differences in experimental procedures in the two studies. In our study the inhibition was of a learned approach response rather than of simple drinking behavior (*5*).

ROBERT L. ISAACSON
WARREN O. WICKELGREN
Department of Psychology,
University of Michigan, Ann Arbor

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Extreme Spindles: Correlation of Electroencephalographic Sleep Pattern with Mental Retardation

Abstract. An electroencephalographic abnormality is described which is relatively common among children below 12 years of age who are mentally retarded. This pattern consists of exaggerated sleep spindles, which are of higher voltage and more continuously present than in normal persons, and it correlates specifically with mental retardation and not with epilepsy or cerebral palsy.

Numerous workers have sought unsuccessfully to find features of the electroencephalogram (EEG) which correlate specifically with mental retardation. Our recent analysis of the waking and sleeping electroencephalograms of 1118 mentally retarded persons without clinical epilepsy failed to reveal such patterns (*1*). However, one of us, (E.L.G.) decided that because the epileptic disorder which correlates most highly with mental retardation, namely hypsarhythmia, is characteristically a disorder of infants and disappears later in childhood (*2–4*), it would be worth while to look intensively at the youngest age group. It has been our standard practice for a number of years to record the EEG in subjects both when they were awake and when they were asleep (*3*). A review of the sleep recordings of young, mentally retarded patients revealed a strikingly distinctive pattern which has been termed *extreme spindles* because it appears as an exaggeration of normal sleep spindles (Fig. 1). The pattern shows a frequency of from 8 to 15 cycles per second and is of much higher voltage and is more nearly continuous than normal spindle activity. In the most severely retarded patients the spindles are continuous. They are diffuse and quite commonly they are seen even in the waking state, though when the patient is awake they are of low to medium voltage and are mixed with waking activity. This abnormality is most usually found among mentally retarded children below the age of 5 years; it has not been observed in any child of more than 12.

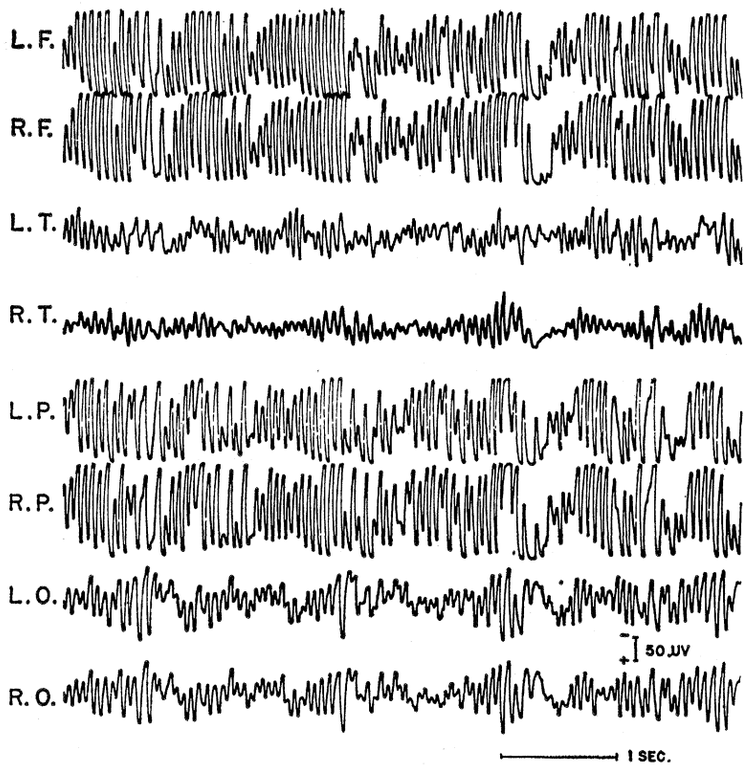

Fig. 1. Sleep recording of young, mentally retarded patient showing extreme spindles.

Extreme spindles do not correlate with epilepsy (*3*, *4*). That they are an abnormality is indicated by the fact that they have been found in only 1 out of more than 3000 control subjects below 12 years of age. A preliminary survey indicates that 70 to 80 percent of children with this pattern are mentally retarded. The pattern was found in 17 percent of 300 noninstitutionalized, mentally retarded children below the age of 8 years. It occurs in 20 percent of cerebral palsy patients classified as ataxics, in 16 percent of athetoids, but in only 6 percent of spastics. Thus extreme spindles are associated with damage to the extrapyramidal rather than the pyramidal system.

There is some suggestive evidence that spindles may be initiated by impulses originating in the intralaminar nuclei of the thalamus (*5*). It seems possible that extreme spindles may be caused by a destructive or irritative lesion. Lindsley has suggested that damage to the reticular formation may be responsible for some types of mental retardation (*6*). Our own studies (*7*) and those of other workers show that high voltage, fast activity, and exaggerated spindles, somewhat like those we have classified as extreme spindles, can be produced by drugs. This pattern may be caused by a metabolic defect and, of course, a combination of structural and metabolic factors may be responsible. A metabolic defect might damage the reticular formation or some other area which regulates the fast activity that appears during sleep.

An immense number of reports have been published relating directly and indirectly in these findings. Literature references can be more meaningful and their significance more properly assessed when our studies have progressed further. The bibliography merely traces our own line of investigation.

ERNA L. GIBBS
FREDERIC A. GIBBS
Neuropsychiatric Institute,
College of Medicine,
University of Illinois, Chicago

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4 September 1962

Increased Sensitivity of Taste and Smell in Cystic Fibrosis

Abstract. Cystic fibrosis is consistently accompanied by the ability to taste and smell salt, sweet, sour, and bitter substances in solution at concentrations much more dilute than those at which the substances are detectable by normal persons. These abnormal thresholds are not affected by the administration of carbohydrate-active steroids.

It has been previously reported that (i) patients with adrenal insufficiency exhibit an increased taste sensitivity for all four modalities of taste (salt, sweet, sour, and bitter) (*1–3*); (ii) thresholds for the corresponding smells are lower in these patients (*4*); and (iii) treatment with carbohydrate-active steroids results in the return of taste and smell thresholds to normal levels, whereas treatment with deoxycorticosterone acetate has no effect on either type of threshold (*1–4*). Because abnormalities in sweat electrolytes in cystic fibrosis are similar to those in untreated adrenal insufficiency, we decided to study taste and smell thresholds in cystic fibrosis and to explore the effect of adrenal cortical hormones on the senses of taste and smell in this syndrome.

Eleven patients, 6 to 20 years old, with cystic fibrosis were studied. All met the usual diagnostic criteria for cystic fibrosis, exhibiting chronic lung disease with obstructive emphysema, steatorrhea, and elevated sweat-electrolyte concentrations. All the patients remained in an air-conditioned ward and ate a normal diet.

Taste was evaluated by measuring the detection threshold in a manner which has been described elsewhere (*1*). Smell was evaluated by a similar technique. The test substance in solution, varying from 0.00006 to 300 mmole/lit., or glass-distilled water was placed approximately 1 to 2 cm below the subject's external nares. The subject was asked to sniff each fluid vigorously, once, for 2 to 4 seconds. Comparison of the fluids—two samples of water and one of test solution—was made after each group of three fluids had been smelled. Threshold was defined as the lowest concentration of test substance which evoked two successive positive responses followed by two consecutive negative responses at the next lower concentration.

The detection thresholds for taste and smell for each patient with cystic fibrosis are presented in Table 1. The median detection thresholds and the ranges of response are indicated for the patients and for normal volunteers 6 to 65 years old. As in the normal volunteers, the median taste-detection thresholds for NaCl, KCl, $NaHCO_3$, and sucrose are all similar (0.3 to 0.1 mmole/lit.) in the group of patients, whereas the values for HCl and urea are quite different (0.006 and 0.8 mmole/lit., respectively). Ten of the 11 patients with cystic fibrosis showed a markedly increased ability to detect all substances. They could detect substances at concentrations 40 to 13,000 times more dilute than the concentrations at which these could be detected by the normal volunteers. In one patient (D.S., age 6) the responses for both taste and smell fell within the normal range. In ten of the 11 patients the range of taste responses did not overlap the range of responses in the normal volunteers, and similarly, in nine of the 11 there was no overlap in the smell responses. Smell thresholds in these patients generally were ten times lower than corresponding taste thresholds.

Since the sensitivity for taste and smell in patients with adrenal insufficiency returns to normal after treatment with carbohydrate-active steroids, four of the patients in our study (C.T., J.B., P.R., and M.D.) were given prednisolone alone (20 mg/day) for 5 days. The values for detection thresholds for taste and smell after treatment are essentially the same as those for

Table 1. Detection thresholds for taste and smell in 11 patients with cystic fibrosis, compared with thresholds in normal volunteers. All patients were Caucasian, and all but D.S. were males. ∞, Inability to smell the substance at any concentration tested.

Patient	Age (yr)	Detection thresholds for taste (mmole/lit.)						Detection thresholds for smell (mmole/lit.)					
		NaCl	KCl	$NaHCO_3$	Sucrose	HCl	Urea	NaCl	KCl	$NaHCO_3$	Sucrose	HCl	Urea
L.R.	13	0.001			0.1	0.00006	0.008	0.001			0.001	0.00006	0.008
B.B.	20	.3	0.5	0.3	.3	.03	.3	∞	300	300	∞	∞	∞
D.B.	13	.3			.1	.03	.8	0.01			0.01	0.01	0.08
C.T.	8	.01			.01	.0006	.8	.001			.1	.01	30
J.B.	9	.1	.01	.01	.01	.0006	.08	.1			.001	.00006	0.008
D.S.	6	60			30	3	150	∞			∞	∞	∞
J.L.	9	0.1			0.1	0.006	0.8	0.6			0.5	0.006	12
P.R.	8	.01			.001	.0006	.008	.01			.001	.00006	0.008
M.D.	8	.01			.1	.06	.08	.001			.01	.00006	.008
R.R.	9	.01			.001	.006	.008	.001			.001	.00006	.008
M.H.	9	.1	.3	.1	.1	.01	.8	.3	0.3	0.1	.1	.006	.8
							*Medians**						
Patients		.1	.3	.1	.1	.006	.8	.01			.01	.006	.08
Normal volunteers:													
$N = 28$		12 (6–60)	21 (6–60)	12 (6–60)	12 (6–60)	3 (0–6)	120 (90–150)						
$N = 8$								∞ (∞–150)	∞ (∞–150)	∞ (∞–150)	∞ (∞–150)	∞ (∞–150)	∞ (∞–150)

* Ranges in parentheses.