Intracranial pressure in the normal monkey while awake and asleep

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Intracranial pressure (ICP) was recorded continuously by telemetry in seven normal monkeys trained to eat, sleep, and live in a primate chair. Electroencephalography, electromyography, and blood pressure were also measured by conventional means. During wakefulness and all stages of sleep except desynchronized sleep, the ICP record showed small short-term variations in pressure. However, during desynchronized sleep, the mean ICP rose on the average to 170 ± 6 mm H2O above the ICP levels in the other states of sleep, and the pulsation pressure variation increased by a factor of three. The episodes occurred 10 ± 2 times during the night and lasted for 6.8 ± 1.4 minutes, during which the average systemic blood pressure decreased by 19 ± 1.6 mm Hg. These ICP waves occurring during desynchronized sleep resemble the plateau waves described by Lundberg, but are of smaller magnitude and they appear to be a normal characteristic of sleep in the macaque monkey. Bilateral sympathectomy of the superior cervical ganglia in four of the monkeys did not alter significantly the duration, amplitude, or frequency of occurrence of the ICP waves during desynchronized sleep.

KEY WORDS • telemetry • plateau wave • REM sleep • intracranial pressure • monkey

The increased use of instrumentation for the continuous recording of intracranial pressure (ICP) has revealed complex temporal patterns of ICP in some neurological disorders. Lundberg found spontaneous, episodic ICP waves in patients with increased ICP secondary to expanding tumors. He identified and defined three categories of ICP waves: A waves (now called plateau waves), B waves, and C waves. The plateau waves are characterized by a rapid rise in ICP to values of 500 to 1000 mm H2O, and remain constant at the high level for 5 to 20 minutes, and then rapidly fall to the original pressure. The B waves are characterized by pulses of pressure ranging between 50 and 500 mm H2O which occur at a rate of about one per minute.

The plateau waves and B waves are said to be associated with pathological conditions. For example, Cooper and Hulme have observed these waves in patients with intracranial tumors, normal-pressure hydrocephalus, and intracerebral hemorrhage. These patients showed large intermittent rises in ICP, sometimes during light sleep, but more frequently during sleep with rapid eye movement (REM sleep). Chawla, et al., and also Symon, et al., have demonstrated the presence of plateau waves in normal-pressure hydrocephalus. The latter workers reported two patients with relatively little variation in ICP during part of the night. In their other patients, large plateau waves and B waves were present, and these waves were used as a factor to decide whether or not a shunt should be implanted. Di Rocco, et al., Crockard, et al., and Maira, et al., have used the presence of A and B waves as an aid for deciding whether or not to perform shunting procedures in patients with normal-pressure hydrocephalus. Pierre-Kahn, et al., and Di Rocco, et al., using continuous ICP recording have observed the presence of plateau waves during REM sleep in hydrocephalic children. Many of the children in another study by Pierre-Kahn, et al., were borderline cases or had arrested hydrocephalus. These reports leave open the question about the form of the ICP profile during various stages of sleep in the normal individual. In a recent paper, Martin offers evidence that the B waves may be a feature of normal ICP.

The effect of REM sleep on the ICP in the normal individual can be inferred from studies of cerebral blood flow (CBF) in humans and animals. In the cat,
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Fig. 1. Recordings of intracranial pressure (ICP), arterial blood pressure (BP), electroencephalographic (EEG) activity, and cervical electromyogram (EMG) in the awake, undrugged monkey. The ICP was at a level of 90 mm H$_2$O with smaller variations in pressure due to the heart beat and respiration.

there is a sharp rise in CBF during REM sleep. The rise relative to slow-wave sleep has been reported as 60% to 80% and 30% to 50%. In measurements in man, Meyer and Toyoda found a rise of 50%. One would, therefore, expect a rise in ICP during REM sleep. Ryder, et al., have shown that an increase in CBF is accompanied by a rise in ICP. This was also shown by Seylaz, et al., in a study of 10 patients who were being prepared for endarterectomy for carotid stenosis. These patients were equipped with flow meters and ICP sensors. During REM sleep there were increases in ICP as well as in CBF. These studies suggest that increased ICP should be expected during REM sleep.

Because of the increased use of 24-hour recordings in patients, and because insufficient information exists concerning the temporal behavior of ICP in the normal mammal during the various stages of sleep, we undertook a study of the ICP profile in normal, undrugged monkeys during sleep and wakefulness.

Materials and Methods

Seven monkeys were used in these experiments. Each monkey from the primate colony was acclimated to a primate chair for approximately 1 week. After acclimatization, a burr hole was placed in the parietal area of the skull while the animal was anesthetized with Nembutal (pentobarbital). An intracranial pressure-sensing device described by Walker, et al., was implanted in the burr hole epidurally, and secured in place with skull screws and covered with acrylic cement. At the same time, electroencephalography (EEG) and electromyography (EMG) electrodes were implanted in the skull and neck muscles, respectively. The leads were brought out to an electronic plug which was secured to the skull with dental acrylic cement. At the same time, a prosthetic halo was installed to restrain the head during recordings of sleep cycles. The monkey's head was restrained for the night-time recording sessions by clamping the halo to a head-restraining block. Throughout the night the EEG, EMG, and ICP were recorded as the monkey passed through his normal sleep cycles. Each monkey had 2 days of baseline ICP recording in addition to EEG and EMG recordings.

Four of the monkeys had an indwelling arterial catheter placed in the brachial artery for recording the systemic blood pressure. The catheter was connected to a Statham pressure transducer for the continuous recording of blood pressure. Heparin was used in the catheter to prevent blockage. All the abovementioned recordings were made with a Grass Model 6 EEG machine† operating at a chart speed of 1.5 mm/sec.

In four monkeys the superior cervical ganglia were totally removed bilaterally after baseline recorded sleep cycles of ICP and arterial blood pressure were obtained. The presence of bilateral ptosis and miosis confirmed that an interruption of the cervical sympathetic chain was achieved. Following the sympathectomy, three to four nights of recordings were made to determine if during sleep there were changes in the temporal profiles of the ICP, EEG, EMG, and arterial blood pressure.

Results

In all seven monkeys, ICP was steady during wakefulness except for transient changes caused by movement, heart beat, and respiration (Fig. 1). The ICP during slow-wave sleep, including stages S1, S2, S3, and S4, as described by Rechtschaften and Kales showed no significant variation except for small pres-

*Statham pressure transducer manufactured by Statham Instruments Co., 2230 Statham Boulevard, Oxnard, California.
†Grass Model 6 EEG machine manufactured by Gradd Instrument Co., Quincy, Massachusetts.
sure changes secondary to heart pulsation and respiration (Fig. 2). However during all desynchronized sleep episodes ICP rose, on the average, to 170.6 ± 6.04 mm H₂O above the pressure levels found in other sleep states. The ICP returned abruptly to the original level at the end of a desynchronized sleep period (Fig. 3). Desynchronized sleep episodes were defined as periods in the sleep cycle in which the amplitude of the EEG potentials had low values and EMG activity decreased markedly. The onset of the pressure waves was closely related in time to the onset of decreased EMG activity and the appearance of the low voltage EEG (Fig. 2). The ICP during the onset rose gradually over a period of 30 to 60 seconds, then reached a more or less constant level of pressure lasting between 2 and 12 minutes.

The cessation of the ICP wave was abrupt. The pressure returned to the original ICP in 5 to 10 seconds at the end of the desynchronized sleep epoch (Fig. 3). During the period of the ICP wave and desynchronized sleep which lasted on the average 6.8 ± 1.38 minutes, the systemic blood pressure decreased on the average by 19.1 ± 1.55 mm Hg. The rate of occurrence of the ICP waves and the concurrent desynchronized sleep states was in these experiments 10.2 ± 2.04 occurrences per night.

Table 1 shows the effect of cervical sympathectomy on amplitude, duration, and frequency of occurrence of the ICP waves during the night as well as the concurrent decrease in systemic blood pressure. The results indicate that there are no significant changes (p > 5) in these parameters as a result of bilateral sympathectomy.

Discussion

The results of our study support the belief that raised ICP during REM sleep is a normal
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### TABLE 1

**Characteristics of intracranial pressure (ICP) and blood pressure (BP) changes during rapid eye movement (REM) sleep**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>After Sympathectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean amplitude of ICP wave (mm H₂O)</td>
<td>170.6 ± 6.04</td>
<td>166.8 ± 7.27</td>
</tr>
<tr>
<td>no. episodes/night</td>
<td>10.2 ± 2.04</td>
<td>7.9 ± 1.23</td>
</tr>
<tr>
<td>duration of ICP wave (mins)</td>
<td>6.8 ± 1.38</td>
<td>7.2 ± 0.38</td>
</tr>
<tr>
<td>decrease in BP during ICP wave (mm Hg)</td>
<td>19.1 ± 1.55</td>
<td>15.5 ± 1.66</td>
</tr>
<tr>
<td>No. of Samples</td>
<td>99</td>
<td>69</td>
</tr>
<tr>
<td>nights</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>nights</td>
<td>101</td>
<td>69</td>
</tr>
</tbody>
</table>

physiological occurrence. The raised ICP is in the form of a pressure wave with the shape and characteristics of the A wave described by Lundberg, but the ICP wave amplitude is roughly double the steady-state pressure, whereas the A wave defined by Lundberg has an amplitude that is five to 10 times what would be considered normal ICP. The speed and magnitude of the pressure change in the ICP wave occurring during REM sleep suggests that the effect is caused by vasodilation of the cerebral arteries. The resulting increase in CBF secondary to the vasodilation and the increased volume of blood in the intracranial space during REM sleep may account for the observed ICP waves. In the normal individual, the ICP reserve will allow the ICP to approximately double. However, this spatial compensating reserve to accommodate the increased blood volume is brought about by expression of fluid from the intracranial space, and most of the fluid loss is accounted for by compression of the cerebral venous system. In a number of neurological disease states the ICP is initially high, thus using up much of the reserve space. Therefore, a small rise in blood volume when the reserve is exhausted will cause a large increase in the ICP. This effect can also be predicted from the fact that the ICP rises exponentially as an increased volume of CSF is infused into the cranial cavity. Under these circumstances, during REM sleep the patient who has little ICP reserve could have, rather than a doubling of ICP, an ICP in the region of 500 to 1000 mm H₂O, that is, the classical plateau wave described by Lundberg. In such cases, the conditions exist for cerebrovascular decompensation, in which these dangerous levels of ICP can depress nervous function.

We explored the possibility that the blood flow in the cerebral arterial system is controlled by neurons in the superior cervical ganglion. Our data did not support this concept. The mode of control over the cerebral arterial vasomotor system has yet to be established conclusively.

The results of our studies indicate that, in neurological patients, continuous recording during the sleep states may be useful for assessing the patients' ICP reserve. A rise in ICP should be expected during REM sleep, and the magnitude of this rise will be a measure of the intracranial compensatory reserve left to the patient. More studies with the use of 24-hour ICP recordings in patients are required to establish what levels of ICP waves in REM sleep are to be considered normal, and what levels are indicative of pathology.

### References

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