Corticospinal Influences on Primary Afferents During Sleep and Wakefulness[1]

The increase in pyramidal discharge which occurs during desynchronized sleep[2] is related in time with the bursts of rapid eye movements (REM)[3]. This effect is due in part to corticofugal volleys arising from the motor cortex because it can still be observed after bilateral ablation of the sensory cortical areas S_I and S_{II}.

The corticospinal fibres, however, are not exclusively concerned with the transmission to α-motoneurones of volleys arising from the motor cortex. Stimulation of the sensory-motor cortex of the cat is also followed by depolarization of the central terminals of the flexion reflex afferents[4,5]. As a result, the afferents involved in the polysynaptic flexion reflex can be inhibited presynaptically[6]. The precruciate gyrus depolarizes these primary afferents only through synaptic activation of neurones in the postcruciate cortex[5].

The present experiments were made to determine (i) whether the phasic enhancement in the pyramidal activity occurring during the bursts of REM could still be observed after unilateral ablation of the motor cortex; and (ii) whether, in the same animal, primary afferent depolarization could still be produced by pyramidal stimulation following degeneration of the corticospinal motor fibres.

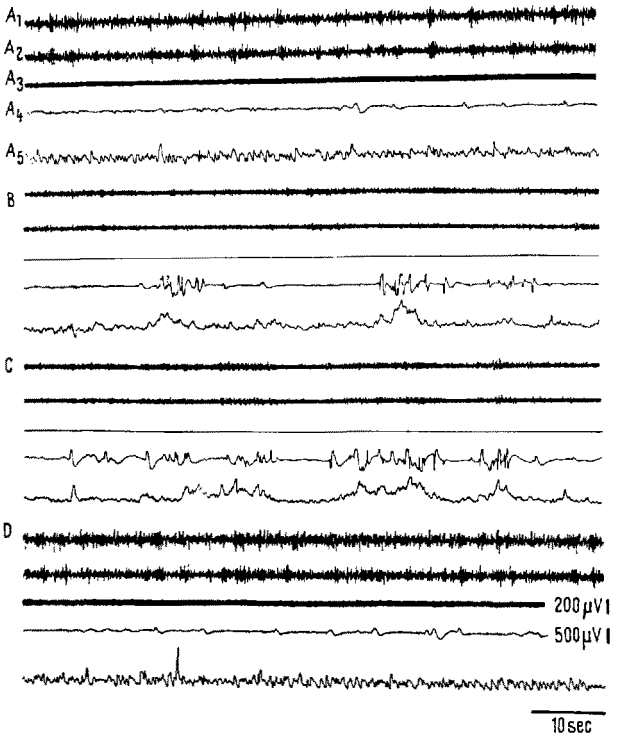

Fig. 1. Pyramidal discharge originating from the sensory cortical areas S_I-S_{II} during sleep. Unrestrained unanaesthetized cat, with chronic (48 days) ablation of left precruciate and rostral postcruciate (motor) cortex. 1, left parieto-occipital; 2, right parieto-occipital; 3, posterior cervical muscles; 4, ocular movements; 5, integrated record from the left pyramid above the decussatio pyramidum. A, during synchronized sleep the pyramidal activity increases synchronously with the EEG spindles and decreases during the interspindle lulls. B, C, phasic enhancements of the pyramidal activity during the REM periods of desynchronized sleep. D, control taken 18 sec after the end of the episode of desynchronized sleep.

Methods. The experiments were performed on 8 unrestrained, unanaesthetized cats, previously submitted to unilateral ablation of the precruciate and rostral postcruciate (motor) cortex. Electrodes for recording the EEG, the EMG of the posterior cervical muscles, the ocular movements and the pyramidal activity were implanted chronically. The integrated pyramidal discharge was recorded with a technique described elsewhere[3]. Following chronic degeneration of the corticospinal fibres stemming from the motor cortex, the animals were decerebrated, paralysed with flaxedil and artificially respirated. In these animals the ventral root discharge and the dorsal root potentials elicited by short-lasting repetitive stimulation of the pyramidal tracts, were recorded respectively from the ventral roots L7–S1 and a dorsal root filament of lower L6 or upper L7 and were compared with similar responses elicited in cats with motor cortex intact.

Results. After ablation of the motor cortex, the pyramidal discharge increased phasically when movements were induced by arousing stimuli, but gradually decreased at the transition from quiet waking to drowsiness. In synchronized sleep the pyramidal activity showed irregular oscillations. In particular the pyramidal activity fell

[1] This investigation was supported by PHS research grant NB-02990-04 from the National Institute of the Neurological Diseases and Blindness, N.I.H., Public Health Service (USA).

[2] E. V. EVARTS, J. Neurophysiol. *27*, 152 (1964). – A. ARDUINI, G. BERLUCCHI, and P. STRATA, Arch. ital. Biol. *101*, 530 (1963).

[3] P. L. MARCHIAFAVA and O. POMPEIANO, Arch. ital. Biol. *102*, 500 (1964).

[4] D. CARPENTER, A. LUNDBERG, and V. NORRSELL, Acta physiol. scand. *59*, 126 (1963).

[5] P. ANDERSEN, J. C. ECCLES, and T. A. SEARS, J. Neurophysiol. *27*, 63 (1964).

[6] J. C. ECCLES, *The Physiology of Synapses* (Springer Verlag, Berlin-Göttingen-Heidelberg 1964).

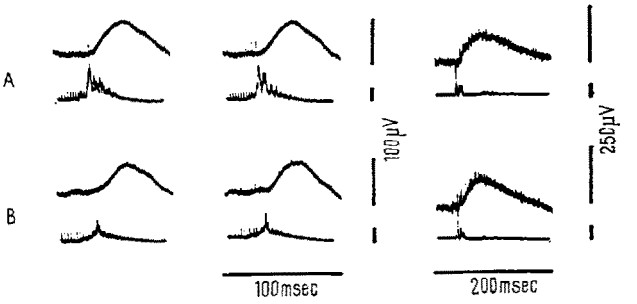

Fig. 2. Dorsal root potentials and ventral root discharges evoked by pyramidal stimulation. The upper traces were recorded from a dorsal root filament in upper L7 on the right side. The filament was cut 15 mm from the dorsal root entry zone and placed on two electrodes, one close to the entry zone and the other on the cut end. Upward deflection denotes negativity of the central electrode. The lower traces were recorded from ventral roots L7-S1 on the right side. A, records taken from cat with sensory-motor cortex intact. B, records taken from another cat with chronic (49 days) ablation of the left precruciate and rostral postcruciate (motor) cortex. Same cat as in Figure 1. The first two records were obtained by repetitive stimulation of the left pyramid at medullary level above the decussatio, with a train of 10 shocks at 440/sec, 1.0 msec pulse duration and 3 times the threshold for the dorsal root potentials. The last record was taken during single shock stimulation of the right common peroneal nerve, with single shock of 0.5 msec, 4 times the threshold for the monosynaptic reflex, to prove that segmental stimulation was equally effective in both animals. The cats were anaesthetized with Nembutal, paralised with flaxedil, and artificially respirated.

to a minimum in the interspindle lulls and reached a maximum during the spindles. When synchronized sleep was replaced by the desynchronized phase, the peaks in the pyramidal record disappeared; and the corticospinal activity became stabilized to a level similar to that reached during the interspindle lulls, provided the REM were absent. As soon as these ocular phenomena occurred, the pyramidal activity increased phasically and reached a level much higher than that seen during the spindle trains (Figure 1). These experiments, together with the demonstration that the ablation of both the motor and sensory areas of the cortex prevented the appearance of changes in pyramidal activity related with the different states of sleep and wakefulness, indicate that during desynchronized sleep there is a phasic increase in the corticofugal discharge which also originates from the somatosensory areas of the cortex (S_I and S_{II}).

In the decerebrate cats stimulation of the pyramidal tract as long as 49 days after ablation of the motor cortex, i.e. when the corticofugal fibres originating from the motor cortex had degenerated and could no longer be excited, produced a ventral root discharge which was strikingly reduced with respect to controls taken in the intact animal. The dorsal root potentials elicited by pyramidal stimulation, on the other hand, resembled those obtained in the control experiment in both size and shape (Figure 2). The fact that outbursts of pyramidal activity still occur synchronously with the REM after degeneration of the corticospinal fibres arising in the motor cortex, suggests that presynaptic inhibitory volleys originate from the sensory areas S_I and S_{II} during the REM periods of desynchronized sleep. They may at least contribute to the phasic depression of the polysynaptic reflex that occurs at the time of the bursts of REM[7].

Riassunto. Nel sonno desincronizzato si osserva un aumento della scarica piramidale originante dalle aree somato-sensoriali della corteccia in corrispondenza dei REM. Queste scariche piramidali depolarizzano le fibre afferenti primarie della via riflessa flessoria e verosimilmente contribuiscono alla depressione fasica dei riflessi polisinaptici che si manifesta durante i REM.

A. R. Morrison and O. Pompeiano

Istituto di Fisiologia della Università di Pisa and Centro di Neurofisiologia e Gruppo d'Elettrofisiologia del Consiglio Nazionale delle Ricerche, Sezione di Pisa (Italy), June 28, 1965.

[7] M. M. Gassel, P. L. Marchiafava, and O. Pompeiano, Rend. Accad. naz. Lincei, Cl. Sci. fis., mat. nat., Ser. VIII, *36*, 543 (1964); Arch. ital. Biol. *102*, 471 (1964).

On the Possibility that Thymus-Mediated Alloantigenic Stimulation Results in Tolerance Response

It now seems firmly established that thymus occupies a privileged position among other lymphoid organs (Miller et al.[1]). The various hypotheses as to whether thymus is an essential source of cells for other lymphoid organs or provides a humoral factor or a local environment required for functional maturation of cells originating elsewhere[2–7] may be complementary rather than contradictory.

One of the features distinguishing thymus from other lymphoid organs is the absence of antibody formation and of morphological symptoms of activation[8–10] which characterizes the response to antigenic stimulation in spleen and lymph nodes. This might simply be due to some sort of afferent blood-thymus bar which prevents extrinsic antigens from entry into the intact organ[11,12]. Especially, this characteristic of thymus led Burnet[2] to place in it a hypothetical mechanism which would ensure immunological tolerance to 'self-antigens'. It was assumed that immunological tolerance results from a collision of an immature lymphoid cell with the appropriate antigen[13,14]; if the 'vulnerable' phase of development of lymphoid cells coincided with their sojourn in thymus, where only autoantigens seem to be available, the potentially self-reactive clones might there be automatically filtered off and prevented from further development to reactivity. Pathological changes of an autoimmune nature following thymectomy[15,16], and some data on the role of thymus in autoimmune conditions[17,18], may be interpreted in favour of this concept even though a different explanation of some of the findings may be preferred[19].

We wished to check this hypothesis by assuming that the respective mechanism might be 'misused' for non-self-antigens if these were artificially introduced into the thymus of adult animals. However, the cell population in an adult thymus seems to involve also a proportion of functionally mature cells, as indicated by the findings of antibody formation in thymus injected with various

[1] J. F. A. P. Miller, Adv. Immunol. *2*, 111 (1962).
[2] F. M. Burnet, Aust. Ann. Med. *11*, 79 (1962).
[3] J. F. A. P. Miller, Proc. Roy. Soc. B, *156*, 415 (1962).
[4] D. Osoba and J. F. A. P. Miller, Nature *199*, 653 (1963).
[5] R. H. Levey, N. Trainin, and L. W. Law, J. Nat. Cancer Inst. *31*, 199 (1963).
[6] C. E. Ford, and H. S. Micklem, Lancet *1963 i*, 359.
[7] J. E. Harris, C. E. Ford, D. W. H. Barnes, and E. P. Evans, Nature *201*, 884 (1964).
[8] M. Björneboe, H. Gormsen, and F. Lundquist, J. Immunol. *55*, 121 (1947).
[9] A. Fagraeus, Acta med. scand. *130*, Suppl. 204, 3 (1948).
[10] T. N. Harris, J. Rhoads, and J. Stokes, J. Immunol. *58*, 27 (1948).
[11] A. H. E. Marshall and R. G. White, Brit. J. exp. Path. *42*, 379 (1961).
[12] S. L. Clark jr., Am. J. Anat. *112*, 1 (1963).
[13] F. M. Burnet, *The Clonal Selection Theory of Acquired Immunity* (Cambridge University Press, 1959).
[14] J. Lederberg, Science *129*, 1649 (1959).
[15] J. de Vries, L. M. van Putten, H. Balner, and D. W. van Bekkum, Rev. Franç. Étud. Clin. Biol. *9*, 381 (1964).
[16] D. E. R. Sutherland, O. K. Archer, R. D. A. Peterson, E. Eckert, and R. A. Good, Lancet *1965 i*, 130.
[17] F. M. Burnet and M. C. Holmes, Nature *194*, 146 (1962).
[18] M. Vojtíšková and Z. Pokorná, Lancet *1964 i*, 644.
[19] I. F. Loutit, Brit. J. Radiol. *36*, 785 (1963).