Cystometric investigations : In the MBP-injected group, the cystometric findings were characterized by three different patterns : 1) Detrusor areflexia / Detrusor hypoactivity (DA) ; 2) DH, and 3) Normal.
Ten (77%) of the 13 rats given MBP showed bladder dysfunctions including 7 DA, 2 DA/DH and 1 DH (Fig. 1). All these bladder dysfunctions were transient and restored to normal by the day 18. All the 5 rats given the vehicle showed normal pattern and their mean micturition volume was 0.44 ml.

Study 2) Correlation between behavioral, cystometric and histological abnormalities

Cystometric investigations showed DA in 10, DH in 1, and normal findings in 9 animals. All the rats with DA showed grade 3 paralysis, whereas among the 9 rats that were cystometrically normal, 1 showed grade 0, 3 grade 1, and 5 grade 2 paralysis. The mean paralysis grade in the DA group was 3.0, whereas the corresponding value was 1.4 in the cystometrically normal group. The difference between the two groups was statistically significant ($p < 0.01$). The mean value of the inflammation score at the level of L6-S1 spinal cord in the DA group was 5.2 ± 0.9, which was significantly ($p < 0.01$) higher than that in the cystometrically normal group (3.3 ± 1.1). The corresponding value in the rat with DH was 2.0. The scores in the brain, and at spinal cord levels C5, Th4, and L2, were much less than at the L6-S1 levels. The degree of paralysis was significantly correlated ($\gamma = 0.563$, $p < 0.01$) with the inflammation score at the L6-S1 spinal cord.

CONCLUSIONS

The present results suggest that MBP can induce bladder dysfunction (DA/DH) in rats. The bladder dysfunction is transient and reversible, occurring concomitantly with hind limb paralysis and inflammatory changes at L6-S1 spinal cord level. Thus, the present rat model seems useful for studies of bladder dysfunction associated with spinal myelitis / demyelinating diseases.

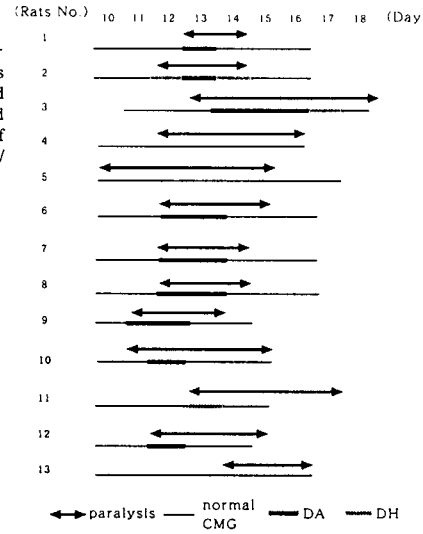

Fig. 1

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SACRAL ROOT NEUROMODULATION INDUCES INHIBITION OF THE HYPERACTIVE C-AFFERENT FIBERS IN A HYPERREFLEXIC ANIMAL MODEL

INTRODUCTION: Sacral root neuromodulation is an impressive new concept that has been used recently for treatment of refractory voiding and storage problems. Unfortunately, the mechanism of action remains to be clarified. We hypothesize that sacral root neuromodulation works through inhibition of the C-afferent fibers. According to the gate theory of Melzack and Wall [1] stimulation of the afferent fibers that is converging on the same dermatome of a smaller size afferents can inhibit the later fibers. Several reports have shown that bladder activity can be inhibited by stimulation of afferents from different sources that converge on the same dermatome of bladder innervation. (2,3,4)

METHODS: Sixty female Sprague Dawley rats have been included in this study. These have been divided into three groups of normal controls, spinalized rats at T10 and spinalized rats that have been subjected to bilateral S1 electrostimulation for 6 hours daily. Three weeks post spinalization, urodynamics was performed and Substance P (SP), Neurokinin A (NKA) and Calcitonin gene related peptides (CGRP) were extracted from the dorsal root ganglia (DRG) of L5 and L6 roots and quantified using radio immuno-assay (RIA). In addition electrophysiological studies for the reflex arcs supplying the urinary bladder

RESULTS: Spinalized rats developed urinary bladder hyperreflexia after 3 weeks of spinalization. This was associated with a significant increase in the neuropeptide content of the DRG of L6. S1 electrostimulation lead to the decrease of the neuropeptide content of L6 significantly. L6 DRG content of SP was 0.050±0.003, 0.063±0.003 and 0.041±0.005 pmole for controls, spinalized group and spinalized stimulated group respectively, while that of NKA was 0.036±0.003, 0.051±0.005 and 0.040±0.005 pmole and that of CGRP was 0.371±0.131, 0.426±0.095 and 0.195±0.019 pmole for the same groups respectively. This was associated with a reduction in the amplitude of the longer latency evoked responses (probably mediated by the C-afferent fibers) without marked affection of the latency. In contrast, spinalization and S1 neurostimulation did not affect the neuropeptide content of L5 DRG except for the CGRP, which increased with spinalization and decreased with neurostimulation.

CONCLUSION: Sacral root neurostimulation abolished the hyperreflexia with a simultaneous drop of the elevated neuropeptide content of L6 root DRG in spinalized animals. This may indicate that blocking of the hyperactive C-afferent fibers is one of the mechanisms of action of sacral root neuromodulation.

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CONTRACTION OR SUPPRESSION OF THE BLADDER BY MAGNETIC STIMULATION OF THE SACRAL ROOTS? RESOLVING THE PARADOX.

Aims of Study Electrical stimulation of the sacral anterior roots through implanted electrodes gives consistently good bladder pressure rises and voiding in patients with a spinal cord injury (SCI) [1] Bladder emptying [2] and detrusor contractions [3,4] are said also to be produced by non-invasive functional magnetic stimulation (FMS) of the sacral nerves in spinal injury but this type of stimulation appears to give equivocal and inconsistent bladder contractions. Paradoxically, FMS of the sacral nerves profoundly suppresses both detrusor hyper-reflexia in SCI [5] and normal voiding contractions in healthy volunteers [6]. The aim of this study was to help resolve this paradox by re-examining the effects of non-invasive FMS of the sacral nerves at different bladder volumes in patients with SCI and comparing the findings with those in healthy volunteers. Local ethics committee approval and informed consent was obtained.

Methods The bladder was filled slowly by catheter to three different levels in 3 patients with SCI and 3 healthy volunteers. Full capacity was indicated by detrusor hyper-reflexia in the patients and a strong desire to void in the volunteers. In both groups, FMS was applied over the sacrum to optimally stimulate the S3 nerve roots (by observing toes and anal sphincter contractions). When the bladder was filled to about half capacity, FMS at 15–25 pulses per second and between 70-100% maximum output of the stimulator for 5 seconds of continuous stimulation was given to attempt evocation of a detrusor contraction. Stimulation was then repeated again after further bladder filling to near capacity. To conclude the experiment, stimulation was given during the beginning of a hyper-reflexic contraction in the SCI patients and a voiding contraction in the normal volunteers to test for detrusor suppression.

Results When the bladder was at *half capacity,* FMS elicited small rapidly occurring artifact in detrusor pressure, probably the result of skeletal movement associated with stimulation, but in neither patient nor healthy volunteer could unequivocal detrusor contractions be seen time-locked to the stimulation (see Figure 1). However, at *near capacity* in the patients only, a hyper-reflexic contraction was occasionally seen but at variable latency ranging from a few seconds to several tens of seconds but always following cessation of the 5s stimulation. In marked contrast, at *full capacity* when hyper-reflexia or voiding took place, a highly consistent time-locked suppression of these detrusor contractions was observed with latencies less than 5s and taking between 10-20s to reach greater than 80% suppression.