Supraspinal Inhibitory Control of Spinal Reflexes during Natural Sleep[1]

Supraspinal modulation of spinal reflex activity occurs during sleep and wakefulness. Both monosynaptic (MR) and polysynaptic (PR) spinal reflexes are slightly depressed during synchronized sleep with respect to relaxed wakefulness[2]. During episodes of deep, desynchronized sleep[3] the MR is completely abolished. Provided the stimulus intensity affecting the high threshold muscular afferents (flexion reflex afferents, FRAs) does not reach the threshold for the arousal, the PRs are also blocked[2].

The aim of the present investigation has been the analysis of the mechanisms responsible for these changes in the mono- and polysynaptic spinal reflexes occurring during the different stages of natural sleep. Particular attention has been devoted to the problem whether the striking changes of spinal reflexes occurring during deep sleep are due (i) to abolition of a descending tonic facilitatory influence or (ii) to descending inhibitory volleys.

The present experiments were performed on unrestrained, unanaesthetized cats. Stimulating and recording electrodes were chronically implanted under barbiturate anaesthesia (see [4]). The spinal reflexes were elicited by stimulating the central end of the medial gastrocnemius nerve and by recording both monosynaptic and polysynaptic responses respectively from the lateral gastrocnemius muscle and the tibialis anterior muscle, following a technique which has been previously described[2]. Short-lasting trains of rectangular pulses at 100/sec, 0.05 msec were used. The nature and the organization of the descending regulatory influences on spinal reflexes were investigated by means of partial and complete sections of the spinal cord. These operations were performed under light ether anaesthesia, which allowed an accurate control of the threshold and of the amplitude of the spinal reflexes soon after the cord transections. The same animals were later decerebrated at a precollicular level and the changes of the reflexes due to stimulation of different supraspinal structures were investigated. The following results have been obtained.

(1) A bilateral and symmetrical section of the dorsolateral funiculi, performed under ether anaesthesia at T_{12}, did not produce any sign of spinal shock, nor did it abolish the changes of MR and PR occurring during synchronized or desynchronized sleep. On the other hand, the threshold for the effects elicited by the FRA volleys (inhibition of extensor motoneurones, facilitation of flexor motoneurones, EEG and behavioural arousal) decreased during relaxed wakefulness or synchronized sleep; also, the threshold for behavioural arousal during desynchronized sleep was lower after this section. These effects were controlled with chronic experiments and cannot be ascribed to irritation. Descending pathways, coursing along the dorso-lateral funiculi, are known to exert a tonic inhibitory control upon the spinal mechanisms influenced by FRAs[5], and it is likely that their interruption was responsible for the lowering of threshold described above. Our experiments show that the changes of flexor reflex occurring during desynchronized sleep are not necessarily mediated by these pathways.

(2) A complete section of the spinal cord at T_{12}, performed under ether anaesthesia, abolished the MR elicited by stimulating the medial gastrocnemius nerve at 100/sec. The impairment of this reflex (spinal shock) lasted only for a short time; it appeared again, partially at least, 1–2 h after the operation. Similar effects were also obtained when the spinal section was not complete, but affected the dorso-lateral and the ventral funiculi of both sides, leaving the ventral half of the lateral funiculi intact. It is known that spinal shock can be elicited by destruction of Deiters' nucleus and that at thoracic levels the vestibulo-spinal pathway courses along the ventral funiculi (see [6]). A short-lasting, reversible depression of the PR also occurred soon after the complete section of the spinal cord.

(3) Although a complete surgical separation of the tonic facilitatory pathways from the inhibitory ones cannot be obtained, the occurrence of spinal shock was taken as an indication that most of the descending facilitatory pathways had been interrupted. This result was obtained by means of one or more (up to 5) sections of the spinal cord, performed in the same animal at different periods of time. As soon as the effects of the spinal shock had disappeared, continuous EEG records were taken until the animal showed episodes of deep sleep. The abolition of MR and PR during desynchronized sleep was never obtained after complete section of the spinal cord, but was present whenever the ventral half of the lateral funiculi had been spared by the lesion. In some animals the section of the spinal cord partially affected also the ventral part of the lateral funiculi. In these cases both MR and PR elicited by 100/sec pulses were reduced during desynchronized sleep. The remaining depressing influence, however, was less profound than in cats having intact ventral halves of the lateral funiculi, as shown by the fact that the blockade could be overcome by raising the rate of stimulation to 500/sec, an observation which was never made when this part of the spinal cord had been completely spared by the lesion.

(4) The animals in which a partial transection of the spinal cord was made as reported under (3), were submitted, after recovery, to a complete section of the spinal cord which was carried out under ether anaesthesia one segment rostrally to the previous lesions. No appreciable manifestation of spinal shock was observed, even *soon* after this total cordotomy. These findings indicate that the abolition of the spinal reflexes, particularly of MR, during desynchronized sleep, observed in the experimental conditions reported under (3), is not due to withdrawal of a tonic facilitatory barrage.

(5) In some of the animals in which the spinal transection had been spared, more or less completely, the ventral half of the lateral funiculi, decerebration was carried out under ether anaesthesia, and both the MR and PR were tested by increasing progressively the stimulus intensities. In these experiments high rate stimulation of the ventromedial region of the medullary reticular formation not only abolished the decerebrate rigidity of the fore-limbs but also inhibited both MR and PR induced by stimulating the medial gastrocnemius nerve. On the contrary,

[1] This investigation was supported by PHS research grant B-2930 from the National Institute of Neurological Diseases and Blindness, N.I.H., Public Health Service (U.S.A.).

[2] S. GIAQUINTO, O. POMPEIANO, and I. SOMOGYI, Exper. *19*, 481 (1963).

[3] M. JOUVET, Arch. ital. Biol. *100*, 125 (1962).

[4] O. POMPEIANO and J. E. SWETT, Arch. ital. Biol. *100*, 311, 343 (1962).

[5] B. HOLMQVIST and A. LUNDBERG, Arch. ital. Biol. *97*, 340 (1959). – B. HOLMQVIST, A. LUNDBERG, and O. OSCARSSON, Arch. ital. Biol. *98*, 60 (1960).

[6] A. BRODAL, O. POMPEIANO, and F. WALBERG, *The Vestibular Nuclei and their Connections. Anatomy and Functional Correlations.* (Oliver and Boyd, Edinburgh 1962).

stimulation of Deiters' nucleus, which increased the decerebrate rigidity of the fore-limbs, was completely ineffective on the electrically induced hind-limb reflexes.

The present experiments show that the striking abolition of the proprioceptive reflexes occurring during desynchronized sleep cannot be explained simply with a withdrawal of a facilitatory influence descending from the the brain stem since (i) this effect could still be observed when the spinal section affected the dorsolateral and the ventral funiculi of both sides, as soon as the effects of the spinal shock had disappeared, and (ii) no appreciable manifestation of spinal shock occurred when a complete section of the spinal cord was later carried out. The experimental evidence suggests, therefore, that the abolition of the spinal reflexes during the episodes of deep sleep is due to descending inhibitory volleys impingeing upon the proprioceptive reflex arcs. These suppressive influences originate from supraspinal structures, localized probably within the inhibitory regions of the brain stem reticular formation; they descend mainly, although probably not exclusively, along the ventral half of the lateral funiculi.

Riassunto. La scomparsa di riflesi spinali mono- e polisinaptici nel corso del sonno desincronizzato è legata a meccanismi inibitori esercitantesi sugli archi riflessi spinali. Questa azione di controllo viene trasmessa da centri sopraspinali al midollo spinale attraverso vie che decorrono principalmente, per quanto non esclusivamente, nei funicoli ventro-laterali.

S. GIAQUINTO, O. POMPEIANO, and I. SOMOGYI

Istituto di Fisiologia della Università di Pisa (Italy), July 8, 1963.

Generalized Inhibition of Spinal Reflexes Induced by Cutaneous Nerve Stimulation in Unrestrained Cats[1]

It was previously reported that low rate stimulation of group II cutaneous afferents, performed in unrestrained unanaesthetized cats, produces EEG synchronization and behavioural sleep[2]. On the other hand, high rate stimulation of group II and low or high rate stimulation of group III cutaneous afferents produces EEG desynchronization and behavioural arousal[2]. A study of the spinal reflexes during sleep and wakefulness has shown, moreover, that in normal, unanaesthetized animal monosynaptic (MR) and polysynaptic (PR) spinal reflexes are completely abolished during deep, desynchronized sleep[3], an effect due to tonic inhibition from supraspinal structures[4].

The present experiments show that the generalized inhibition of spinal reflexes which characterizes episodes of deep sleep may be reproduced by low rate stimulation of the lower threshold cutaneous afferents.

The experiments have been performed on unrestrained, unanaesthetized cats with chronically implanted electrodes (see [2]). EEG cortical electrodes, EMG electrodes recording from the extensor neck muscles, and stimulating electrodes applied on the superficial radial nerve of one or both the sides were implanted under barbiturate anaesthesia. EMG electrodes were also applied to the lateral gastrocnemius and tibialis anterior muscles of one side, in order to record respectively the monosynaptic and polysynaptic reflex responses to graduated stimulation of the central stump of the ipsilateral medial gastrocnemius nerve, following a technique which has been previously described[3]. In order to avoid irritation, the recording sessions never started before the third or fourth day following the chronic implantation of the electrodes. The following results have been obtained.

(1) Low rate stimulation (from 1 to 10/sec, 0.05 msec pulse duration) of the superficial radial nerve, for stimulus intensities capable of activating only the group II cutaneous afferents, does not produce any change in postural tonus when performed on a background of strong arousal. However, when performed on a background of relaxed wakefulnes or of light synchronized sleep, the same stimulation is followed (i) by a decrease of the tonus of the neck musculature and of the lateral gastrocnemius (antigravity muscles), and (ii) by a reduction or abolition of the after-discharge of the tibialis anterior (flexor muscle) following stimulation of the flexion reflex afferents (FRAs) of the medial gastrocnemius nerve. Within the range of 1 to 10/sec, the effects reported above increase in intensity and occur earlier when the rate of stimulation is increased. However, when the rate is raised to 20/sec, the initial decrease in the tonus of the neck muscles is followed by marked enhancement, while at 100/sec only an increase of the electromyographic activity of neck muscles is observed.

(2) The effects on postural tonus may be accompanied by EEG synchronization, but they can be observed independently from it. The synchronized response actually occurs only when the stimulation of the superficial radial nerve is performed on a proper background of EEG activity[2].

(3) Low rate stimulation of group II cutaneous afferents reduces (Figure, A), or abolishes (Figure, B) the MR produced by stimulating the medial gastrocnemius nerve at 100/sec with stimulus intensities ranging from 1.0 to 1.2 times the threshold for the MR. This effect may also outlast the stimulus (Figure, C, D). It is particularly striking when the stimulus applied to the muscular nerve is just supraliminal for the MR, is increased by raising from 1 to 10/sec the rate of stimulation of the superficial radial nerve as well as its intensity, provided the stimulus remains subliminal for group III cutaneous afferents. The reduction or the abolition of the MR are scarcely evident in the aroused animal. They may be accompanied by induced EEG synchronization, but the relationship between EEG and spinal effects is not constant.

(4) The abolition of the MR produced by low rate stimulation of group II cutaneous afferents is the consequence of an inhibitory process which does not depend upon mechanisms of reciprocal innervation, since (i) it is observed by stimulating both the ipsilateral and the contralateral superficial radial nerve, while (ii) the reduction of

[1] This investigation was supported by PHS research grant B-2990 from the National Institute of Neurological Diseases and Blindness, N.I.H., Public Health Service (U.S.A.).

[2] O. POMPEIANO and J. E. SWETT, Arch. ital. Biol. *100*, 311, 343 (1962).

[3] S. GIAQUINTO, O. POMPEIANO, and I. SOMOGYI, Exper. *19*, 481 (1963).

[4] S. GIAQUINTO, O. POMPEIANO, and I. SOMOGYI, Exper. *19*, 296 (1963).