or oscillator formation training [28,32]) which may depend exactly on the synchronizations which functionally define the synfire chains.

Strength of rhythm induction in the α_1 (FF), α_2 (FR) and α_3 (S)-oscillatory firing neuronal networks

According to the approximate correlation between the oscillation period (T) and the number of APs per impulse train (T = 70ms + 30ms • n_{AP}; n_{AP} = number of APs per impulse train), most interneurons are included in the oscillatory firing of α_3-motoneuronal networks and fewest in the α_1-motoneuronal networks. One interneuron in the self-exitatory reverberatory circuit of the α_1-motoneuron represents one unit which probably consists of a set of excitatory interneurons in a short synfire chain (Fig.5), and perhaps some inhibitory neurons. Therefore, one can expect that α_3-oscillators can generate most network rhythmicity, because most interneurons contribute to their networks.

Even though the oscillatory firing of α_1, α_2 and α_3-motoneurons is induced by the afferent input (no supraspinal drive because of the complete spinal cord lesion), the afferent in-
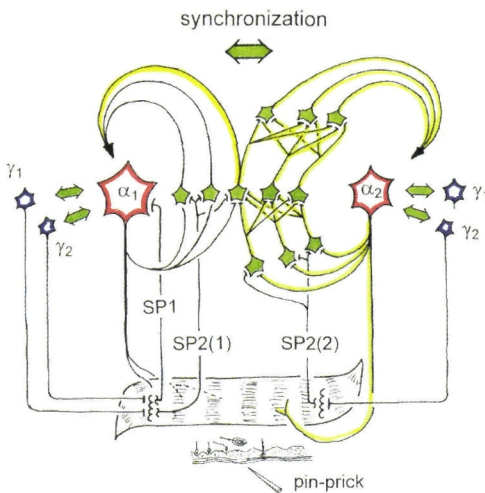

Figure 5. Schematic simplified drawing of how oscillatory firing α_1 and α_2-motoneuronal networks get mono- and oligosynaptic projections from primary and secondary muscle spindle afferents. Phase relations to dynamic (α_1) and static (α_2) fusimotor networks are indicated by double head arrows. Essential in this drawing is that secondary muscle spindle afferents (SP2) project into the synfire chains of premotor oscillatory firing neuronal network of the α_1 and α_2-motoneurons whereas the primary spindle afferent fibre (SP1) bypasses the α_1-oscillatory firing neuronal network and projects directly onto the α_1-motoneuron. The secondary spindle afferent fibre SP2(2) may also project onto other interneurons of the synfire chain of the oscillatory firing α_2-motoneuron. The sets of interneurons in a synfire chain probably consist of more than 3 interneurons. The fringe of subthreshold excited interneurons and inhibitory interneurons are not drawn. Muscle spindle arrangements have not been clarified.

put to the α_3-neuronal network is very unspecific (multimodal) [16], and the α_3-motoneuronal network may not need rhythmic input Probably, the α_2-neuronal network needs some rhythmic afferent input, characterized by a broad-peak phase correlation between the oscillation cycle and, e g , secondary muscle spindle afferent fibres It remains unclear as yet, whether primary spindle afferents essentially contribute to the drive of α_2-motoneurons The α_1-motoneuronal network with little rhythmic properties seems to need rather strong rhythmic input from primary muscle spindle afferents The rhythmicity of the input is generated by the proprioceptive feedback loop in which primary spindle afferents project monosynaptically onto the α_1-motoneurons In the reported case, the broad-peak phase distribution driving secondary spindle afferent fibres could only induce one additional oscillation cycle

Clonus often occurs following complete spinal cord lesion The frequency of repeated dorsal and plantar flexions of the foot range between 4 and 10 Hz Mostly, clonus starts in the low frequency range and then increases in frequency Since clonus also occurs in normal subjects under certain conditions its occurrence following spinal lesion seems to be a dysregulation of a critical regulation circuit Since plantar flexion (reduction of spindle afferent input) stops the clonus in a majority of cases, clonus probably is related to the drive of spinal oscillators by muscle spindle afferents Since the clonus frequency starts below that of the α_1-oscillator, probably α_1 and α_2-oscillators and primary and secondary muscle spindle afferents are involved in the generation of clonus It has been shown that the γ-loop can drive α_2-oscillators and can even be intergrated in α_2-oscillation [27] It seems therefore possible that during clonus excitation travels from the muscle spindles to the oscillators and backwards Since sometimes clonus occurs during surgery on paraplegics (the level of anaesthesia is low, the patient, who feels no pain because of the spinal cord lesion, mainly has to tolerate but the tubus in the trachea), it is a matter of time when the cause of clonus will be clarified by measuring the impulse patterns of oscillatory firing motoneurons and their driving muscle spindle afferents

Probably, the comparable, only little oscillatory firing properties of the α_1-neuronal network are the reason for the important feature of oscillatory firing of human spinal cord neuronal subnetwork having only been discovered recently [16] Spinal oscillators mean those oscillatory firing subnetworks of the medulla which drive single motoneurons (premotor neuronal network, motoneuron included) rather than the propriospinal oscillators, giving rise to the rhythmic properties of spinal networks occurring during locomotion (spinal pattern generator) During rhythmic movements, the premotor spinal oscillators are rhythmically recruited to fire transiently oscillatory Gelfand et al subdivided spinal (pattern) generators into two groups - the rhythm generator and the output mechanism [5] The current research indicates that the motoneuron is a part of the premotor oscillatory firing network and therefore a part of the oscillatory firing network [19], rather than only being driven by it [16] In the occasional firing mode however (low activity firing mode), when the α-motoneurons are occasionally recruited for firing approx every 3 s according to the size principle in each group [17,18], the premotor oscillators are not self organized because of low activity input The problem will be picked up in following papers [27,28]

Research in neurology has mostly concentrated on the firing properties of α_1 motoneu-

rons which show the weakest rhythmic properties among the different types of α-motoneurons. Actually, one of the authors (GS) discovered the oscillatory firing of motoneurons when recording from α_3-motoneurons, which show most rhythmic properties in their network. The term „reflex oscillation" may somehow characterize the weak oscillatory properties of the α_1-network in combination with the monosynaptic drive from primary spindle afferents, and should not be used with respect to the oscillatory firing of α_2 and α_3-motoneuronal networks

Spinal disorders may partly be due to the loss of specificity of spinal oscillators

It has been shown previously that the number of distribution peaks and the bandwidth of oscillation periods and interspike intervals increased following a spinal cord lesion [19,26] Therefore, with the deterioration of neuronal network functions because of nonuse, spinal cord lesion, and missing supraspinal drive or missing synchronization with supraspinal oscillators, most likely the properties of the oscillators and the strength of mutual coupling undergo changes Because of the broadening of the frequency band, the spinal oscillators partly lose their specific functions, namely their ability to interact according to certain afferent input, with certain other oscillators Masses [34] of oscillators will couple and may give rise to mass contractions of muscles (loss of specificity and loss of functional splitting of muscle functions) Because of a reduced strength of coupling, certain stable states of coupled oscillators will not be reached any more (page 156 of [31]) Specific functions are lost and altered Most likely, this increase in unspecific and altered interactions among spinal oscillators is one reason for the dysfunction of the spinal cord following injury, and can give rise to movement disorders Since following injury most α_3-motoneurons change their oscillatory firing property [26] and the corresponding α_3-circuitries include more interneurons than do the circuitries of the α_1 and α_2-motoneurons (see above), the most intensive changes concern the integrative functions of the disconnected spinal cord

Muscle spindle afferent projections onto the different types of motoneurons

It has been argued with respect to animal experiments that with regard to the functional differentiation into types, the proprioceptive muscle-Ia fibre feedback system appears to be organized in a fashion comparable to that of the recurrent Renshaw cell feedback (Fig 39 (page 185) of [30]) It is supposed to be well established that Ia fibres exert homonymous monosynaptic excitatory effects that are stronger on S type than FR and FF type motoneurons ([4,6], page 185 of [30]) At least in this general scope these measurements obtained under artificial experimental conditions are not in accordance with the measurements in patients obtained under rather natural conditions In the continence range, no FR (α_2) and S type (α_3) motoneurons have been found so far to be innervated by primary muscle spindle afferents (Fig 5) It remains to be measured how the muscle spindle afferent projections onto FR and S type motoneurons are in other parts of the human body

Physiological and unphysiological stimulation of the different types of motoneurons

It has been further argued that both, the mean rate and the discharge modulation around the mean of spindle afferents are influenced more strongly by FF than by S type motor units [3,13,30]. Whether this really holds cannot be followed from those measurements, since the different types of motoneurons were stimulated unphysiologically with 40 pulses per second. The FF type motoneurons, firing approximately oscillatory with one AP every 80 to 120 ms (8-12 Hz) were stimulated rather physiologically, even though the frequency of stimulation was too high (40 Hz). The FR type motoneurons, firing physiologically with approximately 3 APs every 160 ms, and the S type motoneurons, firing physiologically, e.g. with 40 APs every second [1 Hz] (Fig.3 of [26]), were stimulated completely unphysiologically. It is unlikely that the modes of oscillatory firing (high mode of activation) are completely different in man as compared, e.g. to cats. If the stimulation pattern of all motoneuron types had been physiologic the results may have been different.

On the other hand, the finding of the different types of motoneurons being enclosed in different network projections is in accordance with these measurements. If one replaces the Renshaw inhibition by neuronal network structures for generating rhythmic patterns, then their S type motoneurons, which obtain more inhibition, are here connected to oscillatory firing networks stronger than do the FF type motoneurons.

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