Basic research meets Manual Medicine

Results of the Conference of physicians for Manual Medicine of German mother tongue in Bad Horn (Switzerland), Lake of Constance, July 22 – 24, 2005

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On the initiative of H. Locher (MWE, Germany) and U. Böhni (SAMM, Switzerland) a conference has taken place in Bad Horn at the Lake of Constance from July 22 – 24, 2005, to which in addition to 20 active physicians for Manual Medicine of German mother tongue the subsequent individuals were invited as referees:

Prof. W. Magerl, Institute for physiology and pathophysiology, University of Mainz
Prof. S. Mense, Institute for anatomy and cell biology, University of Heidelberg
Prof. W. Neuhuber, Institute for anatomy, University of Erlangen
Prof. H. Radanov, Institute of psychiatry, University of Zurich
Prof. J. Sandkühler, Division of neurophysiology, Centre for brain research, University of Vienna
Prof. W. Zieglgänsberger, Max-Planck Institute of psychiatry, Division of clinical neuropharmacology, Munich

On the one hand, on the first day of the conference the physicians for Manual Medicine presented their current view on diagnosis and therapy in Manual Medicine. On the other hand, on the second day the basic researchers exhibited their updated state of the art. On the third day an intensive consensus discussion between both groups, which otherwise obviously do not practice enough mutual exchange, took place.

In the present contribution the results of this consensus discussion – against which there was no contradiction among those taking part – are exhibited. In addition some contributions of the researchers are published. In this issue it is the lecture by Neuhuber on the function of the longissimus muscle as a transmitter of information between occiput and pelvis. The contribution is to be seen in the context of this report.

* Neurophysiology and segmental dysfunction

In discussions on Manual Medicine there arises always the question about the definition of the term «blockage» or «segmental dysfunction», respectively about the meaning

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of the reversible functional disorder accessible to treatment.

The following is a very short description of the segmental dysfunction: «It is a contraction of the short, autochthonous, deep muscles caused by nociceptive and/or other afferents, which induce this segmental or metameric effect via alpha- and gamma motoneurons, whereby the efferents are fed by the nociafferents via the corresponding WDR neuron.»

The idea that has been maintained for decades, namely that a blockage designates an exclusively articular movement problem with one joint segment fixed in one direction and the other one in the opposite direction, has proven to be a misconception. Rather it designates a complex nocireactive patho- logical reflex process, in which one or several segments including all participating structures and in particular the muscular system, are involved.

Hitherto it was not possible to directly derive and thus confirm the effects of the nociceptive afferents on the short, deep paravertebral muscles. Based on the presumption that a painful muscle is not hypertonic, but rather hypotonic, many phenomena of back pain were contradictory and unclear. In particular the phenomenon of the segmental point of irritation could not be explained. After intensive discussion, however, Mense confirmed that a muscle that does not itself function as nocigenerator would naturally react with a hypertonus to a pain stimulus occurring in conjunction with a segmental reflex process.

In a needle electromyography the nociceptive stimulus caused by the needle in the muscle examined is usually so strong that motion-induced changes in the deep autochthonous muscles could so far not be identified. In order to support the above hypothesis, a possibility of derivation of muscle potentials from the autochthonous muscles has further to be searched for. To-date, however, there is no theoretical or practical argument against the opinion that via the mechanism of motoric system activation on the segmental level, the deep autochthonous muscles proportional to the stimulus intensity fall into conditions of increasing tension. According to a unanimous opinion, this is the physical substrate of what is palpated as nocireactive hypertonus of the segmental point of irritation in the deep paravertebral layer of the erector spinae muscle.

In addition to the abovementioned nociafferent other afferents to the WDR neuron can be involved in the induction of a motoric system activaton, i.e. a blockage, or also in an activation of the sympathic system. According to W. Ziegglansberger the converging afferents including the nociafferents originate from one or also from neighbouring segments. As soon as the sum of the afferents of any kind exceeds the threshold, this leads to the described activation reaction of the WDR neuron by the axon collaterals. There is no doubt that non-nociceptive afferents, too, can cause the summation effect via the multifunctional fibre convergence of the WDR neuron so that the blockage becomes manifest. This explains e.g. why patients with whiplash trauma of the cervical spine can react in quite different ways: besides more centrally located mechanisms, the pain radiation via the WDR neuron is influenced in different ways by other, non-nociceptive afferents, which explains why one patient recovers quickly, while another one suffers for a long time.

Not only the «blockage» as segmental reaction is a consequence of the overflow of the WDR neuron. Over the spinothalamic tract central reflections of the summation afferents are created as well. Since the central pain perception is exclusively based on the activation of the WDR neuron, due to the convergence function of the WDR a precise local differentiation of the afferents is not possible. Independent of the (noci-) afferent source, «pain» is localized by the thalamus or the cerebral cortex anywhere in the segment/metamere (respectively in the neigh-
bouring metameres). This can be called a «central perceptive illusion». To the category of central perceptive illusion pertain the pseudoradicular pain\(^7\), the referred pain as described by Simons/Travell\(^{13}\), the projection pain, and also the radiated pain. A scientifically relevant differentiation of these pain perceptions, which have been given different names by different groups, cannot currently be identified. With high probability we are dealing with the same phenomenon of central perceptive failure. In any case, this does not affect the statement that the segmental receptor afferent represents only one of several possible causes of an information pathway through the second neuron – the WDR neuron. Of course, other phenomena such as primary and secondary hyperalgesia equally induce central perceptive disorders with confusing pain projections in the beginning.

Also phenomena from the region of the upper cervical spine, which are otherwise difficult to understand, are to be seen in the context of the abovementioned reactions to a overflow of the WDR neuron. There is a marked trigeminospinal convergence in the region C1-C3 – probably the most distinct convergence investigated so far – with information spreading ipsilaterally and over the cervical central nucleus also contralaterally, encompassing in addition the vestibular, cochlear, oculomotor and hypoglossal nuclei\(^{34}\). Consequences of these convergences in the craniocervical transition are the hitherto controversially discussed perceptive disorders like vertigo, hearing disorders (tinnitus), dysphagia and phonatory disorders, cervical headache and interactions with craniomandibular dysfunction.

Whether only articular or other deep somatic afferents lead to the abovementioned pain reactions, or whether the neurosecretion of the substance P on the WDR neuron is induced by other processes in a different way, could not be clarified so far.

The structural basis of the segmental dysfunction is provided by the nociceptive afferents predominantly over the C fibres and A-delta fibres, the WDR neuron, the axon collaterals into the lateral and anterior horns of the spinal cord, and by the motoric efferents to the short deep autochthonous muscles with their endplates and muscle spindles.

Functionally the nociafferent generates a stimulation of the WDR neuron via substance P and glutamate, which is not only conducted in the central direction over the spinothalamic tract, but via the axon collaterals leads to a motoric and/or sympathetic systemic activation, whereby also inhibitory interneurons appear. Due to the plurifunctional convergence of the WDR neuron, consequences in addition to the local muscular reaction are also central perceptive disorders with pain projections.

The neurophysiological reactions consist in the first place in the directed receptor pain, in the second place in alterations of the first or second neuron corresponding to a primary or secondary hyperalgesia, followed by further alterations in the sense of a conditioning of inhibitory systems which orientate by the inhibitory neurotransmitters GABA, serotonin, endorphins or endocannabinoids. Finally the total condition of the central nervous system for the downregulation predominantly from the periaqueductal grey and the raphe nuclei as well as over the serotoninergic descending paths directly to the WDR neuron is also considered.

The directed receptor pain

The reversible segmental dysfunction is in the first place caused by a receptor pain, which is announced to the WDR neuron via C- and A-delta fibres. At the same time glutamate and substance P are released, which stimulate the second neuron. On the one hand, the information is transmitted in central direction over the spinothalamic tract, and on the other hand to the motoric cells of the anterior horn via the axon collaterals. For pain defence, the alpha- and gamma motoneurons stimulate the agonistic muscles, in particular the extremity muscles from the supply area of the ventral branch of the
spinal nerves. The respective antagonists are inhibited by the RENSHAW interneuron. The agonists also include the short deep rotator muscles of the spinal column, the mono- or oligosegmental autochthonous muscles innervated from the dorsal branch of the spinal nerves. This is the basis of the segmental irritation point in the 3-step diagnosis. It is typical of the receptor pain to produce different reactions with regard to the perceived pain and the muscle tonus depending on the movement direction. Different positioning of the joint causes more or less pain – there is always at least one nearly pain-free or tone-free direction. Here the nomenclature of the different organisations of Manual Medicine in the German-speaking area describe either

- a restricted, painful direction, a sensitivity (MWE); or
- an increase in resistance or tension, tension phenomena (ÄMM); or
- an unilateral restriction, an evaluation of the «end feeling» (FAC, SAMM).

These terms obviously describe reactions to a functional test. This description of function is the right consequence of the turning away from the static model of blockage as a positioning change of the articular surfaces, and even more from the former model of articular dislocation or -luxation. On careful analysis there is a large semantic congruence of the three nomenclatures.

<table>
<thead>
<tr>
<th>Positional diagnosis</th>
<th>Function diagnosis</th>
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<tbody>
<tr>
<td><strong>Examination</strong></td>
<td><strong>Examination</strong></td>
</tr>
<tr>
<td>• palpation of the proc. transversus of a vertebra</td>
<td>• flexion/extension</td>
</tr>
<tr>
<td>• comparison of position in sagittal plane in flexion/extension</td>
<td>• lateral flexion and rotation</td>
</tr>
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<td></td>
<td>• three-dimensional combination</td>
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<tr>
<td><strong>Evaluation</strong></td>
<td><strong>Evaluation</strong></td>
</tr>
<tr>
<td>• change between symmetry or asymmetry</td>
<td>• «Pathologic direction»/end feeling</td>
</tr>
<tr>
<td>• in flexion or extension: prominence of the proc. transversus</td>
<td>- sensitivity (MWE)</td>
</tr>
<tr>
<td></td>
<td>- resistance/tension increase (ÄMM)</td>
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<tr>
<td></td>
<td>- restricted direction (FAC/SAMM)</td>
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<td></td>
<td>- pain increase (all)</td>
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<td></td>
<td>- zone of irritation (SAMM)</td>
</tr>
<tr>
<td><strong>Segment evaluation</strong></td>
<td><strong>Type of segmental dysfunction</strong></td>
</tr>
<tr>
<td>«Vertebra is in»:</td>
<td>«Dysfunction in direction of»:</td>
</tr>
<tr>
<td>A) extension/left/lateral flexion/rotation ERS left</td>
<td>A) flexion and lateral flexion right in direction of divergence zone of irritation = point of irritation left</td>
</tr>
<tr>
<td>B) Flexion/right/lateral flexion/rotation FRS left</td>
<td>B) extension and lateral flexion left in direction of convergence zone of irritation left</td>
</tr>
</tbody>
</table>

*Table 1:* Comparison of diagnostic systems. Attempt of analysis of different terminologies for an identical phenomenon (Böhm). Pain in segmental dysfunction always appears in the initial phase of receptor pain as pain in motion and not as pain occurring in resting meta-position.
At first glance, the osteopathic terminology seems to be diametrically opposed. This, however, depends on the final position of the respective movement, which automatically results in opposed naming. Eventually, the same phenomenon is described, but rather from a static than from a functional point of view.

**Primary hyperalgesia**

In contrast to the receptor pain, primary hyperalgesia consists in an equal motion-evoked pain in all directions. Primary hyperalgesia can either be caused by a strong chronified reversible function disorder or by a structural damage. The latter can e.g. cause an articular hyperalgesia in connection with an artrogenic inflammation.

The clinical picture of primary hyperalgesia is defined as a motion-evoked pain in all possible directions of articular mobility. As discussed before, it occurs in conjunction with a hyperalgesication or hyperactivation of the nocireceptors. In any case the rule «More than three restricted movement directions can no longer be regarded as directed movement pain» is true. An intensified nocireaction in all directions can of course have different causes: hyperalgesia or structural damages (e.g. spondylarthitis, tumour metastasis, spondylodiscitis, etc). If an articular nocireaction cannot be reduced in any direction, a primary hyperalgesia has to be considered – provided that there are no other symptoms corresponding to a secondary hyperalgesia or to a structural damage.

As a new meta-level the notion of primary hyperalgesia clinically designates a chronified dysfunction in the sense of a chronic afferent surplus from the first neuron as well as an activated structural disorder leading to a comparable accumulation of nociceptive afferents, as is demonstrated by the following practical example:

An acute dysfunction C3/4 on the right radiates in the shoulder region on palpation of the irritation point and on provocation in the restricted area: *projection pain*.

A facet «arthritis» C3/4 (primary hyperalgesia) leads to a radiation in the shoulder region already on light movement provocation in practically all directions, maybe even to a spontaneous rest pain in the cervical spine and the shoulder: *primary hyperalgesia in local inflammation; projection pain in the shoulder region*.

Even though conclusive scientific evidence is still missing, there is unanimous agreement nowadays that a pain on motion of a joint occurring in all directions has to be evaluated as a primary hyperalgesia caused by activity of the nocireceptors of the respective joint – considering the differential diagnosis of structural pathologies like primary inflammations, tumour metastases, osteoporosis fractures, etc. Therefore, if every movement of a joint hurts, a primary hyperalgesia on the articular level or caused by comparable deep somatic afferents has to be considered. The common final stage of various articular damages is represented by the change of the receptor (here: C fibre) in the sense of a primary hyperalgesia.

In this connection referral can be made to the various populations of articular receptors, which through a chronic stimulus can change from high- or low-threshold mechanoreceptors into permanent low-threshold nociceptors.

A change has also occurred in the models for explanation of the spinal inhibition insofar as the «old» model of gate control has been replaced by the new model of synaptic long-term inhibition. Only this model on the changing direction of chloride transport between the synaptic gap and the nerve cell is able to explain the functional change of receptor populations observed in practice.
J. Sandkühler\textsuperscript{39, 14} has described the mechanism of this functional change of receptive nerve cells. In the extracellular space between the afferent fibre and the WDR neuron GABA opens a potassium-chloride channel. Chloride flows inwards and the negative charge, i.e. the electro-chemical gradient decreases. This leads to a reduced irritability.

In order to maintain the chloride gradient, the chloride has to be pumped back by means of a potassium-chloride co-transporter-2 (KCC-2) serving as a «pump».

In case of a disorder caused by overstrain of the nervous fibre the outward transportation of the chloride is disturbed and thus causes an inversion of the gradient. GABA is further released, though, binds the GABA receptor and the chloride channel opens again. However, the gradient is inverted and the inhibitory transmitter breaks the inhibitory wall. The chloride ions flow from the inside to the outside and thus the negative charge of the cell increases, i.e. the cell becomes more irritable. This means that:

\textit{An inhibitory neurotransmitter is transformed into an irritating neurotransmitter.}

Sandkühler concludes: In the presence of a reduced inhibition in the spinal cord, all barriers break down. All borders of somatotopy and modality are then abolished in order to enable the spread of irritation – a «worst case scenario» of pain perception.

This contribution on the chloride shift and the relative intra- and extracellular chloride concentrations provides the explanation for the completely unexpected behaviour of nerve cells and nerve cell associations, which according to different environment/milieu phases show entirely different reactions. Thus also phenomena of hyperalgesia can be explained, which on the basis of the mechanisms known so far could not be explained.

Prof. Zieglgänsberger confirms this phenomenon from his research and comments that according to his findings under given circumstances every cell of the body is able
to produce and secrete the substance P. Thus dramatic changes in the behaviour of entire nerve cell populations can be explained.

**Secondary hyperalgesia**

The term nowadays designates a number of proceedings subsumed under the notion of chronication mechanisms, which considerably change the reaction behaviour of the WDR neuron. According to the current state of knowledge the central production of prostaglandin E-2 is essentially involved in this process. To describe the development of this chronic pain, the literature uses terms like «wind-up»\(^\text{18}\), formation of «ephapeses»\(^\text{3}\), formation of «sensitive neuron ion channels»\(^\text{8,11}\) and «acid-sensitive ion channels»\(^\text{22}\), stimulation of neurokinin-I receptors by the nerve growth factor NGF\(^\text{16}\) as well as the abovementioned synthesis of prostaglandin E-2.

The clinical picture of these neurophysiological changes is represented as secondary hyperalgesia. Along with the neuropathic pains goes the allodynia, i.e. a tenderness to touch of the intact, non-inflamed skin. Furthermore symptoms pertaining to secondary hyperalgesia are rest pain and of course all symptoms of primary hyperalgesia, in particular pain on motion in more than three directions.

Also typical is the absence of any kind of local tissue changes, signs of inflammation or other alterations at the topographical projection of pain by the patient – who would not know these «difficult» patients from daily practice?

As cause of secondary hyperalgesia it is nowadays assumed that the chronic induction of nociafferents and also of other afferents leads to a neuroplastic alteration of the 2nd...
neuron, the WDR neuron[^39,40,17]. The WDR neuron starts a permanent spontaneous activity in the sense of a nociafferent path over the spinothalamic tract and can continue this activity in the long run without any further peripheral input. Endocannabinoids are currently discussed as protection of the CNS against this massive stimulus inflow towards centrally[^25,26].

The abovementioned terms are all elements of this permanent change of the 2nd neuron, and unfortunately these changes are hardly reversible. Once the stage of secondary hyperalgesia corresponding to a chronic neuropathic pain has been reached, there are only few ways to stop this development[^14]. In nervous lesions it appears also necessary to prevent a continuous progression of the neuropathic pain. Rostrally (cranially) from a spinal lesion more and more neuroplastically deformed WDR neurons are generated, leading to the threat of a central chronic pain[^48].

A certain effect can be obtained with the tricyclic antidepressant Amitriptylin, the membrane stabilizing anticonvulsant (and Na-channel blocker) Carbamezepin, and Gabapentin acting on neuronal calcium channels[^4]. For hitherto unknown reasons opioids are not at all appropriate for the treatment of chronic neuropathic pain[^36,37].

In any case, though, there is no doubt that the pain patient has to be driven into activity, since inactivity favours the chronification.

For the diagnostic classification, however, the following is important:

- The radiated pain must not be confounded with a secondary hyperalgesia.
- A secondary hyperalgesia is not necessarily a radiated pain.

Even if the pain in the absence of obvious local causes often seems to be identical, the threshold position of the system is decisive for the understanding of both phenomena. Thus a permanent «overflow reaction» of the WDR neuron can either occur when the stimulus threshold of the WDR is considerably reduced and every inhibition is missing, i.e. in secondary neuroplastic hyperalgesia. Or the «overflow» can occur if in the normal WDR neuron the inflow of nociceptive or in addition of non-nociceptive afferents has exceeded the threshold, hence in the «simple» radiated pain.

### Additional anatomical consideration

When analysing clinical symptoms and combining them to a diagnosis one should always bear in mind – regardless of the phenomena described so far – that in the region of the first neuron the differentiation between the region of the ventral branch and the dorsal branch of the spinal nerve has to be considered.

The most common example to illustrate this possible distinction of different reactions to a peripheral lesion is the spectrum of reactions to a decompression of the nervous structures in intervertebral disk surgery or the surgical treatment of a spinal stenosis.

Either the pains in the leg or the back pains or both or neither disappear after a technically «successful» surgery, which means that either the respective component of the spinal nerve or both or neither was under pressure (since the multipotent convergence concerns the dorsal as well as the ventral root).

Also when considering the generation of inhibitory afferents from the periphery and the motoric system activation in the periphery and on the extremity joints, the idea of the ventral and the dorsal branch should not be ignored.

### Hypotheses on the efficiency of muscle-related therapy methods

Based on his own research results and on discussions with A. Mannion on the basis of the scientifically confirmed observations of the latter[^23,24], according to which an increase in rough strength does not correlate with pain
or reduced pain and that a decrease of pain does not correlate with a change of the muscle cross section and an increase in strength, Prof. Mense states that the mechanisms leading to pains within the muscles must be of different nature. He describes free nerve ends running across the muscular or fibre network in the muscular system. According to Mense the adequate stimulus for these nociceptors consists of shearing forces occurring within the muscle.

The muscles cannot be considered as «loose meat in a plastic bag» or as «salami-shaped structure» that is able to produce contractions by means of the anterior and posterior tendon, but rather as a highly complex three-dimensional system that is tightly embedded in the fascia. Hence it becomes evident that based on the above consideration with crosswise interwoven nociceptors already very minor differences of the contractile force or of the length of neighbouring fibre systems can lead to pain caused by shearing of the nociceptors. For the muscle spindle already a change of \(<100 \mu m\) is sufficient. In this light well-known therapeutic methods such as the longitudinal stretching and in comparison the surprisingly even significantly more efficient transversal stretching of the muscles gain a new dimension in the understanding of their therapeutic efficiency. It is assumed that the actual therapeutic agent consists not in the effective change of the muscle length, but in the re-balancing of the various fibre systems in the muscles generated by the described methods.

Also in favour of this viewpoint is the fact that various muscle-energy techniques can be explained to a lesser extent by the motoric interneuron formations and the agonist/antagonist effect, but that the majority of these techniques produce intramuscular synchronisations or balancings leading to a depression of the respective nociceptor fibres. These observations explain why in the so-called myofascial release techniques, which in a general sense mean transversal and longitudinal stretching of the muscles induced by pressure, the main therapeutic agent consists not in the release of the anatomically controversial contractile structures in the fascia, but rather in a harmonisation of the intramuscular contraction systems by means of rolling with the thumb ball (thenar). Also from own experience with manual handling of these techniques this seems much more plausible than speculations on the behaviour of fascial structures, which eventually cannot be verified according to ultrastructural and microfunctional criteria.

Seen from this angle, therapies like myofascial release technique, muscle energy techniques, longitudinal and transversal stretching, certain parts of counterstrain, certain forms of connective tissue massage and depending on the circumstances also some of the lymphatic drainage therapy methods can be classified according to their effect, at least insofar as the muscles themselves are concerned. The neurophysiological basis for the effect of all these techniques is the gamma system of the various types of spindle receptors. Muscle energy techniques (MET) can therefore not be distinguished from postisometric relaxation (PIR, NMT 1), respectively from the two other neuromuscular techniques (NMT).
Fig. 3: Endomysium as communicating fibres of the myofibrils. From: Myers TV: Anatomy Trains. Churchill-Livingstone 2001.

<table>
<thead>
<tr>
<th>Neuromuscular techniques</th>
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<tr>
<td><strong>NMT I:</strong> postisometric relaxation</td>
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<tr>
<td><strong>NMT II:</strong> reciprocal inhibition over isometric activation</td>
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<tr>
<td>• of the antagonist: static tension</td>
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<tr>
<td>• of the antagonist at end of movement</td>
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<tr>
<td><strong>NMT III:</strong> reciprocal inhibition over dynamic activation</td>
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<tr>
<td>• of the antagonist: at end of movement minor forward movements into the locomotion (concentric)</td>
</tr>
<tr>
<td>• slow backward movements ( eccentric)</td>
</tr>
</tbody>
</table>

### Table 2

In any case it has to be considered that the inhibitory proprioceptive afferents are stimulated and that of course central nervous processes above C0/C1 are addressed, which have various complex effects. «Each manual therapy is an interaction with the brain, whereby the anticipation of the reaction by the empathy of the therapist is extremely important» (Ziegglänsberger). Basically each manual action performed on a patient in addition to segmental and local effects has a significant central nervous effect on the brain, where – as it is confirmed – all proprioceptive influences are also pain relieving and pain memory extinctive influences by means of serotonin, endorphins or endocannabinoids\(^1,2,26\). The amygdala plays an important part\(^2,25\). The descending pathways run from the periaqueductal grey over the raphe nuclei to the posterior lateral funiculi of the spinal cord\(^31\). This is consciously formulated as higher hierarchical level as compared to the predominantly GABAergic inhibitory interneurons.

Apart from the above described effect of therapeutic techniques on the muscles there is unanimous consensus that also subliminal mechanical stimuli of a joint at a frequency around 1 Hz corresponding to the already confirmed effect of electric stimulation of 1 Hertz can lead to a long-term depression (LTD), i.e. a longer lasting inhibition of the wide-dynamic-range neuron, whereas high frequency stimulation clearly leads to a long-
term potentiation (LTP), i.e. a permanent stimulus intensification\textsuperscript{14,19,38}.

Zieglgänsberger reports that he was able to deduct inhibitory impulses from the interneuron scene in conjunction with other experiments on anesthetized cats\textsuperscript{50} in small movements performed in flectional end position of the knee joints already 30 years ago.

As it became evident from a decade of experience, the repetitive (15-20 times), soft rhythmic elastic mobilisation in a frequency around 1 Hz in the painless relative end position results indeed in a positive therapeutic effect in addition to the mechanic effects on the articular surface, the muscles and the capsules.

«A blockage eventually designates an area, from which a lacking or uncoordinated inflow of afferents reaches the postcentral gyrus and only there can induce an uninhibited surplus of pain active systems which is finally due to a propioceptive lack of afferents» is a maybe provoking, but nonetheless probably true hypothesis by Zieglgänsberger.

In conclusion manual therapy would consist of any kind of induction of proprioceptive afferents in the entire metamere. The last mentioned theses are so far predominantly confirmed by functional magnetic resonance tomography and are empirically well based on clinical experience with amputation pains, phantom pains etc.

Unfortunately the question how it is possible to efficiently stimulate GABAergic interneurons with manual methods and thus to ultimately explain the effects of various manual therapies remains unanswered. It is stated with certainty that so far there exist no results on in vivo experiments, which derive wide dynamic range neurons or inhibitory GABAergic interneurons in humans. However, our practical experience, according to which the stimulation of proprioceptive afferents activates GABAergic interneurons, is confirmed by animal experiments\textsuperscript{51}. The friction in the neighbourhood of a pain stimulus activates the inhibitory interneurons. This phenomenon is also called «inhibitory receptive field».

\textbf{Abb. 4ab}: MRI-Nachweis des Zuwachs an Beweglichkeit in einem Wirbelgelenk, links vor und rechts nach Manipulation der LWS (au s:10)

\textbf{Fig. 4abc}: MRI-based evidence of increased mobility of a vertebral joint, left prior and right following manipulation of the lumbar spine\textsuperscript{10}.
Inhibitory receptive fields

In the stimulation of proprioceptive afferents in the neighbourhood of a painful body region, the pain reaction can be mitigated or annihilated by stimulation of inhibitory segmental interneurons. The totality of inhibitory potentials is called inhibitory receptive fields.

Inhibitory receptive fields are opposed to the nociceptive fields, which can change due to neuroplastic processes (see central and peripheral sensibilisations/hyperalgesia) with regard to their extension and connecting properties. Generally it can be assumed that secondary hyperalgesic processes lead to an extension of nociceptive receptive fields. The extension of nociceptive receptive fields takes mostly place on account of the extension of inhibitory receptive fields. This means that the development of hyperalgesia can also cause shrinkage of inhibitory potential and even an inversion. Neuroplastic processes can transform inhibitory effective activities into excitative respectively nociceptive receptive fields – inhibitory neurotransmitters transform into pain intensifiers!

From these postulates it can be concluded that in enlarged nociceptive fields the therapeutic strategy must envisage a reduction of these, which goes along with a regression of inhibitory potentials. The mitigation of a secondary hyperalgesia through the administration of centrally effective cyclooxygenase-II inhibitors can result in a dramatic reconstitution of inhibitory potential. Only by adequate pre-treatment with pharmacological COX-II inhibitors a patient can be made accessible to manual therapy methods.

The main argument for the extended indication for manual therapy techniques consists in the idea that chronification mechanisms on the WDR neuron (wind-up etc.) can be interrupted by repetitive proprioceptive inhibitory stimuli and that processes of chronification that have already taken place may regress according to circumstances. This knowledge also justifies the prescription of serial manual therapies of up to 10 administrations in intervals of 1, 2 or 3 days or also longer intervals according to necessity. As a quintessence it is nowadays undisputed that manual therapy methods (in conjunction with other therapies) can also be successfully
administered in chronic pain patients in order to achieve a regression of the chronified neuropathic pain.

In the end: the manipulation

The effect of manipulation (corresponding to osteopathic HVLA technique) is attributed to the fact that the very short and quick/fast impulse can generate special afferent characteristics and in particular frequencies with action potential. This results in a highly effective A-β inhibition of the WDR, which, however, according to Sandkühler and Ziegglänsberger barely exceed the duration of effect of the respective impulses on the WDR. Hypothetically it is required that due to the breakdown of the WDR tension also a reduction of the motoric system activation should take place, which would need some time until it is reconstituted. This would explain the permanent myotonolytic effect of professionally performed manipulations on joint structures, which, however, has not been confirmed by experts.

The current state of the art regarding the better efficacy of manipulative methods as compared to mobilizing and so-called osteopathic techniques without HVLA is amply documented in the literature. At this stage, however, the experts are unable to present a plausible or scientifically confirmed explanation for this observation.

Conclusion for the practice

From the conference between some basic researchers from the fields of anatomy, physiology, pain and neuron research and physicians for Manual Medicine familiar with the therapy of pain of the musculoskeletal system, several useful approaches for the better understanding of pain phenomena hitherto difficult to understand, have resulted. In the first place, it is important to differentiate by means of patient history and the clinical, imaging and if necessary electrophysiological diagnosis between the three following types of pain encountered by the physician for Manual Medicine:

- Directed receptor pain as expression of an acute, reversible dysfunction, with at least one pain free direction of mobility and segmental projection pain.
- Primary hyperalgesia as expression of either a chronified dysfunction or a structural lesion, with no pain free direction of mobility, but with projection pain, which can also be accompanied by a segmental dysfunction due to afferent overflow of the first neuron.
- Secondary hyperalgesia as expression of a neuroplastic transformation of the second neuron, presenting all symptoms of primary hyperalgesia and additional allodynia, with rest pain and absence of any local tissue changes at the topographical pain perception («central perceptive failure»).

The distinction between these three pain phenomena is of utmost importance for any kind of therapy planning. While in the presence of directed receptor pain with «simple blockage» adequate manual therapy methods like manipulation or mobilisation are sufficient, this may not be the case for primary hyperalgesia without the administration of peripherally effective drugs such as analgesics or non-steroidal antirheumatic agents. Eventually, when the effect of the latter is not sufficient in secondary hyperalgesia, centrally effective drugs such as tricyclic antidepressants or anticonvulsants with membrane stabilizing effect (Na-channel blockers) or with effect on the neuronal calcium channels are required, to a limited extent also opioids. However, the truly ideal pharmacotherapy for secondary hyperalgesia does not exist as yet.

Important for the physician of Manual Medicine in practice is the currently confirmed finding that a low frequent mechanic stimulation in the pain-free area ranging around 1 Hz has a considerable therapeutic effect on the chronic pain over a certain period of time (1 – 10 min) due to its long-lasting inhibitory effect (LTD), while a high frequent stimula-
tion has a guaranteed long-lasting pain intensifying effect (LTP). This explains the efficiency of the long-trained «soft rhythmic elastic repetitive» mobilisation and secures its importance for Manual Medicine.

Furthermore we have to take into account that in case of a breakdown of the nocifensive inhibitory systems of the body there is not much time left to prevent the occurrence of a chronification. Neuron researchers find unequivocal neuroplastic changes in vitro in particular of the WDR neuron already after 8 to 48 hours, which can cause serious therapeutic problems. Although from a pragmatic clinical viewpoint we speak of a chronification after 6 weeks only, neuroplastic changes can be detected much earlier.

**Summary**

Painful disorders of the human postural and locomotor apparatus frequently present considerable diagnostic and therapeutic problems.

When analysing clinical symptoms and all other diagnostic information from the point of view of a physician for Manual Medicine, it is important to differentiate between the three following neurophysiological phenomena:

- Directed receptor pain as expression of a reversible segmental dysfunction, also called «blockage».
- Primary hyperalgesia as neuronal change of the first neuron due to a chronified dysfunction or a local structural lesion.
- Secondary hyperalgesia expressing a neuroplastic change of the second neuron, with rest pain and absence of local lesions or tissue changes at the topographical projection of pain.

For the diagnosis it is helpful to know that muscles that are not themselves acting as nocigenerators can indeed contract indicating a segmental pathological reflex dysfunction, while muscles acting as nocigenerators cannot contract at all. Hence the phenomenon of the segmental point of irritation as expression of the reactive hypertonus of the segmentally organized deep autochthonous back muscles as perfect diagnostic tool of segmental dysfunction can be explained.

The development of the chronification of neuropathic pains starting with the discharge of glutamate and substance P over the expression of new ion channels and lowering of the stimulus threshold in the wide dynamic range (WDR) neuron up to the failure of inhibitory systems and the transformation of inhibitory neurotransmitters into pain intensifying neurotransmitters were discussed according to the current state of the art. The inhibitory effects of the neurotransmitters GABA, glycine, serotonin, endorphins and endocannabinoids on the one hand and the mechanic therapeutic possibilities for the improvement of these systems by Manual Medicine on the other hand were widely discussed. From this discussion it has to be pointed out in particular that a low frequent mechanic stimulation around 1 Hz over a certain period of time helps against neuroplastic pain in the sense of a long-term depression (LTD). This confirms the high importance of pain-free repetitive mobilisations «on the barrier» of Manual Medicine.

Regarding therapy it was confirmed that the effect of the majority of methods used in Manual Medicine is obtained in and by the muscles. It is there where the complex three-dimensional structure of the muscle, embedded in the fascia and the tendons, by means of free nerve ends and muscle spindles through change of the contraction force and – direction by shear generates pains which can be successfully treated by adequate methods like neuromuscular techniques as well as the majority of osteopathic techniques up to massage. Besides their local effect on the muscle, all these techniques give a strong proprioceptive afference to the brain and thus prevent the sprouting of the nociceptive neurons in the postcentral gyrus.
Although the better effect of manipulation compared to mobilisation in the treatment of segmental dysfunction is generally undisputed, there is so far no evidence of this observation provided by basic research.

Abstract

The problems dealing with diagnosis and therapy of painful disorders of the human locomotor system are well known and not yet solved at all.

In a conference of basic researchers and physicians for Manual Medicine in July 2005 there was an intensive exchange between both groups. In this and in the following issues of this journal some lectures and the results of the discussion are going to be presented.

Analysing clinical symptoms and all other diagnostic information we have to consider the following three neurophysiologic phenomena:

- Directed pain of receptor, indicating a reversible segmental dysfunction, also called blockage, with almost one pain free direction of mobility.
- Primary hyperalgesia, indicating neural changes of the first neuron by chronic segmental dysfunction or lesions of anatomic structures and no pain free mobility.
- Secondary hyperalgesia, indicating neuroplastic transformation of the second neuron, with rest pain and absence of local lesion or tissue changes at the topographical projection of pain.

In terms of modern diagnostic it is important to differentiate that muscles not acting as a generator of pain can very well contract indicating a pathological segmental dysfunction, while muscles acting as such a pain-generator cannot contract at all. This explains the phenomena of the segmental point of irritation. Therefore the irritation-point gives evidence about the reactive hypertonus of the deep, segmental organized (autochthonous) muscles of the spine. This is the perfect diagnostic information-system about any segmental dysfunction.

The development of chronic neuropathic/neuroplastic pain starting with the discharge of glutamate and substance P continuing with expression of ion channels and loss of inhibition in the wide dynamic range neuron of the dorsal horn of the spinal cord up to complete failure of inhibitory systems and transformation of neurotransmitters from inhibition to increased nociception was widely discussed. The inhibitory effects of the neurotransmitters GABA, glycine, serotonin, endorphin and endocannabinoids were presented. There was a broad discussion about mechanic possibilities for improvement of inhibitory systems especially by Manual Medicine. From this can be pointed out that mechanical stimulation without pain in low frequency around 1 Hz for a certain period leads to «long-term-depression» and helps against neuropathic pain. This confirms the importance of repetitive pain free mobilisation techniques in Manual Medicine.

Concerning the therapy it was confirmed that almost all techniques used today in Manual Medicine have their effects in and by the muscles. The pain is generated in the complex 3-dimensional structure of the muscle, which is imbedded in the fascia and the tendons and filled with free nerve ends and muscle spindles that react on force and direction of contraction by shear. This can be treated by manual techniques, such as the neuromuscular or osteopathic techniques up to forms of massage. Beside their local reaction all these manual techniques give a strong proprioceptive afferece to the brain and therefore also avoid the sprouting of nociceptive neurons in the somatic-sensory cortex.

Better results of manipulation (HVLA) in comparison with mobilisation for the manual treatment of segmental dysfunction are widely known in empirical studies. Hitherto there cannot be given a basic researcher’s explanation or approval for this observation.

Literature


