Effects of sleep on human reflexes with a double component

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Since Kugelberg in 1952 originally described two components of the blink reflex, the initial component was considered to be a proprioceptive or a myotatic reflex because it was briefer in duration and more constant in latency, size, and shape (Kugelberg, 1952; Rushworth, 1962; Gandiglio and Fra, 1967). These reflexes were recorded from the orbicularis oculi muscle and were elicited by tapping the glabella or stimulating the supraorbital nerve percutaneously. During a detailed study of human flexor reflexes, Shahani and Young (1968a, b) noticed a similarity between the two components of the flexor reflex and those of the blink reflex. This similarity pertained to the size, shape, and relative latencies of the two components. In addition, it was possible to evoke homolateral blink reflexes consisting of both components by single brief electrical shocks to the skin of any part of the face supplied by the first division of the trigeminal nerve. It was therefore suggested that the two components of both the blink reflex and the flexor reflex were analogous and that both were cutaneous reflexes.

During extensive studies on human flexor reflexes and the blink reflexes it was noted that, although the first component of these reflexes was relatively constant when the subject was relaxed, apprehension resulted in marked increase in the amplitude of the second component. This phenomenon suggested the possibility that there was differential central control of the two components of these reflexes. The present studies on the effect of sleep on these two human reflexes with a double component have confirmed that impression. In addition to similarities pertaining to size, shape, and relative latencies, the central mechanism responsible for the differential control of the two components of the blink reflex and the flexor reflex is also similar.

METHODS

Nine normal healthy subjects, six males and three females, ranging from 20 to 64 years of age, were studied. Two male patients with Parkinson's disease, aged 62 and 64 years, were also studied.

The subjects lay supine on a comfortable couch in a warm room. For eliciting flexor reflexes, electrical shocks were delivered through two insulated steel needles bared at the tips, which were inserted intradermally approximately 0.5 to 2 cm apart in the medial sole of the foot. The stimuli were fed through an isolation transformer from a DISA Multistim and were 20 msec long trains of 0.1 msec square wave pulses at 500 c/s. Stimulus intensity ranged from 5 to 50 V.

Electromyographic activity was recorded via small clip electrodes with the sharpened tips placed superficially in the skin over the belly of tibialis anterior muscle. For recording single motor unit potentials, double cored (coaxial) needle electrodes were inserted in the tibialis anterior muscle near its tendinous end. The sweep of the oscilloscope was delayed for 50 to 70 msec for recording motor unit potentials from the first component of flexor reflex and 110 to 130 msec for recording potentials from the second component of flexor reflex. The recording electrodes were connected via cathode follower inputs through Tektronix type 122 preamplifiers, further amplified and displayed on a cathode ray oscilloscope, and filmed on 70 mm photographic paper. The individual motor unit potentials were identified by their shape, amplitude, duration, and polarity.

To study the effects of altered consciousness, the subjects were allowed to go to sleep on a comfortable couch in a warm dark room after the control recording of flexor reflex from the tibialis anterior muscle had been taken. The onset of deep rhythmical breathing signalled that the subject had gone to sleep. The flexor reflexes were recorded again while the subject was asleep. The strength of the stimulus for evoking the flexor reflex in sleep was the same as used for recording the control reflex responses.

For recording blink reflexes, small single electrical shocks were delivered to the supraorbital nerve as it emerges through the supraorbital groove, using DISA surface stimulating electrodes. The stimulus was again fed through an isolation transformer from a DISA Multistim and was a square wave pulse with a duration of 0.05 to 0.1 msec and intensity of 5 to 20 V. Electromyographic activity was recorded from the inferior half of orbicularis oculi muscle by means of clip electrodes or silver EEG electrodes attached to the skin overlying the muscle. Subjects lay supine on a comfortable couch in a warm dark room.
As described previously, natural sleep was induced in the same manner. No drugs were used to induce sleep. Low intensity single electrical shocks to the supraorbital nerve were given continuously at the rate of one every 3 sec or one every 5 sec to record the changes in the two reflex components during sleep and consciousness. In some experiments the medial popliteal nerve was also stimulated simultaneously to evoke the H reflex.

For recording the H reflex, the medial popliteal nerve was stimulated in the popliteal fossa using monopolar surface stimulation. Duration of stimuli ranged from 0·5 to 0·7 msec, and intensity from 25 to 40 V. Electromyographic activity was recorded by means of clip electrodes with the sharpened ends placed superficially in skin overlying the distal end of the gastrocnemius-soleus muscle.

RESULTS

As reported previously, electrical stimulation of the supraorbital nerve produced reflexes with two components in the homolateral orbicularis oculi muscle (Fig. 1A). The latency for the initial component ranged from 10 to 14 msec and that for the second component from 23 to 50 msec. Similarly, intradermal stimulation of the sole of the foot produced two reflex discharges in the ipsilateral tibialis anterior muscle (Fig. 1B). The initial component of the flexor reflex discharge had a latency of 53 to 80 msec, whereas the latency of the second component ranged from 110 to 400 msec depending on the strength of the stimulus. In this paper the short latency reflex response will be referred to as the first component and the long latency reflex response as the second component of the blink and the flexor reflex.

BLINK REFLEX There appeared to be an inverse relationship between the size of the first and the second component of the blink reflex, depending on the emotional state of the subject. Apprehension resulted in a marked increase in the amplitude of the second component of the blink reflex. On the other hand, if the subject was relaxed and allowed to stimulate his or her supraorbital nerve using a remote control push button switch, only the first component of the blink reflex was evoked (Fig. 2).

The effects of altered consciousness on the two components of the blink reflex were similar to those for the two components of the flexor reflex. As the subject went to sleep, there was at first diminution in the amplitude of the first component, which soon completely disappeared (Fig. 3). While the first component was absent in sleep, the latency of the second component was usually increased by 5 to 10 msec and its duration was prolonged. Whereas the normal duration of the second component ranges from 20 to 40 msec, in sleep it could be prolonged to...
FIG. 3. Normal subject. A-C: subject gradually going to sleep; D-F: in sleep; calibration time: 20 msec; amplitude: 200 \mu V. Details in the text. (Traces retouched.)

FIG. 4. Normal subject. In each frame lower tracing: direct M response and H reflex from gastrocnemius-soleus muscle. Upper tracing: blink reflex; A: control blink reflex and H reflex; B: in sleep; C: on arousal from sleep; calibration time: 20 msec; amplitude: 200 \mu V. Details in the text.

FIG. 5. Patient with Parkinsonism. A: control blink reflex; B: in sleep; calibration time: 20 msec; amplitude: 200 \mu V. Details in the text. (Trace retouched.)
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100 msec or more. As soon as the subject was aroused from sleep the first component could easily be evoked by the same stimulus. At the same time, the second component reverted to the shorter latency and duration recorded before the subject had gone to sleep.

Simultaneous recording of H reflex from the gastrocnemius-soleus muscle and the blink reflex from the orbicularis oculi muscle showed that the first component of the blink reflex was absent at the stage of sleep when the H reflex remained unchanged (Fig. 4).

In the two patients with Parkinson's disease there was preservation of the first component of the blink reflex in sleep. However, there was marked reduction in the amplitude of the first component and the second component showed characteristic changes of increased latency and prolonged duration (Fig. 5).

FLEXOR REFLEX Like the blink reflexes, apprehension on the part of the subject resulted in marked increase of the amplitude of the second component of the flexor reflex. However, if the subject was relaxed the same stimulus evoked only the first reflex component (Fig. 6).

The effects of altered consciousness on the two components of the flexor reflex were essentially similar to those described for the two components of the blink reflex. During sleep, electrical stimulation of the sole of the foot evoked only a long latency

Fig. 6. Normal man. In each frame lower tracing EMG from tibialis anterior muscle. Upper tracing EMG from gastrocnemius-soleus muscle. Flexor reflex in A: apprehension, and in B: relaxation. Calibration time: 100 msec; amplitude: 200 μV.

Fig. 7. Normal man. In each frame, lower tracing EMG from tibialis anterior muscle, upper tracing EMG from gastrocnemius-soleus muscle. A: normal flexor reflex; B: flexor reflex in sleep; C: flexor reflex on arousal. Calibration time: 100 msec; amplitude: 200 μV. Details in the text.
reflex discharge. However, if the subject was aroused from sleep, the same stimulus was effective in evoking both components of the flexor reflex (Fig. 7). These findings were repeatedly confirmed.

For recording single motor unit potentials, proper adjustment of the intensity of the stimulus was mandatory. Maximal stimuli tended to activate more than one motor unit, which resulted in interference between the potentials. Also it was easier to record single unit potentials from the tibialis anterior muscle near its tendinous end than from the belly of the muscle. Once the recording electrodes were properly placed and the stimulus strength adequately adjusted, the reflex response of a single potential could be repeatedly reproduced. Sometimes, however, it was impossible to record single potentials from a certain area in the muscle, the discharge in these instances consisting of two or more potentials.

**FIG. 8.** Normal man. Left: single unit potentials recorded from the first component. Latency 69, 68, and 68 msec respectively. Right: single unit potentials recorded from the second component. Latency 150, 165, and 148 msec respectively. Calibration time: 10 msec; amplitude 200 μV. Details in the text. (Traces retouched.)

Whereas the latency of the reflex potentials in the first component was relatively constant, that of the potentials recorded from the second component was rather variable (Fig. 8). Not only were the same motor units activated in the two components of the flexor reflex, but also the pattern of recruitment of these potentials was the same. When more than one unit potential was recorded in the first component, the same units were also activated in the second component. The pattern of recruitment was usually the same, although this was not always the case. Sometimes the unit activated first in the first component was second to be activated in the second component and vice versa. However, as a rule, the motor unit activated first in the second component was also the first to be activated in the first component.

**DISCUSSION**

There is a delicate central mechanism which controls the two components of the blink reflex and the flexor reflex. Apprehension results in marked increase in the amplitude of the second component. On the other hand, only the first component is evoked when the subject is relaxed and is certain that the stimulus is not going to be painful.

The central mechanism influencing the two components of the blink reflex appears to be similar to that responsible for the control of the two components of the flexor reflex. During sleep the first component of both the blink reflex and the flexor reflex is absent while the second component is preserved.

Whether or not abolition of the first component of these cutaneous reflexes in man in sleep is due to inhibition or removal of facilitation is not certain at the present time. However, there is some experimental evidence which suggests that the differential effects produced by sleep may be due to release of certain transmitter substances which block short latency paths from the flexor reflex afferents. After injection of L-DOPA (L3,4-dihydroxyphenylalanine) or 5 HT (5-hydroxytryptophane) in acute spinal cats, Lundberg and his collaborators (Andén, Jukes, Lundberg, and Vyklicky, 1964; Lundberg, 1966), showed that, while the short latency component discharge of the flexor reflex was inhibited, there then appeared an intense discharge at long latency. It was assumed that DOPA entered the noradrenergic nerve terminals, activating this pathway in the spinal cord. Recent studies in experimental animals suggest that sleep depends on the activity in the mono-aminergic system (Matsumoto, Nishisho, Suto, Sadahiro, and Miyoshi, 1968). In the light of this experimental evidence, it seems possible that inhibition of the first component of the flexor reflex may be due to activity in the mono-aminergic system which blocks the short latency paths from the flexor reflex afferents. Since the same motor units are activated in the first and the second component of the flexor reflex, the inhibitory effect produced by sleep cannot be due to post-synaptic inhibition of flexor motoneurones. This finding confirms Lundberg’s (1966) suggestion that mono-aminergic pathways act by inhibiting transmission from the flexor reflex afferents at the interneuronal level.

In the two patients with Parkinson’s disease, there was preservation of the first component of blink reflex in light sleep. If, as in the flexor reflexes, the mechanism responsible for the inhibition of the first component is mediated through mono-aminergic nerve endings, it is not surprising to find this effect in these patients. There is evidence of marked depletion
of dopamine in the basal ganglia of patients with Parkinson’s disease (Carlsson, 1964; Kurland, 1967). Rushworth (1962) found preservation of both components of the blink reflex in light sleep and in patients heavily sedated with chlorpromazine. In patients sedated with chlorpromazine, preservation of the first component of the blink reflex may be due to the adrenergic blocking effect of this drug. However, preservation of both components of the blink reflex in light sleep is difficult to explain, unless these observations were made on subjects who were sedated with similar drugs.

Since the first component of the blink reflex was considered to be a proprioceptive or myotatic reflex (Kugelberg, 1952; Rushworth, 1962; Gandiglio and Fra, 1967), it is interesting to note that H reflex can be easily evoked in sleep at a stage when the first component of the blink reflex is absent. This is further evidence against the hypothesis that the first component of the blink reflex is a myotatic or proprioceptive reflex. Existing evidence, in fact, suggests that the first components of the blink and the flexor reflex are similar, as are the second components, and that all are cutaneous reflexes.

The above experiments have revealed the intricacy of the neuronal connections in the central nervous system which control the two components of the same reflex. Although the function of the second component of the cutaneous reflex is withdrawal, that of the first component has remained obscure (Brooks and Fuortes, 1952; Shahani and Young, 1968a). Lundberg (1966) in his review on the integration in reflex pathway, suggests that the late effects evoked from the flexor reflex afferents are inhibited at the interneuronal level by the activity in the short latency pathway. It is probable then that the first component in the human cutaneous reflexes acts as a modulating force on the second component, resulting in a smooth, purposeful withdrawal movement.

**SUMMARY**

The central mechanism responsible for the differential control of the two components of the blink reflex and the flexor reflex is remarkably similar. During sleep there is abolition of the first component of these reflexes in man. Although the first component of the blink reflex is absent during sleep in normal subjects, this is not observed in patients with Parkinson’s disease. The possible role played by the mono-aminergic system in the differential control of human reflexes with a double component has been discussed.

I take this opportunity to thank Professor W. Ritchie Russell for his constant encouragement and advice. I thank Dr. G. Rushworth for giving me the laboratory facilities and for his useful criticism. I am grateful to Dr. P. B. C. Matthews and Dr. D. G. Lawrence for their valuable discussion.

**REFERENCES**


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*J Neurol Neurosurg Psychiatry* 1968 31: 574-579
doi: 10.1136/jnnp.31.6.574

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