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SELECTIVE COGNITIVE IMPAIRMENT DURING FOCAL AND GENERALIZED EPILEPTIFORM EEG ACTIVITY

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SUMMARY

It is well established that generalized epileptiform EEG discharges unaccompanied by overt clinical change may nevertheless be associated with transitory cognitive impairment (TCI) detectable by appropriate psychological testing. However, the tests employed in most research studies of this phenomenon are of little use for routine clinical application. They are suitable for administration only over short periods of time and are therefore applicable only to patients with a high discharge rate, a serious limitation, as the discharges are generally depressed by the tests themselves.

We have developed two short-term memory tasks, one using verbal, the other nonverbal material presented in the form of television games which patients are generally prepared to perform for up to an hour or longer. Forty-six patients with subclinical EEG discharges have been studied. They were screened by video monitoring before and during testing to exclude any with overt clinical changes during the discharges. Despite this rigorous selection, in 50 per cent TCI was demonstrable with a confidence level (within the individual patient) of 10 per cent. Discharges during stimulus presentation were most disruptive of performance and those confined to the period when the patient was responding were without demonstrable effect. A significant association was found between the laterality of focal or asymmetrical generalized discharges and impairment of one or other task, left-sided discharges being associated with errors in the verbal task and right-sided with impairment of the nonverbal test.

Two case histories are cited illustrating patients who were clearly handicapped by TCI and whose functioning improved when the subclinical discharges were suppressed by medication. To determine how many patients suffer such disabilities or can be helped by appropriate medication, further prospective studies are required.

INTRODUCTION

Epileptiform EEG discharges occur without evident clinical concomitants in many patients with epilepsy, and also in some persons who are not known to suffer from seizure disorders. The discovery by Berger (1933) of generalized 3 Hz high voltage activity accompanying the absence seizure was rapidly followed by the realization (Gibbs *et al.*, 1936) that this relationship was not invariable and that brief generalized spike-wave bursts could occur without apparent clinical change. This view had in turn to be qualified when Schwab (1939) succeeded in demonstrating

that 'subclinical EEG discharges' were often accompanied by an increase in reaction time or indeed by complete failure to respond to a stimulus. Many subsequent studies have reported transitory cognitive impairment during subclinical spike-wave activity. Most, however, gloss over the problem of distinguishing overt absence seizures with global unresponsiveness from EEG discharges accompanied by subtle cognitive changes detectable only by suitable testing. A minority of authors (*see* Shimazono *et al.*, 1953; Kooi and Hovey, 1957; Yeager and Guerrant, 1957; Davidoff and Johnson, 1964; Guey *et al.*, 1965; Porter *et al.*, 1973; Goode *et al.*, 1970) have documented behaviour during the investigation and few have compared performance during subclinical discharges with that during visible absences. This is regrettable as it has been shown (Tizard and Margerison, 1963*a*; Goode *et al.*, 1970) that the probabilities of detecting a cognitive deficit and of observing an absence both increase with duration of the discharge. Very few studies are specifically restricted to patients exhibiting no overt seizures during the investigation (Hutt and Gilbert, 1980) or include patients not considered to suffer from epilepsy (Ishihara and Yoshii, 1967).

The concept of 'subclinical' EEG discharges has been used, sometimes under other names such as 'larval seizures', by many authors (Gibbs *et al.*, 1936; Shimazono *et al.*, 1953; Kooi and Hovey, 1957; Yeager and Guerrant, 1957; Tuvo, 1958; Tizard and Margerison, 1963*a*; Davidoff and Johnson, 1964; Grisell *et al.*, 1964; Hutt and Fairweather, 1973), but itself presents difficulties. Involuntary movements during a seizure will not readily be recognized by an observer unless they differ from the patient's interictal behaviour. Stereotyped ictal movements falling within the subject's normal behavioural repertoire may be detectable only by careful analysis of simultaneous EEG and video recordings. Impairment of normal functions may be even more difficult to recognize: during routine EEG recordings there is little behaviour to be seen. Conversely, during telemetric monitoring a patient may be engaged in activities too unpredictable for the observer to be able to detect a momentary decrement of performance. An EEG discharge can therefore be classified as 'subclinical' only in so far as the available methods of clinical observation, applied under particular circumstances, fail to show any change in the patient. In the present text the term 'transitory cognitive impairment' (TCI) is used to designate functional deficits demonstrable by suitable testing, during spike or spike-wave discharges, which are subclinical in the operational sense indicated above.

Some authors consider that generalized spike-wave activity is always accompanied by impaired performance (Kooi and Hovey, 1957), or that 'interseizure discharges probably do not occur in absence seizures' (Delgado-Escueta, 1979). Others have been unable to demonstrate TCI during such discharges (Milstein and Stevens, 1961; Prechtl *et al.*, 1961). Various authors, notably Tizard and Margerison (1963*a*) and Mirsky and Van Buren (1965), have demonstrated that some tests are more sensitive to the effects of epileptiform activity than others: simple motor tasks such as rhythmic tapping, simple reaction time, or tracking, are relatively little

affected by generalized spike-wave activity (Schwab, 1941; Cornil *et al.*, 1951; Shimazono *et al.*, 1953; Yeager and Guerrant, 1957; Tuvo, 1958; Hauser, 1960; Tizard and Margerison, 1963*a*; Davidoff and Johnson, 1964; Grisell *et al.*, 1964; Mirsky and Van Buren, 1965; Chatrian *et al.*, 1970; Goode *et al.*, 1970; Porter *et al.*, 1973; Browne *et al.*, 1974), whereas choice reaction time (Tizard and Margerison, 1963*b*; Sellden, 1971; Hutt *et al.*, 1977), signal detection (Tizard and Margerison, 1963*a*; Mirsky and Van Buren, 1965; Hutt *et al.*, 1976) and short-term memory tasks (Shimazono *et al.*, 1953; Jus and Jus, 1962; Geller and Geller, 1970; Hutt, 1972; Hutt and Gilbert, 1980) are more sensitive.

Although any attempt to equate epileptiform activity with epilepsy is in general to be deplored, the occurrence of a paroxysmal change in cerebral electrical activity simultaneously accompanied by cognitive impairment meets generally accepted definitions of an epileptic seizure (Lennox, 1960). Whether or not the conclusion of Tizard and Margerison (1963*b*) is accepted, that such an event 'should be considered evidence of a seizure', TCI is likely to be of practical importance. Such episodic impairment may be a disability (causing problems of education or at work) or a danger (when the patient is driving, or is exposed to common domestic hazards). There appears therefore to be a clinical indication to test for TCI in patients exhibiting frequent generalized epileptiform discharges without overt seizures. Indeed an evaluation study of a clinical EEG and video monitoring service (Binnie *et al.*, 1981) showed that patients were often referred with the request to determine whether or not known EEG discharges were accompanied by clinical changes. Often the video recordings revealed brief minor seizures which had not previously been observed, but to address the question adequately in patients without visible attacks it seemed necessary to add psychological testing to the monitoring techniques.

Most published studies of TCI concern highly selected patients with frequent epileptiform discharges and the tests used were hardly suitable for clinical purposes. A routine test for TCI should fulfill the following criteria (Binnie, 1980). (1) The task must not so suppress epileptiform activity that testing is impossible. A high level of arousal generally reduces epileptiform activity, moreover intense stimuli may abort the discharges and elicit normal responses (Schwab, 1941; Shimazono *et al.*, 1953; Tizard and Margerison, 1963*b*; Goode *et al.*, 1970). (2) The test must be acceptable for administration over a period sufficiently long for the effect, if any, of an adequate number of discharges to be observed. In practice, patients must generally be willing to perform the task for at least half an hour. (3) The difficulty must be adaptive to the patient's level of performance. Easy tasks are relatively insensitive to TCI (Hutt, 1972; Hutt *et al.*, 1977), but increasing task difficulty may either decrease or increase the amount of epileptiform activity (Tizard and Margerison, 1963*b*; Hutt, 1972). (4) The task must continuously test cognitive activity (Guey *et al.*, 1965; Goode *et al.*, 1970); if it is intermittent, discharges may fall in the intervals between trials. Intermittent testing triggered by the discharges themselves (Binnie and Lloyd, 1973; Porter *et al.*, 1973) is not an acceptable solution. Discharge probability is influenced by the state of awareness, and epileptiform activity may therefore occur preferentially

when the patient is inattentive. (5) The test should have face validity. The clinical relevance is more obvious if the cognitive impairment demonstrated is of practical importance, as for instance impaired verbal memory in a school child or increased reaction time in a motorist. (6) To give greater insight into the nature of TCI, the test, or tests, should differentiate between different psychological functions and between different regions of the brain.

The authors have developed several tests intended to meet these criteria but only the two which have proved to be most satisfactory will be described. Both were short-term memory tests presented as television games. The material to be recalled was topographic in one case and verbal in the other.

MATERIAL AND METHODS

Tests

In the topographic task, the patient was presented with 7 randomly coloured rectangles (height 23 mm, width 35 mm) distributed irregularly against a dark green field on a 440 mm colour TV monitor. These flashed off and on in a random sequence, one rectangle at a time being blacked out for 650 ms with a 250 ms interval between extinctions of successive rectangles. The extinction of each rectangle was accompanied by a tone. On completion of the sequence all the rectangles became white. The patient was then required to reproduce the sequence by pointing at the rectangles in turn with a light-pen. Each correct response elicited the tone previously presented with that rectangle. An incorrect response elicited a low frequency tone and flashing of the rectangle which should have been selected, and terminated the current test run. The next trial began 4 s after completion of the correct sequence or after the occurrence of an error. The task was therefore self-paced. The sequence length was adaptive to performance: when two consecutive sequences were correctly reproduced the entire series length was increased by one; two consecutive errors resulted in the sequence being reduced by one. Colour and sound effects were used to make the task entertaining and a correct response caused a simple tune to be played. However, sound and colour did not provide information which could be used to assist recall of the sequence: the sounds and colours associated with each rectangle were randomly changed after every trial and during the response phase the display was colourless. The task, it will be noted, had some similarity to Corsi's blocks test (Milner, 1971) and also to a popular computer toy.

The second, verbal, task used so far as possible a similar form of presentation and response. Words of four letters (height 14 mm, width 9 mm) were displayed consecutively in the centre of a television screen, each for 650 ms separated by intervals of 250 ms. The sequence had then to be reproduced by means of the light-pen from a list of 7 words arranged vertically in the middle of the screen. The words were selected as being simple, emotionally neutral, not readily assembled into sequences based on meaning or alliteration, and containing no repetitions of characters. The following (Dutch) names of animals were used: duif, hond, geit, mier, spin, poes, kalf.

Both tasks were presented by means of a microcomputer, which also annotated the EEG chart with a pulse code indicating stimulus presentation and correct or incorrect responses. The program, written in BASIC with assembler subroutines, currently runs on an Apple II computer, and is available from the authors. A revised version for a Z80 with colour graphics (Kontron Psi 80) is in preparation.

Patients

The patients were all in the first instance referred to the Department of Clinical Neurophysiology, Instituut voor Epilepsiebestrijding, Heemstede, for investigation of epilepsy. Patients were selected for possible testing on the basis of the following criteria. (1) Presence of paroxysmal EEG discharges, either frank epileptiform activity (spikes or spike-wave complexes or sharp waves) or paroxysmal theta

or delta bursts, whether generalized or focal, in the eyes open condition, exclusive of findings during hyperventilation, photic stimulation or after sleep deprivation. (2) Absence of overt clinical manifestations accompanying such discharges. The routine practice of the department includes such measures as recording with the patient seated in an upright position, asking the patient to count or press regularly on a button or to repeat simple phrases to determine whether performance is impaired, or muscle tone lost, during subclinical discharges (Binnie *et al.*, 1982). Patients in whom clinical changes were detected by such methods were excluded. (3) Mental and physical capacity considered to be compatible with performance of the tests (children of average intelligence from 8 yrs upwards were generally able to perform both tasks). (4) Agreement of the referring neurologist that a clinical indication existed for determining whether or not the patient's discharges were accompanied by TCI.

Procedure

Prior to testing, preliminary EEG recording of some 30 to 60 min duration was performed by 16- or 20-channel cable telemetry (Kamp *et al.*, 1979) with continuous video monitoring in a sitting room which provided a normal domestic environment (Binnie *et al.*, 1981). During monitoring the patients sat with eyes open, read, talked or played card or board games. If the number of discharges occurring under these conditions was considered inadequate (generally less than 1 per 5 min) patients were excluded from further study, as were any exhibiting overt epileptic seizures during this period.

During testing, the patient was seated in an upright chair in front of the television monitor in a quiet room with subdued lighting. Behaviour was monitored and tape-recorded by closed circuit TV in order to exclude any patients exhibiting overt seizures. As indicated above, it may be considered that the phenomenon of TCI itself calls in question the definition of a seizure. However, the operational criterion employed was the occurrence during an epileptiform EEG discharge of abnormal movements or behaviour, staring or obvious akinesia, eyelid flutter, or subjective changes resembling the patient's habitual ictal phenomena. In practice only 2 patients were excluded on these grounds: one had absence attacks (staring and eyelid flutter), the other displayed massive myoclonus, which strikingly increased in frequency with task difficulty. During the period of the study 1059 patients of more than 8 years of age attended for EEG investigation; 62 were rereferred for evaluation of possible TCI, 53 were considered to meet the criteria for testing and 2 of these were eliminated because of overt seizures during the test. One patient had to be excluded due to a lack of discharge-free trials and 4 others exhibited too little epileptiform activity to permit assessment.

Data Analysis

The test may be considered as a series of trials, each comprising, first, the presentation of the stimulus sequence and then the response. Each record was analysed to determine whether any association existed between errors and the occurrence of paroxysmal activity during a particular trial. Because the level of task difficulty (sequence length) was adaptive giving a 50 per cent error rate, most of the testing involved only 2 or 3 sequence lengths. Separate 2×2 contingency tables were drawn up for each sequence length, showing the incidence of correct or incorrect trials with or without epileptiform activity. For each table with a determinate association (i.e. with all marginal totals greater than zero) χ^2 was then calculated without correction for continuity according to the conventional formula $(O\text{-}E)^2/E$. The square root of the value of χ^2 for each table yielded a value of z, which was given a sign corresponding to that of any association between error and discharge. The values of z were then summated and the sum divided by the number of values contributing to the sum. This provided a new value of z from which a probability level was obtained. The strength of association was estimated by calculating the mean value of Yule's coefficient of association.

RESULTS

Forty-six patients were testable; their principal clinical characteristics are summarized in Table 1.

The effects of testing on discharge frequency are summarized in Table 2. In 7 patients there was an increase in discharge incidence. As none of these patients was photosensitive, there is no reason to suppose that exposure to the TV monitor as such was responsible for this effect. One patient became untestable, showing no trials without epileptiform activity, so the control condition of no discharge could not be tested. Another (not included in Table 2) developed myoclonic jerks and therefore no longer fulfilled the admission criteria for the study. In 28 there was no change and in 16 there was a decrease. However, in only 4 of these 16 was the suppression so marked as to render statistical analysis impossible. In 2 patients there was a change in the morphology of the discharges during the task. In both cases the spikes disappeared and slow waves remained.

TABLE 1

Age Mean 25 ± 11, range 10 to 46 yrs	
Sex Male/Female 26/20	
Type of epilepsy	
Primary generalized	3
Partial	20
Secondary generalized	18
Unclassified	5

In analysing the test results, it seemed appropriate to employ more stringent statistical criteria for research than for clinical purposes. An association of error with epileptiform activity was accepted as evidence of TCI for the management of an individual patient at a significance level of 0.1 (for a one-tailed test). By this criterion, TCI was demonstrable in 11/22 patients with focal or asymmetrical discharges and in 13/24 with symmetrical generalized epileptiform activity (Table 3). For a more detailed analysis for research purposes a 0.05 level on a two-tailed test was regarded as significant. This criterion was satisfied by 7/22 patients with focal or asymmetrical epileptiform activity and by 9/24 with symmetrical discharges.

In Table 3 data for patients with generalized epileptiform activity that had a unilateral predominance have been grouped with the data for patients exhibiting focal activity on the same side. Nine of the 12 patients with left-sided activity who were tested on both the verbal and topographic tasks showed a stronger association between errors and epileptiform activity for the verbal task than for the topographic. The association between epileptiform activity and errors on the verbal test reached significance in 3 of the 14 patients.

The opposite pattern obtained for 4 of the 5 patients with right-sided epileptiform activity who were tested on both tasks. In 3 of the 6 patients who received the topographic test the association between errors and epileptiform activity reached significance. The single patient with a significant positive association of right-sided focal discharges and errors on the verbal task was left-handed.

For patients with symmetrical generalized epileptiform activity (Table 3B) the pattern of results was midway between the extremes obtained for patients with asymmetrical discharges. For the majority of those patients who performed both tests (12/16) the association between errors and epileptiform activity was stronger for the topographic test. For the remaining patients the reverse was the case. In 7/23 patients the association reached significance on the topographic test, as compared with 3/17 on the verbal test. In one patient the association was significant on both tests.

TABLE 2. SEIZURES AND DISCHARGE RATE DURING TESTING

Eliminated because of seizures during testing	2
Change in discharge rate	
Increase, testable	6
untestable	1
No change	28
Decrease, testable	12
untestable	4
Total patients	51
Patients testable	46

The effect of the degree of asymmetry and its lateralization on the strength of the association between errors and epileptiform activity is summarized in Table 4. In patients with asymmetrical discharges, the association between greater impairment of the verbal task and lateralization of the discharges to the presumed dominant hemisphere is significant ($P < 0.02$ by Fisher's exact probability test, two-tailed).

The preceding results were based on a comparison of error rates in trials with or without paroxysmal activity, regardless of the timing of the discharges. Table 5 presents a more detailed analysis of the relationship between errors and the occurrence of discharges at different points in each trial: within 2 s prior to the stimulus, during stimulus presentation, during the interval between stimulus and response, during both stimulus and response, during response and within 2 s after completion of response. These categories are mutually exclusive: discharges during the stimulus are taken to include those commencing earlier or continuing into the stimulus response interval, and discharges during the response include those commencing in the stimulus response interval or continuing after the response. Only error rates differing from the basal interdischarge level are shown; ties are excluded, as are missing data (due to the nonoccurrence of discharges in a particular phase of

TABLE 3A PATIENTS WITH FOCAL AND ASYMMETRICAL GENERALIZED PAROXYSMAL EEG ACTIVITY

Paroxysmal activity		*Topographic task*		*Verbal task*	
Distribution	*Type*	*Mean Yule's coefficient of association*	*z*	*Mean Yule's coefficient of association*	*z*
Focal right					
	S-W	0.22	2.79**	−0.80	−1.37
	S-W	0.24	2.45*	0.17	1.06
	Sp	0.30	0.34	0.88	2.44**
	S-W	0.2	1.52†	0.19	1.06
	S-W	0.33	2.05*	—	—
Generalized right maximal					
	T	0.07	0.53	−0.02	−0.28
Focal left					
	S-W	0.50	0.52	0.27	0.49
	T	−0.26	−1.47	0.44	0.21
	D	−0.29	−0.81	0.53	2.01*
	S-W	0.20	0.58	−0.16	−0.17
	Sh	0.09	0.54	0.21	0.64
	S-W	—	—	1.0	1.49†
	T	0.16	0.44	1.0	0.35
Generalized left maximal					
	T	−0.41	−1.20	−0.18	−0.16
	S-W	−0.11	−1.32	0.49	1.36
	S-W	0.79	1.85†	−0.57	−0.85
	S-W	0.25	0.37	0.50	1.29
	S-W	0.21	1.16	0.75	2.81**
	S-W	0.19	1.46†	0.82	3.60**
	S-W	0.52	1.02	—	—
	S-W	1.0	1.67†	—	—
	S-W	—	—	0.22	−0.45

the trials in some individuals). The error rate when discharges occurred during the stimulus is also compared with that observed when paroxysmal activity coincided with the response. Significance of any apparent effects was evaluated by the sign test (two-tailed).

It will be seen that the error rate associated with discharges during the stimulus was strikingly higher than the basal level ($P < 0.001$) and than that when discharges occurred during the response ($P < 0.002$). Indeed paroxysmal activity during response did not produce any apparent increase in errors. Intermediate effects are seen with discharges in the stimulus response interval or continuing from

TABLE 3B. PATIENTS WITH SYMMETRICAL GENERALIZED PAROXYSMAL EEG ACTIVITY

Paroxysmal activity	*Topographic task*		*Verbal task*	
Type	*Mean Yule's coefficient of association*	*z*	*Mean Yule's coefficient of association*	*z*
S-W	0.30	0.01	0.14	1.49†
T	−0.20	−0.16	−0.07	−0.81
S-W	1.0	1.49†	0.22	0.69
S-W	0.48	0.35	0.12	0.03
D & T	1.0	2.85**	−0.43	−1.09
T	0.29	0.47	0.22	0.64
S-W	0.90	1.51†	0.89	3.34**
S-W	−0.63	−0.44	0.05	0.33
S-W	−0.26	−1.00	−1.0	−1.00
S-W	0.58	2.86**	0.55	2.37*
S-W	0.78	2.00*	0.31	0.08
D	Excessive increase in PA		0.66	0.34
S-W	−0.35	−0.26	0.2	2.82**
S-W	0.71	3.48**	0.23	0.64
D	0.16	0.57	0.08	0.13
S-W	0.29	0.28	0.58	0.17
S-W	0.5	0.44	0.47	0.864
S-W	−0.38	−0.33	—	—
S-W	1.0	−1.80	—	—
S-W	0.80	4.07*	—	—
S-W	1.0	2.64**	—	—
S-W	−0.37	−0.04	—	—
S-W	0.20	1.64†	—	—
S-W	1.0	3.64**	—	—

Key to types of paroxysmal activity. S-W = spike-wave. Sp = spikes. T = theta bursts. D = delta bursts. Sh = sharp waves.

† $P < 0.1$ single-tailed (positive associations only). * $P < 0.05$ two-tailed. ** $P < 0.01$ two-tailed.

TABLE 4. ASSOCIATION BETWEEN ERRORS AND EPILEPTIFORM ACTIVITY

Epileptiform activity	*Greater on topographic task*	*Greater on verbal task*
Right-sided	4	1*
Symmetrical	12	4
Left-sided	3	9

* Left-handed patient.

TABLE 5 ERROR RATES

	Discharge during			
	Topographic task		*Verbal task*	
	Less	*Greater*	*Less*	*Greater*
Error rate relative to interdischarge level				
2 s before stimulus	12	21	19	6 $P < 0.02$
Stimulus	8	34 $P < 0.001$	6	24 $P < 0.01$
Stimulus-response interval	11	22 $P < 0.1$	10	19
Stimulus and response	6	13	13	13
Response	18	16	15	16
2 s after response	8	10	5	2
Error rate relative to that when discharge occurs during response				
Stimulus	7	27 $P < 0.002$	6	20 $P < 0.02$

the stimulus through to the response. There appears to be an increased error rate (not significant) with discharges in the 2 s prior to the topographic stimulus; however, the opposite effect is observed with the verbal task. Otherwise the two tests give similar results.

Finally, the clinical context of TCI will be illustrated by two examples.

Case History 1

A 35-year-old male librarian had an excellent academic record up to the age of 18. However, when he attempted to read law at university he became subject to an inability to concentrate which forced him to abandon his studies. He continued to have the same difficulties in his work as a librarian. When stressed, he could not answer reader's enquiries and had particular difficulty in cataloguing. A psychological examination suggested that his problems were due to obsessionality; at one time a diagnosis of schizophrenia was considered. The possibility of epilepsy first arose when an ENT surgeon astutely noted that a letter from the patient contained repeated hesitations, where the writing trailed away. A decision to carry out EEG and video monitoring in combination with performance tests was made more in the expectation of excluding than of establishing an epileptic basis for his complaints. Indeed, during a period of 5 h monitoring without intellectually demanding activities no EEG abnormality was observed. However, during the performance of the topographic task, generalized 3 Hz spike-wave discharges appeared, their duration increasing with task difficulty. During these discharges no obvious ictal behavioural changes were observed apart from an inability to continue the task and some evident perplexity which continued 10 s or more after each discharge. He was treated with sodium valproate (1800 mg daily) which was followed by a marked improvement in his complaints of poor concentration and a striking reduction of epileptiform EEG activity during performance testing.

Case History 2

A 13-year-old boy complained of difficulty with his school work. The EEG contained repeated runs of generalized sharp waves or irregular spike-wave activity maximal in amplitude over the frontal regions. Both the topographic and the verbal task showed significant ($P < 0.01$) transitory cognitive impairment. Due to the repeated errors associated with the EEG discharges he never advanced beyond a series length of 2 blocks or 2 words. Diazepam (7.5 mg) was then administered by slow intravenous injection, suppressing the epileptiform activity. After 15 min performance testing was repeated.

Although the patient was now extremely drowsy the EEG contained no epileptiform discharges and he repeatedly achieved two consecutive correct responses to series of 3 blocks. An hour later he was again tested. Epileptiform activity was still absent, he was less drowsy and responded correctly to series of up to 4 blocks. Sodium valproate (900 mg daily) was prescribed; his school work improved, but a year later he relapsed with frequent overt absences.

DISCUSSION

The tests described appear to satisfy the main requirements for a means of investigating TCI as a routine clinical service. Of those 51 patients who had sufficient discharges under control conditions for testing to be attempted, 90 per cent were both willing to perform the tasks for an adequate period of time and exhibited a sufficient discharge rate to permit a conclusion concerning the presence or absence of TCI demonstrable by these tests. Behaviour was monitored by video recording and subjects exhibiting overt seizures during the investigation were excluded. This implies that selection was more rigorous than in most, arguably all, previous studies. Nevertheless, TCI was established with a frequency similar to that generally reported by other authors. Cognitive impairment was demonstrable with 10 per cent confidence in 50 per cent of patients overall: in 50 per cent of those with symmetrical and 40 per cent with asymmetrical generalized discharges, and in 58 per cent of those with focal epileptiform activity. This finding was unexpected: the occurrence of TCI during generalized discharges is well documented but its presence during subclinical focal epileptiform activity has, so far as we are aware, been suggested only by Kooi and Hovey (1957). Tuvo (1958), Prechtl *et al.* (1961), Sellden (1971) and Hutt *et al.* (1977) found no evidence of TCI during discharges variously described as unilateral, focal or localized. An association of increased reaction time with localized increase in low frequency components of EEG power spectra has been demonstrated, however, by Stevens *et al.* (1972), and these 'ramp spectra' in turn were associated with spiking at depth electrodes.

The effects of focal discharges were specific to the task lateralized to the appropriate hemisphere. This suggests that TCI is not necessarily a consequence of a general impairment of attention but can reflect disruption of specific psychological functions located in the region or regions where the epileptiform discharges arise. The selective nature of the impairment further suggests the possibility that when TCI was not demonstrable by the present tests, the discharge involved structures different from those affected when TCI was found. Effects of these discharges too might have been detected by different tests.

The practical clinical importance of TCI during focal discharges is uncertain. The small numbers of subjects with focal discharges in the present series (despite the fact that some 70 per cent of patients attending the Instituut have partial epilepsy) reflects a low incidence within and between subjects of focal interictal epileptiform activity in the eyes open, alert state. This in turn may suggest that very few patients with only focal interictal discharges will suffer any important disability due to TCI. The finding of impairment during focal discharges, does, however, have other,

practical implications for the use of psychological testing in patients undergoing surgical treatment of partial epilepsies. Corsi's block-tapping test, for instance, was specifically used for evaluating pre- and postoperative memory deficits (Milner, 1971), apparently on the assumption that these reflected anatomical lesions, not paroxysmal dysfunction. The interpretation of the results of such testing may be difficult if there are frequent interictal discharges in either the pre- or postoperative EEG. The association between lateralization of epileptiform activity and the verbal or nonverbal nature of the TCI that it produces may further confuse the assessment. The patient may trade a selective cognitive deficit, due to a focal dysfunction, for a qualitatively similar impairment produced by the operative lesion.

In accordance with the findings of previous workers, the morphology of the paroxysmal activity was an important determinant of TCI (fig. 1). Ten patients were included with paroxysmal delta or theta bursts without frank spikes or sharp waves and only 2 exhibited evidence of TCI. If these subjects are excluded, then the incidence of TCI in the remaining 36 with epileptiform activity was 61 per cent. It

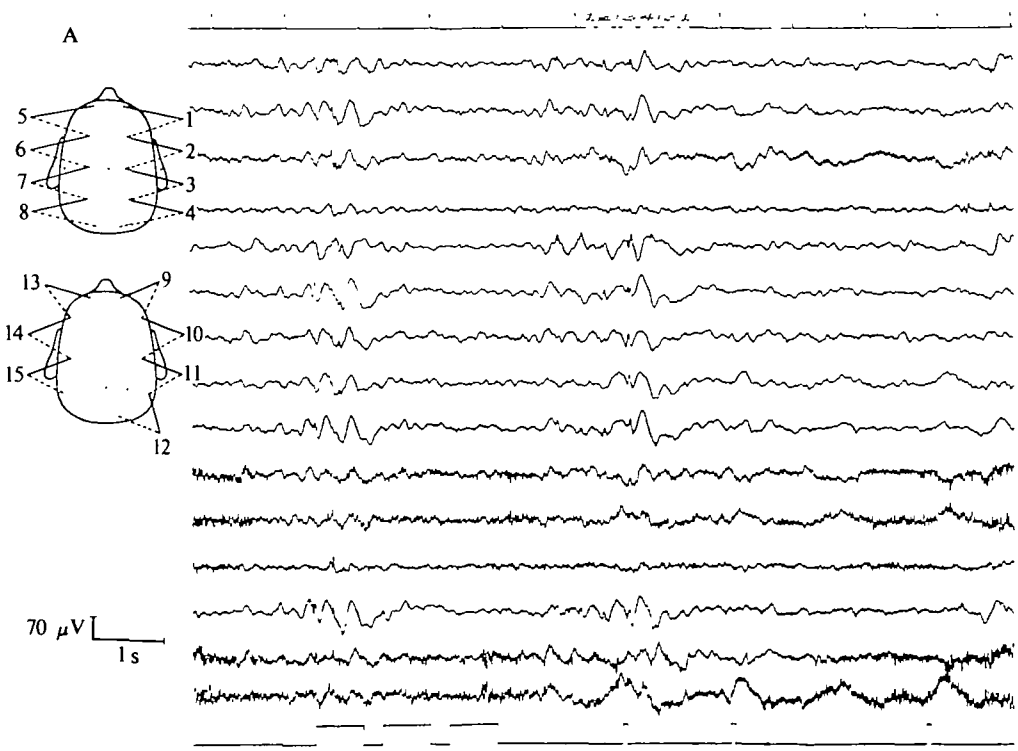
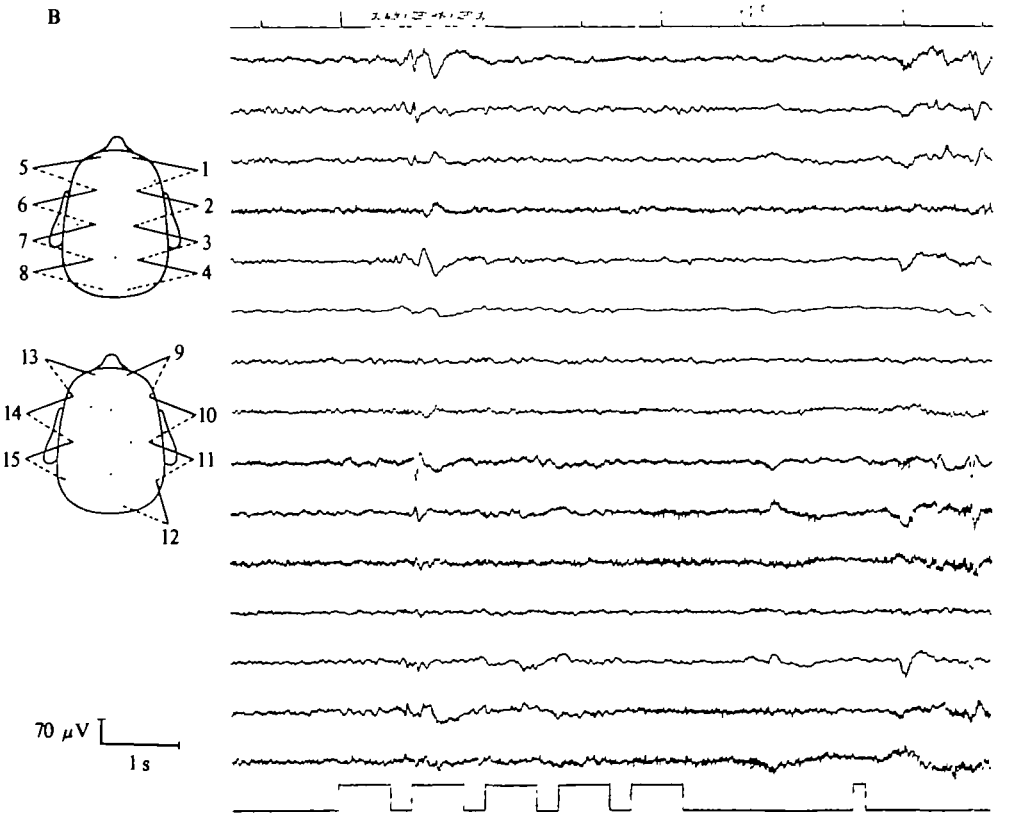


FIG. 1. Epileptiform discharges during performance testing. A, generalized asymmetrical spike-wave discharge in a subject showing no evidence of TCI. The marker channel (16) indicates the stimuli (each large square-wave corresponds to presentation of a block) and correct responses (short pulses). B, (p. 305), focal right-sided discharge in a subject demonstrating TCI on the topographic task. A single incorrect response is indicated by a wider pulse. Time constant 0.3 s, HF response 30 Hz for both A and B.

should further be noted that the Instituut is a centre of third referral: patients with typical petit mal absences are rarely seen in our EEG Department and had moreover been excluded by the selection of subjects without overt seizures during their EEG discharges. Of the 19 patients with symmetrical spike and wave activity, none exhibited those 'classical' regular 3 Hz discharges which previous authors have shown to be most strongly associated with TCI.

It is interesting that the effects of epileptiform activity were greatest when the activity occurred during the presentation of the stimuli. One possible reason for the selective nature of the disruption might be that the presentation of the stimuli was paced, whereas the production of responses was not. Another possibility is that this result is an expression of the more general finding that a concurrent task during stimulus presentation produces a greater effect on errors than one during recall (A. Baddeley *et al.*, in preparation). Discharges during the stimulus could disrupt attention or perception or interfere with 'working-memory' as suggested by Hutt and Gilbert (1980).



The case histories cited indicate that some people suffer a clear social disadvantage as a consequence of TCI and may be benefitted by antiepileptic medication intended to suppress the discharges. It would be regrettable, however, if the present findings were in any way considered to justify the practice of treating EEGs rather than patients. The advice of Browne *et al.* (1974) that 'therapy should be aimed at suppressing all spike-wave paroxysms' may prove to be correct, but is premature. It has yet to be determined what proportion of all patients exhibiting subclinical discharges are significantly handicapped due to TCI. Further work will also be required to establish in how many the possible benefits of antiepileptic drugs to suppress the discharges, or of appropriate counselling to take account of the consequences of TCI, outweigh respectively the side-effects or the social disadvantages of such management. A necessary preliminary to further research was the development of an appropriate method for detecting TCI in routine clinical EEG practice and this, we suggest, has now been achieved.

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