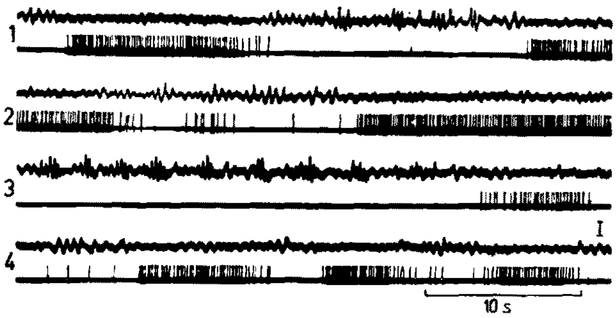
cerebral cortex and gamma motor system by a common relay system within the reticular formation of the brain stem.



Rabbit. Chloralose-urethane. EEG from left motor area. Muscle spindle afferent from left gastrocnemius. Note high frequency irregular spindle discharge simultaneously with periods of desynchronized EEG. Muscle spindle silent when slow waves appear in EEG.

Occasionally a muscle spindle was inhibited synchronously with cortical "arousal" when stimulating the midbrain tegmentum, indicating that the activating relay system of the brain stem may be functionally subdivided, or may be less functionally uniform than is often believed. Another consideration that has to be borne in mind is that the single spindle afferent sampled in such an experiment may not be typical of the gamma system as a whole. Electroencephalogram gives statistical information of the activity in a great number of neurones. The muscle spindle test might, on the contrary, tell us about the situation in a restricted part of the motor system only. Considering this the good correlation generally obtained is still more impressive.

C. von Euler and U. Söderberg

The Nobel Institute for Neurophysiology, Karolinska Institutet, Stockholm 60, Sweden, April 9, 1956.

Zusammenfassung

Es wurde gezeigt, dass die Weckreaktion im EEG meist mit Erregung der Muskelspindeln verknüpft war. In tieferer Narkose konnten die Muskelspindeln bei Erwärmung des Hypothalamus noch beeinflusst werden, ohne dass im EEG nennenswerte Veränderungen auftraten. Thermische Reizung im Hypothalamus konnte aber auch bei der «encéphale isolé»-Katze langsame, grosse Wellen in Grosshirnrinden-Ableitungen hervorrufen. Wahrscheinlich werden die Muskelspindeln und die Aktivität der Grosshirnrinde dabei über dasselbe System vom Hirnstamm beeinflusst.

—

Excitability Changes and Muscle Atrophy After De-afferentation

The problem of muscle atrophy has absorbed the interest of a large number of experimental and clinical workers. In spite of many new facts in this field it is not possible, at the present time, to state precisely, which factors are most important in determining the onset and rate of muscle atrophy. A disturbance of the trophic influence of the nervous system is generally assumed, but the term "trophic influence" lacks a physiological definition.

A number of papers published by Gutmann and his collaborators show that the basis of nervous trophic influence is in the activation of metabolic recovery processes following muscle stimulation (Gutmann, Vodička and Vrbová[1]; Bass, Gutmann and Vodička[2] and others). These recovery processes differ in rate and extent in normal innervated and denervated muscles. They have been found to be influenced by the functional state of nerve centres. For example, coffein activates these recovery processes, while bromides depress them. Myleotomy (Gutmann, Vodička and Vrbová[1]), as well as reflex nociceptive stimulation (Gutmann and Vodička[3]) have a similar depressing effect on these metabolic recovery processes.

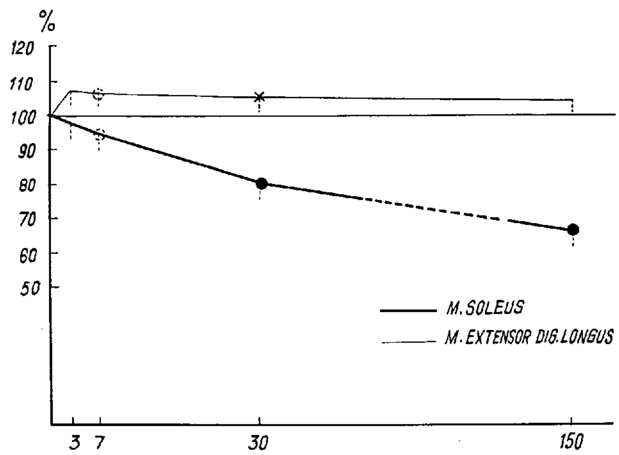
After section of the dorsal roots in the cat and the rat, a tendency to extension develops, which is in accordance with observations described in literature (Hering[4], Ranson[5] *et al.*). We have had ample opportunity of observing exaggerated reflex activity of the de-afferented hind limb, e.g. crossed extensor reflex etc. (see also Trendelenburg[6], Bremer[7], Ranson[5] *et al.*). From our observations, we have been able to conclude that tendency to extension after de-afferentation does not develop immediately after the operation but by the 7th–10th day, and is not dependant on the presence of spinal ganglia. It seems probable, therefore, that these changes of excitability are of central (spinal) origin and that tendency to extension is not mediated by the spinal ganglia as Ranson[5] postulated. Extirpation of spinal ganglia leads to a similar tendency to extension of section of the dorsal roots proximal to the ganglion.

It is possible to interpret these findings in terms of Cannon's Law of Denervation (Cannon and Rosenblueth[8]) and consider them to be the result of afferent denervation of spinal neurones. Drake and Stavraky[9] have postulated this extension of the Law of Denervation to de-afferentation. We have offered the following explanation. Antigravity muscles are mostly connected to the myotatic 2-neurone reflex arc, so that degeneration of the central stump of the dorsal roots leads to the destruction of synaptic endings on extensor motoneurones, while flexor motoneurones are, most probably, to a great extent protected by their interneurone pool.

We have further evidence for the increased excitability of extensor motoneurones after de-afferentation. Changes of chronaxy in cats before and after de-afferentation were studied. Chronaximetric difference between flexor and extensor muscle groups is well marked under normal conditions in cats, similar to man (Lapicque[10]), and is present until about the 10th day after the operation. By this time we noted a gradual decrease in chronaximetric

[1] E. Gutmann, Z. Vodička, and G. Vrbová, Physiol. Bohemoslov. *3*, 182 (1954).
[2] A. Bass, E. Gutmann, and Z. Vodička, Physiol. Bohemoslov. *4*, 267 (1955).
[3] E. Gutmann and Z. Vodička, Physiol. Bohemoslov. *2*, 389 (1953).
[4] H. E. Hering, Neurol. Zbl. *17*, 1077 (1897).
[5] S. W. Ranson, Arch. Neurol. Psychiat. *19*, 201 (1928).
[6] W. Trendelenburg, Arch. Physiol. *1906*, 1.
[7] F. Bremer, Ann. Physiol. Physicochim. Biol. *4*, 750 (1928).
[8] W. B. Cannon and A. Rosenblueth, *The Supersensitivity of denervated Structures. A Law of Denervation* (New York, 1949).
[9] C. G. Drake and G. W. Stavraky, J. Neurophysiol. *11*, 229 (1948).
[10] L. Lapicque, *L'excitabilité en fonction du temps* (Paris 1926).

values for extensor muscles, which led to a levelling out of the flexor-extensor difference. These results, together with observations described above, are considered as evidence for the increase of excitability of motoneurones in the anterior spinal horns for extensor muscles after de-afferentation.



Weight changes in m. soleus and m. extensor digitorum longus after section of the dorsal roots L_1-S_1 proximal to the spinal ganglia in the rat. The results are expressed in percentage of control muscle weight of the contralateral extremity (y axis). Muscles were weighed 3 days (7 animals), 7 days (26 animals), 30 days (32 animals) and 150 days (5 animals) after the operation (x axis). Values marked with a cross are statistically significant for $p = 0{\cdot}05$, with a ring for $p = 0{\cdot}01$ and with a dot for $p = 0{\cdot}001$.

These changes in excitability lead to muscle atrophy in extensor muscles after de-afferentation. We studied weight changes in m. soleus (physiological extensor, antigravity group) and m. extensor digitorum longus (flexor group) after de-afferentation in cats and rats. It was found that m. soleus progressively atrophies after de-afferentation, while no weight changes were noted in m. extensor digitorum longus (see Fig.). Similar results, only less marked, were obtained on m. gastrocnemius and m. tibialis anterior.

The differences due to changes in excitability are further shown in experiments in which muscle hypertrophy or recovery of weight was evoked. On the one hand, we used unilateral amputation and daily "exercise" of the remaining de-afferented extremity by running rats (13 animals) in a rotating drum as a means of provoking muscle hypertrophy. On the other hand, reinnervation of de-afferented muscles 10, 20, and 30 days after crushing the nerve in 45 rats served as a model for weight recovery after denervation. In both cases the results were in agreement with our previous findings. In the amputation experiments, it was found that m. soleus atrophies, while m. extensor digitorum longus hypertrophies significantly more than in control animals. Weight recovery during reinnervation is significantly slower in m. soleus and a little faster in m. extensor digitorum longus than in control muscles.

These experiments also show that the atrophy of m. soleus after de-afferentation is not so much due to the loss of adaptational ability of de-afferented muscles to increased work exertion, as to the increase of excitability in extensor motoneurones in the anterior spinal horns following de-afferentation. De-afferentation atrophy of extensor muscles of the cat and rat may be considered to be a peripheral metabolic consequence of this increased excitability of extensor motoneurones. We do not agree with KURÉ[11], WYBURN[12] and others, according to whom dorsal roots contain trophic nerve fibres, because a similar course of muscle atrophy was noted in extensor muscles after spinal gangliectomy in the rat as after section of the dorsal roots proximal to the spinal ganglia.

We may conclude that metabolic recovery (trophic) processes are influenced by the functional state of nerve centres, and that inactivity *per se* cannot fully explain the onset and rate of muscle atrophy.

P. HNÍK

Physiological Institute, Czechoslovak Academy of Sciences, Prague, February 21, 1956.

Zusammenfassung

1. Die Deafferenzierung der hinteren Extremität bei Ratten und Katzen verursacht eine Neigung zur Extension, welche sich 7–10 Tage nach der Operation zu entwickeln beginnt; diese sehr ausgeprägte Neigung wird durch eine erhöhte Erregbarkeit der motorischen Vorderhornzellen erklärt, welche die Extensoren innervieren.

2. An der deafferenzierten Extremität atrophieren die Antigravitationsmuskeln (m. soleus und m. gastrocnemius), während man bei den Flexoren (m. extensor digitorum longus und m. tibialis anterior) kein Anzeichen von Atrophie findet.

3. Die Deafferenzierungs-Atrophie der Antigravitationsmuskeln ist als eine in der Peripherie eintretende metabolische Folge des veränderten Funktionszustandes der Nervenzentren aufzufassen. Diese Ansicht konnte mit Hilfe weiterer Experimente (Reinnervation und Arbeitshypertrophie) bestätigt werden.

[11] K. KURÉ, Y. NITTA, H. MATSUURA, and M. TSUJI, Z. ges. exper. Med. *60*, 250 (1928).

[12] R. WYBURN-MASON, *Trophic Nerves* (London, 1950).

On the Stability and the Reactions of the H_2O^+ Ion in Aqueous Solution

The existence of the H_2O^+ ion in the gaseous state has been fully established by mass-spectrometric observations. From a knowledge of the ionisation potential of the water molecule (12·6 e.v.)[1] and of other well known thermo-chemical data, it can be shown that H_2O^+ itself should have considerable stability since the association process:

$$H^+ + OH \longrightarrow H_2O^+ + 6{\cdot}1 \text{ e.v.} \qquad (1)$$

is highly exothermic.

In aqueous systems, however, the situation might be different, since here one has to take into account the hydration energies; under these conditions, therefore, the equilibrium:

$$H_2O^+ \text{ aq} + H_2O \rightleftharpoons H_3O^+ \text{ aq} + OH \qquad (2)$$

should be of considerable importance. With regard to the position of this equilibrium, it can be said that in view of the structural similarity of the H_2O^+ and H_3O^+

[1] *Cf.* W. C. PRICE, Chem. Rev. *41*, 257 (1947).