Polygraphic sleep study in craniopagus twins (Where is the sleep transmitter?)

H. G. LENARD AND F. J. SCHULTE

*From the Department of Pediatrics, University of Göttingen,
Göttingen, West Germany*

SUMMARY By means of polygraphic recordings complete independence of the sequence of sleeping and waking and of the two sleep states (REM and NREM) could be demonstrated in twins extensively conjoined at the skulls. Functionally important connections in the circulation of the two babies were found during subsequent preoperative investigations. These observations are at variance with the hypothesis of an extraneuronal humoral sleep-inducing factor based on crossed-circulation experiments in animals; moreover they raise a new question about the transportation of the sleep-regulating biogenic amines.

The union in craniopagus twins may be of any extent from a small superficial connection of two apparently complete individuals to a malformation resulting in the impression of a single head with two faces. Whether surgical separation is a possibility or not depends primarily on the extent and intimacy of the union. Before the necessary meticulous information on anatomical details is obtained in preoperative diagnosis, the crucial question has to be answered whether the twins are two complete individuals with two separate brains or not.

We could quickly demonstrate two independently functioning brains in twins extensively conjoined at the skull by polygraphic registration of their behaviour, especially of their sleep states and stages.

Crossed circulation experiments in animals have led to the postulation of an extraneuronal humoral sleep-inducing factor. Our results with polygraphic and further diagnostic procedures do not appear to be consistent with such a hypothesis.

CASE HISTORY

A pair of female craniopagus twins was delivered by caesarian section, and transferred to our hospital at the age of three days. It could not unequivocally be established whether their gestational age was 36 or 40 weeks. The combined weight of the twins was

4,200 g, one (twin 1) being slightly larger than the other (twin 2). Twin 1 had, as additional malformations, club feet and an atrial septal defect. Twin 2 showed club feet, a coloboma of the right upper eyelid, a flat broad nose with a medial sulcus, and an incompletely developed os sphenoidale. The skull of twin 2 appeared microcephalic, irregularly deformed in its lateral portions, and telescoping with its parieto-occipital parts into the right parietal portion of the skull of twin 1. From the clinical aspect alone it was uncertain whether twin 2 would have a complete brain (Fig. 1).

A lumbar pneumoencephalogram was performed in twin 1 and 30 minutes later in twin 2. Twin 1 showed a cyst of the septum pellucidum and a deformation and enlargement of the right lateral ventricle. In twin 2 the air collected in the subarachnoid space and did not enter the ventricular system. No air passed from one infant into the other. Protein values in the cerebrospinal fluid (CSF) were very similar in both infants (111 and 114 mg/100 ml.).

Cerebral arteriograms, carried out from the aortic arch after catheterization of the femoral artery, showed in both infants a deformed but complete arterial system and an arterial connection with shunting from twin 1 into twin 2 (Fig. 2). No shunt could be demonstrated in the other direction (Fig. 3). Small venous connections were found during sinography in twin 1 (Fig. 4).

After injection of 4 μ Ci of 125 I-hippuran into a cubital vein of twin 1, 50% of the radioactive substance was found in the venous blood of twin 2.

FIG. 1. The smaller twin 2 is on the left.

14 minutes later. When anaesthesia was performed for angiography in twin 1 with small amounts of NO_2 and halothane, twin 2 reached the same stages of anaesthesia at the same time as twin 1. Renal excretion was carried out exclusively by twin 1; twin 2 passed almost no urine and had a negative intravenous pyelogram in spite of a morphologically normal urinary system at necropsy. The results from haematological and biochemical investigations of the blood were, if not identical, always very similar in the two babies.

The twins underwent a short period of respiratory difficulties immediately after birth. They were lively and fed well thereafter. From their behaviour and their reactions towards the environment they appeared to be completely different personalities. During angiography on day 12 ventricular fibrillation occurred in twin 1 which could be stopped by electrical defibrillation. In the following days twin 1 had recurrent spells of cardiorespiratory problems. Probably because of the doubled task of renal excretion, there was a continuous cardiac enlargement in twin 1. Decubital ulcers developed at the

skulls despite all precautions because the babies could lie in one position only. These increasing difficulties led to the attempt of a surgical separation, with the aim of saving twin 1. The twins were now aged 21 days. The twins died of cardiac arrest during the first stages of anaesthesia before the operation.

POLYGRAPHIC INVESTIGATIONS Polygraphic recordings on the fourth and 11th day of life were carried out with an 8-channel Offner type T dynograph. Silver-silver chloride electrodes were fixed on the skulls with gauze strips dipped into collodion. The electroencephalograph (EEG) was recorded bipolarly from both twins from positions corresponding roughly to F_3-C_3 and F_4-C_4 . Horizontal eye movements and respiration were recorded simultaneously from each twin.

The EEG pattern, with a 'spiky' *tracé alternant* during non-rapid eye movement (NREM) sleep, corresponded to a gestational age of 36 weeks. In twin 2 the EEG showed some abnormal high amplitude sharp waves. Spindles, abnormal for the age, with a frequency of 16–18 Hz, were present in

FIG. 2. Cerebral angiography in twin 1. Arterial connections reaching into the brain of twin 2.

the EEG of both babies. Both babies had periodic respiration for long periods and irregular respiration prevailed even during NREM sleep. The eye movements appeared to be normal in number and distribution.

The sequence of the behavioural states and the sleep cycles was normal for each twin. Longer rapid eye movement (REM) epochs (with low amplitude continuous EEG and with rapid eye movements in the oculogram) alternated with shorter NREM epochs (classified by the *tracé alternant* pattern in the EEG and the absence of eye movements); wakefulness occurred mainly before feeding time. There was, however, a complete independence of wakefulness and sleep and of the two sleep states in the two babies. One twin could be awake or even moving and crying, while the other one continued to stay in either sleep state. Figures 5 to 7 give examples from the original records. The course of the sleep states in the two polygrams is shown in Fig. 8.

DISCUSSION

In several reports on craniopagus twins independent EEG activity is listed as evidence for the

presence of independent brains (Grossman, Sugar, Greeley, and Sadove, 1953; Franklin, Tomkinson, and Williams, 1958; O'Connell, 1964; Wolfowitz, Kerr, Levin, Walker, and Vetten, 1968). It may, however, not always be easy to ascertain the degree of independence of the brain waves of conjoined twins. In the awake state or during REM sleep the EEG over two hemispheres of one individual may appear as independent as that of normal identical twins. This independence becomes obvious during NREM sleep when the bursts of the *tracé alternant* pattern occur asynchronously, and more so when the two individuals are in different behavioural states during the recording. The latter case can be conveniently and accurately demonstrated by means of a polygraphic recording. Besides proving independence of cortical activity, this proves the presence of two brains with complete neuronal systems for the complex regulation of the sleep-waking cycles and of the sleep stages.

FIG. 3. Cerebral angiography in twin 2. A large parieto-occipital portion of her brain is lying in the posterior fossa of twin 1. No shunting demonstrable.

Besides these diagnostic aspects, the results of our investigations have some theoretical implications concerning a possible humoral regulation of the sleep states and cycles. In crossed-circulation experiments in animals it was found that sleep, indicated by EEG synchronization, occurred also in the recipient animal after thalamic stimulation in the donor animal (Kornmüller, Lux, Winkel, and Klee, 1961; Monnier, Koller, and Graber, 1963; Monnier and Hösli, 1964 and 1965; Monnier and Hatt, 1971). The concept of a sleep-inducing extraneuronal humoral factor put forward by these authors has regained great importance during recent years when the role of biogenic amines for the regulation of sleep has become apparent (Jouvet, 1966; Koella, 1970). Without meaning to doubt the importance of biogenic amines for the regulation of sleep, we find it difficult to accept the relevance of the crossed-circulation experiments for the condition of normal sleep. Robertson (1953), Baldwin and Dekaban (1958), O'Connell (1964;

1968), together with Franklin *et al.* (1958) and Wolfowitz *et al.* (1968), have observed in six pairs of craniopagus twins independence of sleeping and waking in spite of extensive connections in the circulation of the babies. In two of these cases even a continuity of brain substance was found at operation. In ours, in addition to independence of sleep and wakefulness, independent alternation between REM and NREM sleep could be shown in the presence of functionally important connections in the circulation. An exchange of more than half of the blood volume occurred between the twins within 14 minutes, which is still within the range of time that the hypothetical humoral transmitter in crossed-circulation studies needed to become effective. It is possible, of course, that EEG synchronization does not constitute an analogue of slow wave or NREM sleep (Mandell, Spooner, and Brunet, 1969) and that sleep, induced by thalamic stimulation, is a state essentially different from natural sleep.

FIG. 4. Sinography in twin 1. A small vessel drains into twin 2.

FIG. 5. Polygraphic recording. Twin 2 in NREM sleep (regular respiration, no eye movements, tracé alternant in the EEG), twin 1 in REM sleep (irregular respiration, slow and rapid eye movements, low amplitude continuous EEG).

Baby II (17days old)

RESP.

EOG

EEG $F_4 - C_4$ EEG $F_3 - C_3$

Baby I

RESP.

EOG

EEG $F_4 - C_4$ EEG $F_3 - C_3$ 50 μ V
1 sec

FIG. 6. Polygraphic recording. Twin 2 in REM sleep, twin 1 in NREM sleep.

Baby II (17days old)

RESP.

EOG

EEG $F_4 - C_4$ EEG $F_3 - C_3$

Baby I

RESP.

EOG

EEG $F_4 - C_4$ EEG $F_3 - C_3$ 50 μ V
1 sec

FIG. 7. Polygraphic recording. Twin 2 in NREM sleep, twin 1 crying.

FIG. 8. Sequence of behavioural states during two polygraphic recordings. Alternation of wakefulness and sleep, and of the two sleep stages (REM and NREM) occurs independently in the two babies.

Concerning the monoaminergic regulation of natural sleep, the findings in the 'natural' experiment of craniopagus twins raise the question of how serotonin and noradrenaline are transported. Apparently this does not occur via the cerebral circulation. A mediation by the CSF could be possible. However, an argument against this assumption is provided by the first case of O'Connell (1964) where a connection of the two ventricular systems was shown during pneumoencephalography. We could not demonstrate an actual continuity of the CSF spaces of our twins, but the separation of the two brains by thin pia-arachnoid membranes only and the almost identical composition of the CSF of the two babies pointed to a very close connection. Thus sleep studies in craniopagus twins add another presently unanswered question to the theory of humoral sleep-inducing mechanisms.

REFERENCES

- Baldwin, M., and Dekaban, A. (1958). The surgical separation of Siamese twins conjoined by the heads (cephalopagus frontalis) followed by normal development. *Journal of Neurology, Neurosurgery, and Psychiatry*, **21**, 195-202.
- Franklin, A. W., Tomkinson, J. S., and Williams, E. R. (1958). A triplet pregnancy with craniopagus twins. *Lancet*, **2**, 683-685.
- Grossman, H. J., Sugar, O., Greeley, P. W., and Sadove, M. S. (1953). Surgical separation in craniopagus. *Journal of the American Medical Association*, **153**, 201-207.
- Jouvet, M. (1966). Sommeil et monoamines. *Bulletin der Schweizerischen Akademie der medizinischen Wissenschaften*, **22**, 287-305.
- Koella, W. P. (1970). Serotonin oder Somnotonin? *Schweizerische medizinische Wochenschrift*, **100**, 357-364.
- Kornmüller, A. E., Lux, H. D., Winkel, K., and Klee, M. (1961). Neurohumoral ausgelöste Schlafzustände an Tieren mit gekreuztem Kreislauf unter der Kontrolle von EEG-Ableitungen. *Naturwissenschaften*, **48**, 503-505.
- Mandell, A. J., Spooner, C. E., and Brunet, D. (1969). Whither the 'sleep transmitter'. *Biological Psychiatry*, **1**, 13-30.
- Monnier, M., and Hatt, A. M. (1971). Humoral transmission of sleep. 5. New evidence from production of sleep dialysis. *Pflügers Archiv. European Journal of Physiology*, **329**, 231-243.
- Monnier, M., and Hösl, L. (1964). Dialysis of sleep and waking factors in blood of the rabbit. *Science*, **146**, 796-797.
- Monnier, M., and Hösl, L. (1965). Humoral transmission of sleep and wakefulness. *Pflügers Archiv. European Journal of Physiology*, **282**, 60-75.
- Monnier, M., Koller, T., and Graber, S. (1963). Humoral influences of induced sleep and arousal upon electrical brain activity of animals with crossed circulation. *Experimental Neurology*, **8**, 264-277.
- O'Connell, J. E. A. (1964). Surgical separation of two pairs of craniopagus twins. *British Medical Journal*, **1**, 1333-1336.
- O'Connell, J. E. A. (1968). An operation to separate craniopagus twins. *British Journal of Surgery*, **55**, 841-850.
- Robertson, E. G. (1953). Craniopagus parietalis. Report of a case. *Archives of Neurology and Psychiatry*, **70**, 189-205.
- Wolfowitz, J., Kerr, E. M., Levin, S. E., Walker, D. H., and Vetten, K. B. (1968). Separation of craniopagus twins. *South African Medical Journal*, **42**, 412-424.