HANDBOOK OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

EDITOR-IN-CHIEF A. REMOND

VOLUME 13

Clinical EEG, III

EDITOR: H. GASTAUT
Hôpital de la Timone, Marseilles (France)

PART B

Mental diseases

EDITOR: M. DONGIER
Allan Memorial Institute, Montreal (Canada)

ELSEVIER

HANDBOOK OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

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Elsevier Scientific Publishing Company – Amsterdam – The Netherlands

International Federation of Societies for EEG and Clinical Neurophysiology

ISBN 0-444-41259

Elsevier Scientific Publishing Company, Jan van Galenstraat 335, Amsterdam
Printed in The Netherlands

Sole distributor for Japan:
Igaku Shoin Ltd.
5-29-11 Hongo Bunkyo-ku
Tokyo

All other countries:
Elsevier Scientific Publishing Company
Amsterdam, The Netherlands

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A great need has long been felt for a Handbook giving a complete picture of the present-day knowledge on the electrical activity of the nervous system.

The International Federation of Societies for EEG and Clinical Neurophysiology is happy to be able to present such a Handbook, of which this is a small part.

The decision to prepare this work was made formally by the Federation at its VIIth International Congress. Since then nearly two hundred specialists from all over the world have collaborated in writing the Handbook, each part being prepared jointly by a team of writers.

The Handbook begins with an appraisal of 40 years of achievements by pioneers in these fields and an evaluation of the current use and future perspectives of EEG and EMG. The work subsequently progresses through a wide variety of topics—for example, an analysis of the basic principles of the electrogenesis of the nervous system; a critical review of techniques and methods, including data processing; a description of the normal EEG from birth to death, with special consideration of the effect of physiological and metabolic variables and of the changes relative to brain function and the individual's behaviour in his environment. Finally, a large clinical section covering the electrical abnormalities in various diseases is introduced by a study of electrographic semeiology and of the rules of diagnostic interpretation.

The Handbook will be published in 16 volumes comprising 40 parts (about 2500 pages altogether). For speed of publication most of the 40 parts will be published separately and in random order.

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PART B

MENTAL DISEASES

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Section I. Aspects and Pecularities More or Less Specific to EEG in Psychiatry

The early expectation of electroencephalographers who anticipated finding characteristic patterns of common mental disorders in the conventional EEG has been of some disappointment. Although EEG proved to be one of the tools in the detection of organic underlying processes, it has brought little to the theory or practical application of the classification, diagnosis and prognosis of the primary functional psychoses and neuroses. Even though EEG shows changes during some somatic therapies, it may not help in the selection of treatment. Many of the claims have to be reexamined and reappraised. The notion of functional electroencephalography (Liberson 1945b) reactivated by recent techniques (averaged evoked potentials, slow potential changes) seems more promising than the classical standard record. None, so far, have reached general recognition, and many techniques need to be refined and differentiated. On the other hand, it must be emphasized that even the routine technique applied in the framework of a psychiatric evaluation is (or at least should be) more deversified than the routine technique used in neurology. Even the definition of a "normal" EEG is much easier in the latter field, and is mostly negative, namely the absence of certain well-defined abnormalities. Interpretation in the field of psychiatry is a more complex task, since topography and variability of various components of alpha rhythms, reactivity and habituation of evoked potentials and subjective reactions of the patient may have to be taken into account, although no general agreement has been reached so far as to the definition of criteria to be used (*e.g.*, see review of C. Walters 1964).

In the research field, quantitative data will often be required to be more convincing as conflicting opinions are commonly due to imprecision in both clinical and EEG criteria. The use of computers has recently helped in individuating electrophysiological patterns which were missed before (drawing together elements previously unrelated and giving them significance, or extracting them from the "background noise").

One of the most difficult tasks is to differentiate the more permanent characteristics such as personality diagnosis, psychiatric nosology and their EEG correlates, from fluctuating, unstable psychophysiological factors such as emotion, attention, alertness and their EEG correlates. In this respect, one of the main deficiencies of the literature is the lack of longitudinal studies establishing the permanent characteristics, if any, of a given group of patients.

Both the physiology and the psychophysiology underlying most of the aspects under review are still poorly understood and their possible value in psychiatry has to be defended on purely empirical and statistical grounds. This of course is largely due to our lack of knowledge of objective topography underlying normal mental processes.

For the practicing electroencephalographer it is also necessary to bear in mind the possibility that particular effects, observed in individual patients, may be due to drugs rather than to intrinsic physiological factors. The use of psychotropic agents is so common nowadays, and the fact of their use is so often unknown to the physician, that it is probably one of the most common sources of error in interpretation. Fortunately, some old literature is available concerning observations made prior to the introduction of psychotropic drugs. In addition, it must be emphasized that, although many of the following results have been shown to be highly significant statistically, their variability within a given clinical group is generally too great to give them much *diagnostic* significance in individual cases.

A. STANDARD, SPONTANEOUS EEG IN THE WAKING STATE

1. *Posterior activities*

(a) Alpha rhythms

Alpha rhythms are as often absent in a neurotic or psychotic population as in a normal group. This corresponds to the "alpha minus" type in Walter's classification (Golla *et al.* 1943). However, Liberson (1951) claimed that alpha activity was often better organized in the paranoid than in hebephrenic or catatonic schizophrenics. Neither complete nor incomplete alpha blocking on opening of the eyes or under the influence of other stimuli has significant correlation with psychiatric conditions. The topography of alpha activity has mostly been studied in schizophrenics, and in children with various dysfunctions of higher nervous activity (see these two Sub-sections).

Frequency. Normal subjects have a dominant frequency averaging 10 c/sec, with a normal distribution curve around this mode. Psychoneurotic patients do not give a normal distribution, but have a weighting on both the slower and the faster frequencies (8.5 and below, or 11.5 and above) (Brazier *et al.* 1945; Fischgold and Gastaut 1957); however, Ellingson (1954) in his review argues that no EEG abnormalities of frequency have been established in neurosis. In patients 60–70 years of age with "functional" mental disorders, a peak at 8.5 c/sec and another at 11.5 c/sec were found by Liberson (1951). Although this is still controversial, the peak in high frequencies would seem to relate to anxiety states; the peak in low frequencies is not so clear, these patients being distributed in various diagnostic groups such as hysteria, reactive depression, mixed psychoneurosis, etc. Automatic frequency analysis, cross- and auto-correlation and toposcopy are technical refinements which obviously hold promise, but yield no concrete results in clinical psychiatry to date.

Amplitude. Quantitative analysis has been concerned essentially with the frequency of brain waves: amplitude has been almost completely neglected, although Drohocki (1948) proposed a simple device which performs such analysis continuously and automatically (amplitude integration). Goldstein *et al.* (1965) have compared with this method the occipital EEGs of non-psychotic volunteers and of schizophrenics, and shown that the normal EEG is characterized by an *amplitude variability* which is twice as great (see also Chweitzer *et al.* 1936). The low variability (stability) in patients is seen from week to week as well as from minute to minute. Changes in position (recumbent or sitting), in the recording situation, and on opening the eyes affect the results in non-psychotics: schizophrenic records remain relatively invariable. Similar features have been identified in chronic alcoholics (Rimland 1964; Goldstein *et al.* 1965). Marjerisson *et al.* (1969) confirmed these observations in schizophrenia and made the interesting discovery that variability was particularly low during hallucinatory episodes in schizophrenic patients.

The mean energy content does not differentiate various male populations (normal controls, reformatory inmates and schizophrenics) but normal females show a significantly smaller mean energy. The relative invariability of the EEG of schizophrenics is interpreted by Goldstein *et al.* (1965) as a manifestation of hyperactivation, or of "information input overload". The schizophrenia-like effect of LSD given to normal subjects is accompanied by a marked decrease in variability. This is in agreement with much earlier findings of Chweitzer *et al.* (1936) who found both depression of the amplitude of alpha waves and a decrease of the variability following ingestion of mescaline inducing hallucinatory states.

(b) Slow posterior rhythms

"Posterior theta rhythm" (Gastaut *et al.* 1967a) seems a better term than "4 c/sec rhythm" sometimes used in the literature. Liberson (1945a, 1956) described in adults a bisynchronous occipital slow dysrhythmia at 5–6 c/sec, often predominant on the right side. It is found mostly in adult psychiatric patients with depression, particularly over 40 years of age. In these individuals, sleep studies show an "occipital beginning" of sleep theta waves instead of the usual onset in the region of the vertex. Later, slow posterior rhythms at 4 c/sec, plus or minus 1 c/sec, were correlated with hysterical personality (Dongier *et al.* 1964), and with emotional and autonomic instability. A possible interpretation of their relative (although controversial) predominance after head injury could be related to accident proneness.

(c) Slow posterior waves or pi waves

They are normally present in children's records, mostly on the non-dominant hemisphere, and to a lesser degree in young adults. Aird and Gastaut (1959) have found them in 10% of normal adults in the 19–22 years of age group. They have been correlated by Cohn and Nardini (1958) with aggressive behaviour. They may have some relationship with the "posterior temporal foci" described by Hill in anti-social personalities (see this Part). According to Timsit and Koninckx (1968) they are not, as one would expect, correlated with immaturity, but with hysterical personality among neurotic patients.

2. *Central activities*

(a) Beta rhythms are accentuated in various groups of neurotic and psychotic patients, compared with normal groups, and seem mostly related to anxiety, Liberson (1951) claimed that this activity was most prominent in patients with involutional

psychosis, paranoid type. Its incidence tends to decrease in groups (such as obsessional neurosis) where anxiety is less prominent. The tendency of barbiturates and anxiolytic drugs to induce beta rhythms must be considered in an EEG differential diagnosis.

(b) Mu rhythms, although as frequent in normal as in neurotic groups, have been described in the latter as correlated with hyper-emotionality (Gastaut *et al.* 1957, 1959; Dongier and Gastaut 1963; Timsit and Koninckx 1968). There are some arguments in favour of the view expressed by Bostem *et al.* (1964) that the physiological interpretation of mu rhtythms may be a superficial cortical inhibition. If this is so, a psychophysiological (as well as morphological) connection between the meaning of mu rhythm and of fourteen-and-six-per-sec positive spiking might be proposed.

(c) Excessive *theta rhythms* have been repeatedly related to symptoms of immaturity, aggressiveness, lack of emotional control, in various diagnostic categories. In some patients, Liberson (1956) found an association of theta activity in the anterior and lateral areas of the brain coexistent with well-organized alpha rhythm in the posterior regions and suggested that this pattern was a sign of immaturity. Mundy-Castle (1957) attempted to distinguish the significance of different types of theta activity, but this distinction does not seem to have found clinical applications. According to Timsit and Koninckx (1968), in a psychiatric group sinusoidal theta bursts seem to have little, if any, clinical significance, whereas sharp theta bursts ("theta angulaire") are usually correlated with other meaningful abnormalities (pi waves, excessive reaction to hyperventilation, photomyoclonic response).

3. *Anterior activities*

(a) Fast frontal rhythms of above normal amplitude have been related in children and adults to character disorders (Nekhorocheff 1952; Schneider 1957). In many respects they resemble the fast activities induced by drugs (barbiturates and diazepam derivates in particular); waxing and waning bursts of 10–20 μV, 25–30 c/sec, bilaterally synchronous and uninfluenced by eye opening. They are found in a very small proportion (0.5%) of routine records of the average EEG laboratory, and usually in patients with psychomotor restlessness, sleep disturbances and hypomanic or hypochondriacal tendencies.

(b) Slow waves (burst of theta–delta rhythms) have been described by Hill (1963) especially in catatonics (periodic catatonia), and also in acute schizophreniform states.

4. *Paroxysmal activities (spike and wave complexes)*

(a) Paroxysms of spikes and waves in neurotics without brain damage are always subclinical and generally isolated and not rhythmic. Seizures in these patients (*e.g.*, hysterical or anxiety attacks) are not concomitant with EEG discharges. The classical 3/sec spike and wave bursts, in which the spike is usually maximal in the frontal areas,

is traditionally regarded as "idiopathic" or inherited. It is usually correlated with epileptic seizures, mainly in children and adolescents.

The problem of the meaningfulness of spike and wave complexes (especially "phantoms") in psychiatry is far from being solved. In every individual case the organically-minded psychiatrist still systematically suspects a latent epilepsy, even in the absence of suggestive history. The more dynamically-minded, as Dell and Lairy (1960), will remind us that it is not difficult to induce a seizure in any human brain and that spike and wave phantoms may merely imply a low convulsive threshold, more frequent in hysteria than in other psychiatric conditions (at least according to a few authors). Here it is necessary to keep in mind the many psychiatric conditions in which low convulsive thresholds have been described (in particular, hysteria and catatonia). Unfortunately, in any individual, marked fluctuations in convulsive threshold are induced, for instance, by fatigue, lack of sleep, etc. This emphasizes the need for standardizing the conditions under which convulsive thresholds are estimated, and limits their diagnostic value to a considerable extent.

(b) The 6/sec spike and wave is a much rarer electrographic pattern (0.4% in 12,000 records) studied by Hughes *et al.* (1965), which Walter (1950) had previously called "wave and spike phantom". Usually maximal in the occipital areas, it is seen mainly in young adult females. As mentioned by Hughes *et al.* (1965) the majority of patients with the 6/sec spike and wave pattern have a history of some external precipitating factor, like trauma or excessive drug usage. The incidence of psychiatric symptoms, mostly chronic, is very high (78%), while convulsive attacks (grand mal essentially) occur in 62% and vegetative attacks in 72%. Silverman (1967) has given convincing arguments for a relationship between the 6/sec "phantom spike-waves" and the 14 and 6/sec positive spike phenomena, the former being subsumed for the most part by the latter.

B. REACTIVITY AND ACTIVATION

Reactivity to various stimuli, including pharmacological activations and conditional stimuli has been one of the most rewarding aspects of EEG in psychiatry, as shown by the Marseilles Colloqium (Frischgold and Gastaut 1957), which still remains a basic source of references. Psychiatric correlations with slow potential changes preceding and/or following various types of stimulation also show that the reactions to external or internal stimuli (such as decision) are more informative than the study of the brain "at rest".

1. *Intermittent photic stimulation (IPS)*

The use of photic stimulation is very pertinent in a laboratory working in the psychiatric field, with attention paid to several aspects:

(a) Subjective reactions such as anxiety and other symptoms are a valuable index of

anxiety proneness (Ulett *et al.* 1953). However, on a pragmatic level they are more interesting in psychology (for instance, in personnel selection) than in the psychiatric field proper, and later publications from the same group contain sobering commentaries on the variability of findings on repeated follow-up examination (Ulett *et al.* 1958, 1959). Nonetheless, in a minority of cases of hysteria, stimulation (especially at 4–7 flashed/sec) induces various subjective feelings such as intense anxiety (Bert and Courjon 1949).

(b) Driving in psychoneurotic states has been found to be less than normal within the range of 8–12 c/sec, but more with slower and faster frequencies. This has been related to differences in resting EEG rhythms between neurotics and normals (Mundy-Castle 1957), since it is easiest to "drive" at the frequencies predominant in the resting record.

(c) Paroxysmal discharges are induced by IPS in about 6% of a neurotic population against 1% of a normal control group, provided that IPS is applied for long enough and at a sufficient range of frequencies. These paroxysms may take the form of sharp waves or degraded spike and wave complexes localized to the posterior region, where they mix with the driving phenomena. They often appear either at the beginning or at the end of a series of flashes, or they may reach the whole scalp, generally with a posterior or central predominance, taking the shape of actual polyspikes and waves. They have been mostly related to the hysterical group of neuroses (Gastaut *et al.* 1959; Dongier *et al.* 1961), although contradictory data exist. In particular, a history of possible minimal brain damage may be found in a number of cases.

(d) The photomyoclonic response (PMR) described by Gastaut *et al.* (1951) is a phenomenon which the muscular component (Bickford *et al.* 1952) makes distinct from the photoconvulsive response, of purely cortical origin. What is recorded are the artefacts due to myoclonic jerks induced by IPS. They may be localized either to periorbital muscles alone, or include ocular musculature, or diffuse to the upper limbs or to the whole body.

Most authors agree that PMR are especially frequent in mental diseases, occurring on average in 1% of normal controls, 5% of neurones, 12% of psychoses. They are also more frequent in females and in alcoholics. Diffuse PMR are more significant (as far as severity of mental disturbance is concerned) than PMR localized to ocular or periorbital musculature. PMR seem to be of greater clinical significance when associated with posterior paroxysmal discharges on IPS and also with muscular startle on auditory stimulation (Timsit and Dongier 1970). The neurophysiological dysfunction underlying the PMR may undoubtedly be due to an organic lesion or stress (Shagass 1954b) but in most cases it can be interpreted as an abnormal accentuation of the normal, subclinical, photomotor microreflex (Bickford *et al.* 1964). How and why this reflex becomes exaggerated in a variety of "functional" mental disturbances remains a problem.

(e) The averaged evoked response (AER) to photic stimulation has so far given only inconclusive results in the psychiatric field. However, Heninger *et al.* (1966) have found a prolonged recovery cycle to paired stimuli in schizophrenics: the amplitude of the AER to the second flash is reduced, for the same interval as in the normal controls. The finding is analogous to that of Shagass (1972) with somato-sensory AER.

2. *Auditory stimulation*

(a) The *startle reaction* studied without summation technique includes:

i. A vertex sharp wave followed by a general desynchronization of the cortical rhythms (Bancaud *et al.* 1953; Y. Gastaut 1953). The latency of this wave approximates 90 msec. It is probably a sign of the "orienting reaction" described by Russian authors. The EEG nature of this potential has been questioned by Bickford *et al.* (1964), arguing that it might be of muscular origin. However, Davis has shown that distinction must be made between the early photomyoclonic potential (latency 6 msec) and the later components (latency 90 msec) of cerebral, non-specific origin. The latter are increased by muscular relaxation, whereas the former is decreased. There is a suggestion that it bears some relationship to the V wave of the K complex as seen in sleep (same latency (100 msec), localization and distribution).

ii. A jerk of variable intensity, recorded by actogram and/or EMG (EMG of periorbital muscles appears quite often as an artefact in the EEG record).

iii. A GSR and other autonomic changes. Repetition of stimulation normally induces a quick decrease in all these components (habituation). Lack of habituation has been described in psychiatric patients (Dongier *et al.* 1957) and in the "startle disease" described by Gastaut and Villeneuve (1967b), characterized by jerks of abnormal intensity and/or frequency following unexpected stimuli.

(b) Auditory AER. Callaway (1965) has developed a method to detect through the auditory AER one of the thought disorders characteristic of schizophrenia. Half-second tones of 600 and 1000 c/sec are sounded in haphazard order, and the high tone AER and low tone AER are computed separately. In non-schizophrenics, these two AER are almost identical; by contrast schizophrenics "seem unable to avoid wasting physiological energy in attending to the physical differences between the tones: correlation between high tone AER and low tone AER is lower than in non-schizophrenics". Jones *et al.* (1965, 1970) have used this test as a diagnostic and prognostic measure in schizophrenia (the two-tone AER correlations increase when schizophrenic patients improve). These studies still await confirmation.

3. *Somaesthetic stimulation; evoked potentials*

Somato-sensory AER. Shagass and Schwartz (1966) have reported that age (amplitudes of AER tend to increase with age) and sex factors were probably responsible for their earlier findings that patients with psychoses (schizophrenia, psychotic depression) and asocial personality disorders showed larger amplitude early components of the somato-sensory AER than normal individuals and psychoneurotics for the same intensity of stimulation. The stability of these potentials at rest is underscored by a study of Liberson (1966) who showed that these potentials may remain within the normal limits (on the involved hemisphere) in hemiplegics without aphasia.

4. *Event-related slow potentials (ERSP)*

All the various stimuli discussed in the previous Sub-sections are without meaning for the subject (or at least devoid of intended meaning). Standardized psychological situations have been proposed, such as word association tests (Liberson 1945b) and projective techniques (Faure 1950), but have not led very far for diagnostic purposes. More recently the discovery of the contingent negative variation (CNV) by Walter *et al.* (1964) has provided psychiatric EEG research with a new tool by which simple stimuli (such as clicks or flashes) are charged with semantic (symbolic) value (such as warning, action required from the subject, etc.). Study of slow potential changes, preceding or following these stimuli, requires of course special equipment (long time constants, averagers or computers: see special Part on technique and description of ERSP) and appears as a most promising field in psychiatry.

(a) CNV. The Bristol group (especially Grey Walter and McCallum) assumed from the beginning a probable relationship of CNV (expectancy wave or E wave) and psychiatric phenomena; Walter directed two international colloquia (Dargent and Dongier 1969; Knott and McCallum 1973) devoted to this topic. Most workers were initially interested in *amplitude* of the CNV, and McCallum found it reduced in psychopaths and variably influenced by a distracting sound (recovery is quick in

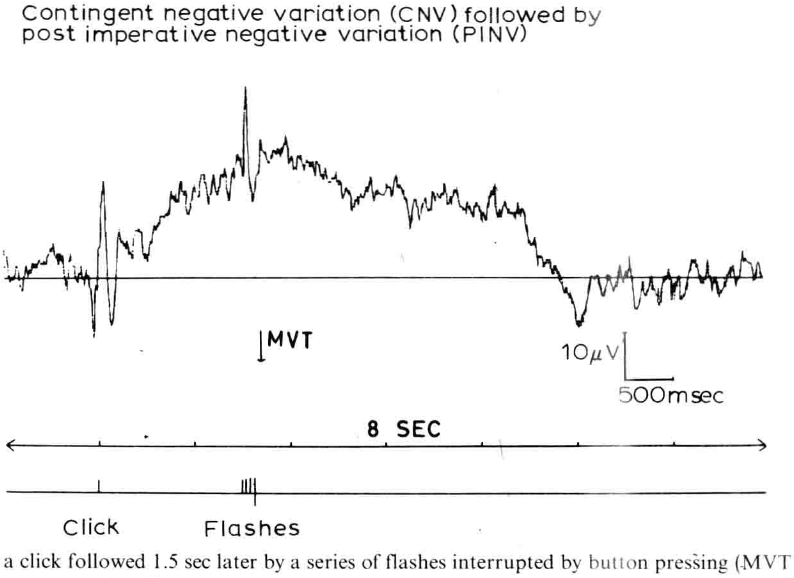

Fig. 1. S_1 is a click followed 1.5 sec later by a series of flashes interrupted by button pressing (MVT). 3 sec elapse before return to baseline.

normals, partial or absent in chronic anxiety cases and schizophrenia). However, the amplitude of the CNV is very much influenced by various psychophysiological factors, and hence liable to fluctuate considerably from moment to moment. For this reason studies of variability deserve exploration for psychiatric diagnostic use.

(b) Post-imperative negative variation (PINV) or C wave ("C" for conflictual) is a term which has been proposed for the prolonged negativity which follows the subject's response to the second stimulus in the CNV paradigm. It has been mostly observed in psychotic and less often in neurotic patients. It initially appeared in CNV experiments as a prolongation of the E wave, but it soon became manifest that it does not depend, like the CNV, on as association of stimuli, but appears after a single imperative stimulus, especially in psychiatric patients (Fig. 1 and 2) (Dongier *et al.* 1973).

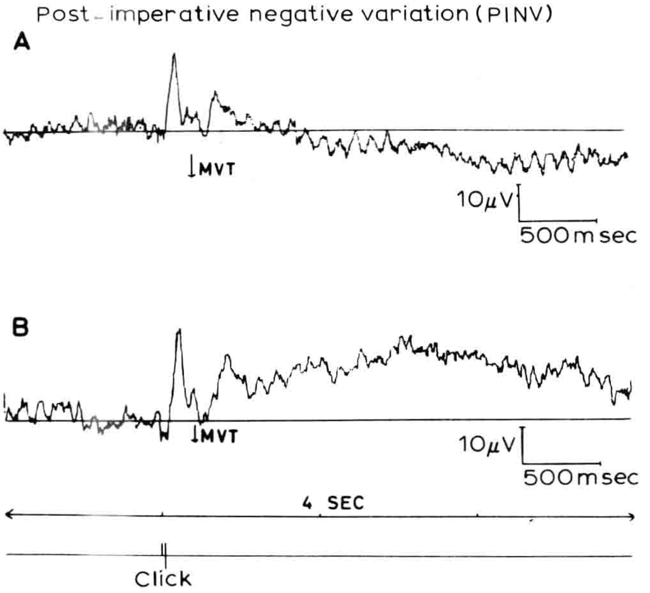

Fig. 2. There is no warning stimulus, the paradigm is limited to sound interrupted by button pressing (MVT). *A*: Normal subject: no lasting negativity following the evoked potential. *B*: Schizophrenic patient (same as Fig. 1): PINV lasting about 3 sec.

(c) Readiness potential. Grey Walter proposed to call intention wave or P wave ("P" for preparation) a phenomenon described by Kornhuber and Deecke (1965) under the name of Bereitschaftspotential (readiness potential): a negative slow wave preceding any voluntary movement. After the movement a positive potential follows. Timsit-Berthier (1970) described the changes in this potential frequently observed in psychotic patients (Fig. 3).

(d) Transcephalic DC potentials. Cowen (1968) recorded a transcephalic prolonged potential between the frontal and occipital midline regions. A negative frontal shift occurred when the subject attended to an exteroceptive or proprioceptive stimulus.

Anxiety increased variance without imparting a specific polarity to the potential. Thus, says Cowen, "the potential appears to monitor certain aspects of the reality testing processes".

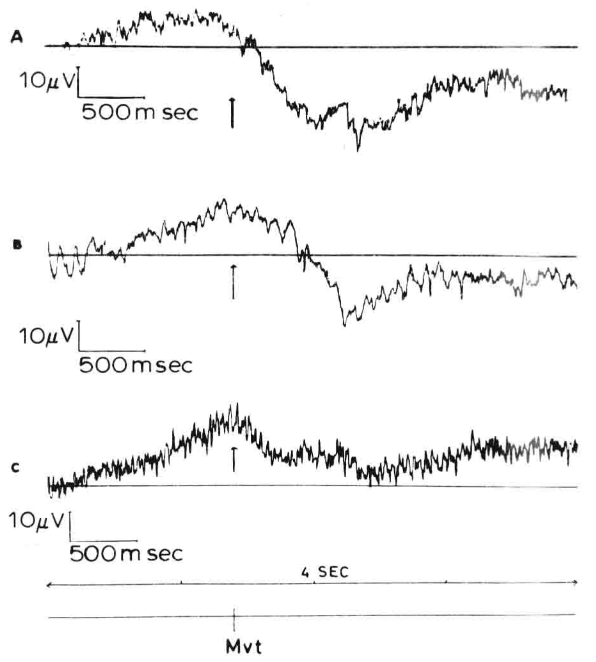

Fig. 3. Summation of 20 spontaneous voluntary button presses. *A* is a normal control, *B* and *C* psychotic patients. In all three cases there is a normal pre-motor negativity (readiness potential) lasting about 1 sec. In subject *A* it is quickly followed by a post-motor positivity; this is delayed for about 600 msec for patient *B* and the positivity does not occur in case *C*, both patterns being considered abnormal.

Schizophrenics were reported to differ markedly from both normal and non-schizophrenic mental hospital patients (catatonics being significantly more abnormal). For instance, schizophrenics with hallucinations had unusually large negative trans-cephalic DC potential peaks in comparison with other schizophrenics.

5. *Convulsive threshold*

The convulsive threshold, whether measured with intravenous Metrazol or other convulsant agents, must be considered among the EEG aspects which are too dependent on psychophysiological factors such as fatigue, vigilance, etc., to be given much confidence as a diagnostic test. However, the photo-Metrazol threshold is often low in schizophrenia (Leffman and Perlo 1955). Chamberlain and Gordon-Russell (1953) found a relationship in schizophrenics between the photo-Metrazol threshold and body build: leptosomatic patients had significantly lower thresholds than those of pyknic habitus. We do not know of similar studies in non-schizophrenic patients.

Alpha chloralose activation

Abnormalities (mostly generalized paroxysmal slow waves) were induced in 40 to 60% of psychiatric patients with no symptoms of epilepsy, and only in 21.7% of volunteers (Monroe and Mickle 1967). These abnormalities were more frequent in psychopaths (75%) than in patients with central nervous system lesions (66.7%); they are also found in schizophrenics (59.3%), affective psychoses (42.4%) and neurotics (37.5%). The authors comment that activation is less frequent in records of older patients, suggesting that it may reflect some CNS immaturity.

6. *Hyperventilation and hypoxia*

Overbreathing is the most common method of activation, but the proportion of clinically useful findings is small. Hysterics, psychologically immature individuals and aggressive psychopaths react with more slow waves on hyperventilation than the average normal subject (Gastaut *et al.* 1957). The percentage of abnormal reactions decreases with age in these groups, suggesting once more a delayed maturation (Liberson and Strauss 1941). (Liberson (1951) claimed that the presence of hyperventilation responses in involutional psychosis was of poor prognostic significance.)

7. *Barbiturates and sedation threshold*

Barbiturates have been used as an activating method, not only to induce sleep (see next Section) but also to measure various reactions of the brain. For instance, Shagass (1954a), Goldman (1959), Itil (1966) and Murphree *et al.* (1967) proposed various procedures of measurement.

(a) Sedation threshold (Shagass 1954a). An intravenous injection of 0.5 mg/kg of sodium amytal is repeated every 40 sec until slurring of speech is obtained. The amount of fast activity (15–30 c/sec) in the frontal region is measured either visually or with a frequency analyser. The sedation threshold (corresponding roughly to the onset of slurred speech, but in fact occurring often substantially later) is determined when the additional amount of fast activity produced by further increments of the drug is sharply diminished. The threshold is low in organic psychotic states and in endogenous depressions, high in schizophrenia and in neurotic depression.

The validity of Shagass' results has been questioned by several workers, for instance Ackner and Pampiglione (1959), but confirmed by a majority of others such as Kawi (1958), Nymgaard (1959) and Seager (1960). Probably one of the main problems with the method is that it is not as objective as was initially hoped. It does require specially trained personnel.

(b) In Goldman's (1959) technique, 100 mg of thiopentone sodium (Pentothal) is administered rapidly up to four times at two minute intervals, and produces characteristic EEG changes in schizophrenics. These comprise bilaterally synchronous theta activity with an amplitude of 100 μV appearing soon after the injection, fast activity