Technical Papers

The Thalamus and Temporal Orientation

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Disturbances of temporal orientation have been observed chiefly in conditions causing diffuse impairment of cerebral function, sometimes in diseases affecting the parieto-occipital region or large areas of the brainstem. We had occasion to observe such disturbances in the initial stages after dorsomedial thalamotomy (*1*). Although these symptoms were only transitory, they seem of sufficient general interest to warrant a more detailed description and analysis (*2*). Since we find in our material a rather elementary disturbance of orientation in time, we have avoided the term *agnosia,* which we reserve for more complex types of dysfunction, and have chosen instead the term *chronotaraxis* (confusion in time) to indicate that confusion in temporal orientation is the most prominent symptom.

Since a study of this symptom in patients who preoperatively show severe defects of intelligence or disturbances of orientation is, of course, hardly possible, our material is restricted to 30 cases, patients who underwent thalamotomy for the relief of chiefly emotional disturbances or intractable pain. Before operation these patients were well oriented in time and place and they were in good contact with their environment. Of the 30 cases studied, 19 showed more or less pronounced chronotaraxis, four showed disturbance of orientation in time and place, and seven showed no such disorders. In most instances the chronotaraxis lasted a few days or weeks; in only one case did it last 6 mo.

The patients were confused regarding the date, the season, and the time of the day; they misstated their age and/or that of their children. They made serious errors regarding the duration of the time elapsed since operation, their stay in the hospital, or their home. Each individual's mistakes were usually in a definite direction: some showed a tendency to overestimate, others to underestimate the duration of their experiences. Furthermore, as observed by Heimann in scopolamine poisoning (*3*), a dissociation between the estimation of time by "feeling" and its judgment by empirical, intellectual factors was observed after the thalamic lesions; for example, 2 mo after thalamotomy, one patient knew from repeated discussions with her family and with the interviewers that she had lived in her home for 5 yr; but she expressed the feeling that she had resided in her home for only a few weeks.

Another patient reported postoperatively a peculiar feeling that the day finished within a few hours, although she knew that only a short time had elapsed since morning; this feeling was repeated several times during the same day. These observations seem to support the view that isolated disturbances of the immediate perception of time duration do exist; they also show that such disturbances may be caused by circumscribed thalamic lesions. Although a constant relationship to anosognosia or to emotional changes could not be established, there were usually memory defects affecting recent, as well as remote, events. These memory defects may be an important component of the temporal disorientation; however, they seem insufficient to explain the aforementioned syndrome.

The operative coordinates and postoperative x-ray studies of pantopaque droplets injected at the site of the lesion indicate that the dorsomedial nuclei were chiefly involved. Since temporal disorientation was observed in single cases after prefrontal lobotomy (*4*), it seems possible that interruption of the circuit that connects the dorsomedial nuclei with the frontal lobe plays an important role in the genesis of the temporal disturbance after lesions of these nuclei.

However, since these disturbances do not appear in all cases and, if present, are only transitory, the possible participation of other circuits in the underlying mechanisms must be considered. The lesion may encroach upon parts of the diffuse thalamocortical projection system such as the intralaminar nuclei. It seems, however, somewhat doubtful that the depression of cortical activity caused by lesion of these latter nuclei plays an important part in the production of our syndrome, for this system seems dispensable for cortical activation on stimulation of the reticular formation of the brainstem (*5*). If asymmetric lesions are produced inadvertently, so that on one side medial parts of the lateral nuclei are affected, the nuclei lateralis dorsalis and lateralis posterior may be injured where parietopetal fibers originate. Associated lesions of this latter system may be significant in view of the fact that temporal disturbances were observed in lesions of the parietal lobe (*6*).

An extension of the lesion in frontal direction to the anterior nuclei-mamillary body system is still more important. This is illustrated by a case in which transient temporal disorientation following lesion of the dorsomedial nuclei reappeared several months later when a more cranial lesion including the anterior nuclei was added. Furthermore, in single instances, localized processes in the area of the mamillary body were associated with a Korsakoff syndrome (*7*) that is, at least in some respects, similar to our syndrome. However, it should be emphasized that severe lesions of the mamillary bodies do not necessarily induce a Korsakoff syndrome (*8*). In view of these various observations, it does not seem possible to relate the mechanisms involved in temporal orientation to single nuclei or their cortical connections. The observations seem to be explained best by the assumption that multiple circuits participate in the mechanism of temporal orientation, so that a lesion of a single thalamic nucleus produces only transitory disturbances.

Following lesions of other subcortical regions (midbrain in the area of the spinothalamic system; pallidum) chronotaraxis was not observed.

References and Notes

1. E. A. Spiegel and H. T. Wycis, *Proc. Royal Soc. Med.* **42**, Suppl., 84 (1949).
2. This investigation was supported by a research grant MH-372 from the Institute of Mental Health, National Institutes of Health, U.S. Public Health Service.
3. H. Heimann, *Die Scopolaminwirkung* (Karger, Basel, 1952).
4. M. Partridge, *Prefrontal Leucotomy* (Blackwell, Oxford, 1950); R. W. Hyde and A. C. Wood, *Occup. Therap. and Rehabilit.* **28**, 109 (1949).
5. T. E. Starzl, C. W. Taylor, H. W. Magoun, *J. Neurophysiol.* **14**, 461 (1951).
6. H. Ehrenwald, *Z. ges. Neurol. Psychiat.* **132**, 519 (1931).
7. E. Grünthal, *Conf. Neurol.* **2**, 64 (1939); M. Remy, *Monatschr. Psychiat. Neurol.* **106**, 128 (1942).
8. Y. Tsiminakis, *Arb. Neurol. Inst. Univ. Wien.* **33**, 24 (1931).

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Lack of Lens Induction by Eye Cup

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In amphibian embryos, trunk ectoderm can be induced to form a lens at the neurula stage; in later stages, depending on the species involved, lens potency is restricted to the ectoderm surrounding the eye and, then, is lost altogether (*1*). However, the eye cup still retains its lens-inducing ability for some time, and in *Triturus,* even in adults, the eye cup can induce a neoformation of a lens from the upper rim of the iris. In a series of publications, several Soviet authors (*2–4*) reported that the trunk ectoderm of early and late embryonic stages, and even tadpole ectoderm, could be transformed into lens tissue when transplanted into the eye cavity of the tadpole. According to later reports, the chordomesoderm and the tail skin of the metamorphosing tadpole reacted in the same manner (*5*).

Somewhat different were the experiments of Törö (*6*). He cultured embryonic chick and rat iris epithelia *in vitro*; after some 10 explant generations he implanted them back into the eyes of the young animals, after the lens had been removed. Well-formed lenses could be observed in these eyes a few days after operation. Törö supposed that the iris epithelium dedifferentiated in tissue culture and acquired the ability to be converted into a lens when exposed to the induction of the eye. The reported experiments demonstrated both lens potency in tissues that were believed unable to form a lens and strong lens-inducing properties in fully developed eyes. These interesting observations deserved independent confirmation, and we tried to repeat the experiments, using locally available amphibians and chicks (*7*).

The types of experiments performed are summarized in Table 1. In *Rana pipiens,* tadpoles with posterior leg buds, or slightly younger, served as hosts. The lens of one eye was removed through an opening in the cornea. Pieces of trunk ectoderm from the neurula or early or late tail-bud stage, were then introduced with a micropipette into the lenseless eye. In the majority of experiments, the implant could not be found in fixed preparations of tadpoles killed 1 wk or later after operation. When the implant was not expelled or resorbed, it showed an epithelial vesicle with no indication of lens formation. The cells partially lost their pigment, and the center of the vesicle contained expelled yolk and pigment granules.

Removing the lens in *Ambystoma gracile* and *A. maculatum* larvae was easy, and implanting other tissues was successful in most cases. The operative technique was similar to that previously described for *Triturus* (*8*). The hosts were larvae with three- or four-toed hind legs. Trunk ectoderm from the neurula or early or late tail-bud stage, was implanted into the eye. The implanted piece rounded into a vesicle that usually settled near the pupil. Four days after the operation, a general depigmentation of the vesicle was observed. Some cells lining the center of the vesicle still contained pigment granules, but the cells facing the eye cavity were free of pigment. The yolk granules and most of the pigment were expelled, either into the central cavity of the vesicle, or into several smaller cavities inside the vesicle wall (Fig.

Table 1. Implantation of embryonic ectoderm and iris epithelium into lensless eyes. Harrison stages for *Ambystoma,* Shumway stages for *Rana pipiens.* Iris tissue culture from 12-day-old embryos was implanted in *Gallus gallus.*

Host	Stage of donor	Duration of experiment (days)	Eyes operated	Successful implantations
Rana pipiens	20	5	6	5
		7	8	3
		14	13	2
		21	12	7
Ambystoma gracile	22	4	7	4
		7	10	4
		10	8	7
		14	12	12
A. maculatum	20	7	11	8
		14	10	8
		21	10	9
	30	7	14	14
		14	12	12
		28	20	18
	38	14	14	12
		28	14	13
Gallus gallus		9	1	1
		14	6	3
		28	4	2