Intracranial pressure and related phenomena during sleep¹

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In patients with raised intracranial pressure, headache, vomiting, and visual disturbance are often at their worst on first awakening and clinicians are familiar with the deterioration which sometimes occurs during the night. This suggests that in such patients further increases of pressure may occur during sleep. It therefore seems pertinent to investigate the alterations in intracranial dynamics which occur during sleep.

A number of investigators have recorded spontaneous variations in intracranial pressure superimposed on the main resting level in patients with intracranial lesions (Guillaume and Janny, 1951; Lundberg, 1960; Ingvar and Lundberg, 1961). Lundberg and his colleagues have identified several types of ventricular fluid pressure waves. During some of these, especially the large 'plateau' waves, intracranial pressure approached or exceeded the diastolic blood pressure and they were considered to be indicative of a serious disturbance of intracranial vascular function. Our observation that pressure changes of this nature and other phenomena are closely associated with certain phases of sleep forms the basis for this communication.

METHODS

Pressure transducers were inserted by a method already described (Hulme and Cooper, 1966). At the same time gold electrodes (4 mm. long, 150 μ diameter) and thermistors (less than 0.5 mm. diameter) were placed in the subdural space.

One or more of the electrodes were used to measure oxygen availability by a polarographic method (Clark, Misrahy, and Fox, 1958; Meyer and Portnoy, 1959; Cooper, 1963). In the present study the bare electrodes were polarized with a 1 volt negative potential with respect to a silver/silver chloride electrode on the scalp. The mean current flowing through each electrode was 'backed off' and the changes of oxygen availability (O_2a) were displayed on a polygraphic recorder.

The electrical impedance (electroplethysmograph) of

two electrodes in the subdural space is primarily determined by the thickness of the layer of cerebrospinal fluid which is of low impedance compared with blood and other tissue (Robinson and Tompkins, 1964; Porter, Adey, and Kado, 1964). The impedance rises if brain volume increases, as in generalized cerebral vasodilatation (Moskalenko, Cooper, Crow, and Walter, 1964). In these studies the impedance was measured at 1 kc/s or 20 kc/s.

The temperature of the subdural thermistor beads was raised about 1.5°C above blood temperature by direct current and the change of temperature as measured by the resistance used to indicate blood flow.

Heart rate was determined by expressing the beat to beat (E.C.G.) interval as an equivalent heart rate, and displayed as a deviation from a chosen norm. Respiration was indicated by chest expansion. Blood pressures have been taken only occasionally during sleep recordings because of the disturbance caused by inflation of the cuff. The E.E.G. was recorded from scalp electrodes; we have used the classification of Dement and Kleitman (1957) to distinguish the stages of sleep.

RESULTS

Recordings of intracranial pressure during many nights have been obtained from 24 patients in whom continuous monitoring of intracranial pressure was clinically indicated. All these records showed changes of intracranial pressure similar to the plateau waves described by Lundberg. Polygraphic recordings during sleep were obtained from 15 patients, (13 cases of intracranial tumour, one of so-called benign intracranial hypertension, and one of spontaneous intracerebral haemorrhage). Figure 1 shows a polygraphic recording of a plateau wave in a 55-year-old man who had an infiltrating glioma in the left cerebral hemisphere. Intracranial pressure, shown in channels 3 and 4 at low and high gains respectively, rose gradually over a period of about five minutes to a peak level some 600 mm. of water above the mean resting pressure of 400 mm., and fell abruptly in less than one minute to the previous level. The amplitude of the transmitted cardiac pulse

¹Based on a paper presented at the 73rd meeting of the Society of British Neurological Surgeons, 27 May 1966.

FIG. 1. Polygraphic recording of plateau wave (E.P.G. = electrical impedance; I.C.P. = intracranial pressure; O_{2a} = oxygen availability).

FIG. 2. Plateau wave accompanied by rapid eye movements and change in pattern of E.E.G. There was a rise of impedance (E.P.G.) and the low frequency fluctuations of available oxygen (O_{2a}) disappeared at the height of the pressure wave. During the periods of high pressure there were sustained increases of heart rate and a doubling of the respiration rate.

FIG. 3. All-night recordings of changes of intracranial pressure before, during, and after a course of deep x-ray therapy. Note increase in frequency and duration of pressure waves during treatment.

wave increased fourfold as the pressure rose. The increase of pressure was preceded by an increase of impedance (channel 2), indicating an increase of brain volume. There was a fall in the level of available oxygen and the spontaneous low frequency oscillations disappeared (channels 5 and 6). An increase in heart rate and depth of respiration commenced about 30 seconds before the end of the pressure wave and continued for about two minutes (channels 7 and 8). As the pressure fell there was a marked increase in the level of available oxygen and the oscillations returned. There was a rapid fall of impedance. The E.E.G. throughout this pressure wave showed low-amplitude fast activity.

Plateau waves were rarely seen when the patients were awake, or during periods of deep sleep characterized by widespread high-amplitude, low-frequency activity in the E.E.G. (stage IV sleep). They occurred most frequently on transition from a phase of deep (stage IV) sleep to paradoxical sleep as shown by desynchronization of the E.E.G. and the appearance of rapid eye movements (Fig. 2).

The frequency, amplitude, and duration of

pressure waves recorded during sleep in any individual patient tended to increase as the clinical condition deteriorated (Fig. 3).

In patients whose mean resting pressure was less than 400 mm. of water the waves usually occurred in groups of two or three, with a few minutes' interval between each and periods of one or two hours between the groups. The amplitude of the waves was roughly proportional to the mean resting pressure, and small waves were recorded even when the intracranial pressure was low (Fig. 4). Recordings from patients with mean pressures in excess of 500 mm. of water showed large plateau waves during light sleep (stage II), and often these patients awakened before entering the deep phase (stage IV) of sleep as indicated by the E.E.G. (Fig. 5).

Peak values for intracranial pressure of 1,500 mm. water were recorded for long periods during light sleep in a 42-year-old woman who had an infiltrating glioma spreading through the corpus callosum (Fig. 6). In this patient the heart rate was much more constant than in the other patients and the collapse of the pressure waves much slower.

FIG. 4. Low-amplitude waves were observed in a patient whose intracranial pressure was low. The whole group of pressure waves occurred during a period of paradoxical sleep following deep sleep. The pressure waves ceased when the patient went into stage III sleep characterized by high and low frequency E.E.G. activity (upper traces). The changes of pressure were accompanied by changes of heart rate and respiration.

FIG. 5. Record showing a rise of pressure occurring shortly after the patient went to sleep. There was a marked fall in available oxygen and flow and an increase in depth of respiration for the period of the pressure wave. For most of this wave the heart rate showed only small changes. Later in the night there were small plateau waves each associated with changes of heart rate, E.E.G., and available oxygen. At the end of the record the pressure increased and was relieved by opening a ventricular drain. There was no marked difference between the blood pressure during the pressure wave and when the drain was open. This patient had a neurilemmoma of the acoustic nerve.

FIG. 6. Long periods of high pressure were recorded during periods of light sleep (stage II) with decreases of flow and available oxygen and increases of impedance. The heart rate during the second wave when peak values of 1,500 mm. of water were recorded was steady at 80 beats/min. The respiration did not change significantly.

DISCUSSION

Despite differences in individual pathology the many similarities in the records suggest that certain general principles apply. The relative abundance of large pressure waves in recordings during sleep, in contrast to those taken in the waking state, implies that in some patients intracranial function is seriously disturbed during sleep.

It is generally agreed that intracranial pressure begins to rise above the normal range when the magnitude and rapidity of an expanding process exceeds the available compensation from distension of covering membranes or displacement of other contents of the craniovertebral cavity. Any further acute increment, such as the swelling of the brain which accompanies cerebral vasodilatation, will cause an additional sharp increase of intracranial pressure even though the actual changes in volume may be very small (Evans, Espey, Kristoff, Kimbell, and Ryder, 1951; Langfitt, Kassell, and Weinstein,

1965; Langfitt and Kassell, 1966). During ventriculography we have observed that the injection of 3 ml. of air can increase the pressure from 400 mm. to 800 mm. of water.

Several investigators have demonstrated that when intracranial pressure rises above a critical level, estimated at between 350 and 500 mm. of water, total cerebral blood flow becomes significantly diminished (Kety, Shenkin, and Schmidt, 1948; Ferris, 1941). In the majority of patients in this series the resting intracranial pressure was over 400 mm. of water, and we have observed decrease of blood flow and available oxygen during each high pressure wave. The primary cause of pressure waves appears to be swelling of the brain (as shown by the increase of electrical impedance) caused by vasodilatation due to accumulation of CO_2 . The disappearance of the spontaneous fluctuations, which are believed to be caused by local variations in vascular tone, supports this hypothesis, since these are known to cease if cortical pCO_2 is increased (Clark *et al.*, 1958;

Cooper, Crow, Walter, and Winter, 1966). The paradoxical effect of vasodilatation in these conditions is to cause a reduction in blood flow owing to the rise in intracranial pressure and vascular resistance. This effect may be offset to some extent if it is accompanied by a rise in systemic blood pressure, but in these investigations we have found no close correlation between intracranial and blood pressures. The absence of an increase in blood pressure is probably related to the chronicity of the intracranial hypertension in the patients examined. Experimental and clinical observations indicate that the pressor response is a feature of acute increase in intracranial pressure to levels in the region of the diastolic blood pressure, but is often absent with more gradual increases (Cushing 1901, 1902; Browder and Meyers, 1938; Evans *et al.*, 1951; Greenfield and Tindall, 1965; Langfitt *et al.*, 1965).

At high levels of intracranial pressure the reduction in blood flow occurs mainly in the non-pulsatile component (Greenfield and Tindall, 1965), so that cerebral circulation becomes increasingly dependent on the pulsatile flow accompanying each systolic wave. A tachycardia, even without a rise in systemic blood pressure would therefore increase the total blood flow through the brain and reduce cerebral $p\text{CO}_2$. We have noted that the fall in pressure at the end of a wave is regularly preceded by a tachycardia and often by increased depth of respiration. We believe that these autonomic changes are initiated by stimulation of the medullary centres by the hypoxia or hypercapnia, and this may be the mechanism by which a pressure wave is terminated. As the mean pressure rises, however, this protective mechanism becomes less effective and ultimately fails at the stage of complete vasomotor paralysis postulated by Langfitt and his associates (Langfitt *et al.*, 1965; Langfitt and Kassell, 1966).

The increased incidence of pressure waves during sleep is probably related to the metabolic activity of the brain. Recent work on animals indicates that large increases of metabolic rate (above that of the normal alert state) occur during the paradoxical (rapid eye movement) stage of sleep (Kanzow, 1965; Kawamura and Sawyer, 1965; Kety, 1965; Rechtschaffen, Cornwell, and Zimmerman, 1966). Brebbia and Altshuler (1965) have shown that oxygen consumption in man is greatest in the paradoxical stage of sleep, least in stages III and IV (deep sleep), and intermediate in stage II. Although these measurements are of whole body consumption of oxygen it is probable that the changes of oxygen consumption are due to increases of cerebral metabolic rate (since the musculature is notably relaxed during paradoxical sleep) and support the hypothesis

that the intracranial pressure waves are due to increases of cerebral metabolic rate above that of the alert state.

Since the cerebral circulation is seriously compromised during each high pressure wave, it must be considered that repeated episodes of relative ischaemia and hypoxia occur and that these may have a cumulative effect on neurones, eventually causing irreversible damage.

The findings in this investigation provide a physiological explanation for the clinical facts as stated in the opening paragraph and underline the urgency of measures to relieve intracranial pressure when this approaches the critical range.

SUMMARY

Symptoms of intracranial hypertension are commonly accentuated during sleep. Continuous monitoring of intracranial pressure during sleep in 15 patients has shown that large intermittent increases of pressure occur. These are most frequent during the paradoxical stage of sleep but may also occur during light sleep (stage II) in patients with a high mean resting intracranial pressure. These increases are accompanied by reduction of cortical blood flow and available oxygen. It is suggested that they are caused by intermittent cerebral vasodilatation associated with an increased metabolic rate during certain stages of sleep.

The authors wish to express their appreciation for the assistance given by the Research Grants Committee of the United Bristol Hospitals and the South Western Regional Hospital Board and the W. Clement and Jessie V. Stone Foundation. Mr. W. J. Warren provided invaluable technical assistance.

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