Cyclic Variation in the Amplitude of a Brain Stem Reflex during Sleep and Wakefulness

In recent years, attention has been drawn to variations in the amplitude of spinal reflexes which occur during the different stages of sleep and wakefulness[1-6]. We were interested in determining if similar variations take place in reflex activity at a brain-stem level. For this purpose we chose as a test reflex the masseteric monosynaptic reflex[7,8]. It is our intent to determine the fluctuations in brain-stem reflex transmission during various behavioral states; the initial ones studied were sleep and wakefulness. A second objective of these studies arose as the result of experiments in acute preparations in which we observed complete inhibition of this reflex and others following orbital-cortical[9-10] or basal forebrain stimulation[9]. We are presently investigating the behavioral conditions during which the orbital cortex and basal forebrain may induce this reflex inhibition. Our first step, however, was the documentation of the normative variations in the amplitude of the masseteric monosynaptic reflex during sleep and waking states in unanesthetized, unrestrained cats.

Each of the 8 adult cats which were studied was prepared in the following manner. While the animal was under sodium methohexital (Brevital) anesthesia, electrodes to induce and record the reflex response, as well as others to monitor the EEG, eye movements, and posterior neck muscle EMG, were permanently fixed in place for chronic recording and stimulation. Anesthesia was then discontinued, the incisions closed, and the animal allowed to recover for a period of 1 week.

Data were collected while the animal was within an environmental chamber to which he had been habituated (see reference [11] for details of chamber and recording apparatus). The length of each recording session was approximately 5 h. During these sessions a liminally-induced reflex was evoked continuously at the rate of 2/sec. In addition to oscilloscopic records of the reflex potentials, we were able to obtain, with the aid of a peak-reading amplifying circuit, simultaneous polygraphic records of the amplitude of the reflex motor potential along with the activity of the EEG, eyes, and neck muscles. This method of data collection allowed us to correlate closely variations in reflex amplitude with the specific state of the animal. Sleep and wakefulness were divided into the following 4 states: (1) alert; (2) drowsy; (3) quiet sleep; (4) active sleep (see references [11] and [12] for details of this classification).

The amplitudes of the reflex motor responses are plotted in histographic form in Figure 1 for the 4 states of sleep and wakefulness. During the alert state a large number of moderate and high-amplitude reflex potentials was observed (Figure 1A). The drowsy state was characterized by a decrease in the frequency of the higher-amplitude potentials (Figure 1B), as compared with the alert state. During quiet sleep the mean amplitude of the reflex response decreased when compared with the drowsy state (Figure 1C). At times during quiet sleep reflex responses failed to occur following stimulation of the mesencephalic nucleus. These events are indicated by the frequency of zero amplitude potentials (arrow at zero in Figure 1). The majority of the reflex responses was completely suppressed during active sleep (Figure 1D).

A statistical analysis of the change in mean amplitude of the reflex during the successive states in the sleep cycle utilized planned comparison tests based on an analysis of variance. The changes in state – waking compared with drowsy, drowsy with quiet sleep, and quiet sleep with active sleep – were each marked by a significant reduction in the amplitude of the reflex response ($p \leq 0.05$).

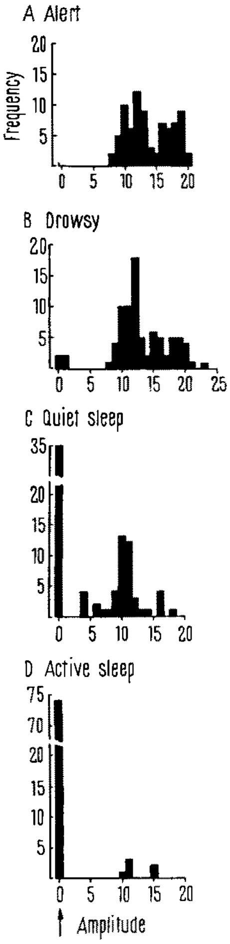

Fig. 1. Frequency histograms of the amplitudes of 80 consecutive masseteric reflex responses. These potentials were obtained during the (A) alert, (B) drowsy, (C) quiet sleep, and (D) active sleep states. The amplitudes of the motor responses are plotted on an arbitrary scale as a function of the frequency of their occurrence. High amplitude potentials are reduced and then almost totally abolished as the animal progresses from wakefulness, through drowsiness and quiet sleep, and into active sleep.

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We were able to follow the phenomenon of complete reflex suppression which was observed during quiet and active sleep more closely by plotting the % occurrence of the reflex, minute by minute, during consecutive cycles of sleep and wakefulness (Figure 2). In this aspect of our analysis no marked variations were noted during short episodes of the alert or drowsy states. In quiet sleep, however, and especially during those episodes which terminated in active sleep, a gradual reduction in the % occurrence of the reflex response was observed. As clearly indicated in both Figures 1 and 2, there was almost complete suppression of the masseteric reflex during active sleep. With suprathreshold stimuli during active sleep, we frequently observed an additional phasic reduction in the reflex amplitude concomitant with bursts of rapid eye movements.

In summary, as an initial step in the analysis of the functional significance of central inhibitory systems during behavioral states, we investigated the spontaneous fluctuations of a brain-stem reflex during sleep and wakefulness. We observed a gradual, but statistically significant, decrease in the amplitude of the reflex response as the animal passed from the alert state through the drowsy and quiet sleep states, and into active sleep. During active sleep the reflex response was almost completely abolished. The studies on spinal reflexes similarly report reflex depression during active sleep and during bursts of rapid eye movements, but note only slight or no change during quiet sleep when compared with wakefulness[1-6]. There are a number of possible explanations for this discrepancy: (1) the techniques of reflex excitation and recording have differed slightly, (2) in the present study a liminally-induced test reflex was used, (3) we analyzed and treated statistically a large population of reflex amplitudes, and (4) previous studies on spinal reflexes did not differentiate between the drowsy and quiet sleep states[13,14].

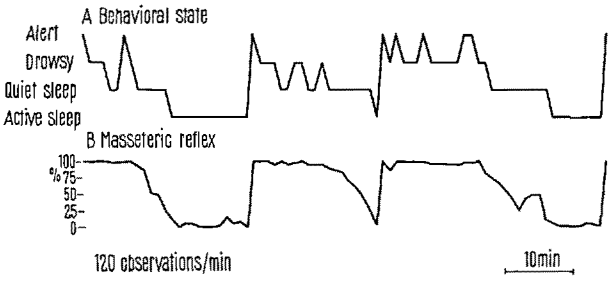

Fig. 2. This figure shows the % occurrence of the masseteric reflex (B) during consecutive sleep cycles (A). In this analysis the reflex responses were counted as either present or absent. Note the gradual decrease in the % response during the periods of quiet sleep preceding active sleep.

Zusammenfassung. In frei beweglichen Katzen wurden Veränderungen des Reflexes zum Musculus massetericus während des Schlafes und im Wachzustand untersucht. Eine graduelle Abnahme der Amplitude des Reflexes wurde beobachtet, wenn die Tiere vom Wachzustand über eine «schläfrige Phase» (drowsy state) in die sogenannte «ruhige Schlafphase» (quiet sleep) gelangten. Während des paradoxalen Schlafes (active sleep) waren die Amplituden der Reflexpotentiale hochgradig herabgesetzt.

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The Effects of Primary Afferent Depolarization on Excitability Fluctuations of Ia Terminals within the Motor Nucleus

We have recently reported[1] that stimulation of group I muscle and of low-threshold cutaneous afferents can reduce the fluctuations of successive monosynaptic reflexes elicited by constant afferent volleys. The time course of this effect and its sensitivity to picrotoxin suggested that the paths leading to primary afferent depolarization (PAD) were involved in variability reduction. It was then proposed that variability of the monosynaptic reflex resulted mainly from membrane potential fluctuations of the Ia afferent terminals. This would affect the amount of transmitter substance released by each presynaptic knob[2] and/or the number of afferent terminals invaded by the presynaptic impulse[3]. To test this possibility further we studied the effects of conditioning afferent volleys on the excitability fluctuations of Ia afferent terminals within the motoneuronal nucleus.

Methods. The experiments were performed in 10 cats made spinal (at the first cervical level) under ether anaesthesia and with head circulation occluded. All animals were immobilized with gallamine triethiodide (Flaxedil) and maintained on artificial respiration. The lumbosacral spinal cord was exposed and the right S1 and L7 ventral roots sectioned. The lateral (GL) and medial (GM) gastrocnemius, as well as the plantaris flexor digitorum and hallucis longus (PL-FDHL) and common peroneal (P) nerves on the right side were sectioned and their central ends prepared either for stimulation or recording. Neural responses as well as stimulating current pulses were electronically integrated and their mean areas ($\bar{A}$) and corresponding variances (σ^2) continuously calculated with an analogue computer[1].

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