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MULTIPARAMETRIC OUTLINES WITH CNV APPLICATION TO DEPRESSIVE SYNDROMES

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The contingent negative variable (CNV) is a slow component recorded at scalp during temporal conditioning (Walter *et al.*, 1964; Picton and Stuss, 1980). It is an event-related slow potential which is considered to be endogenous (Donchin *et al.*, 1978). Studies show the importance of degree of vigilance, anxiety, motivation and resistance to stress to this wave (Knott and Irwin, 1973; Paty *et al.*, 1980), and also the modification of static characteristics of the CNV in some mental illnesses (Lelord, 1973; Timsit-Berthier, 1970; Usdin *et al.*, 1977).

Our work is based upon a more dynamic approach to the CNV using new indices and allowing an elaboration of different emotional and motivational levels during a sequence of several conditions. The CNV appears useful as an index of cerebral plasticity and of behavior adaptation of particular interest in psychopathological evaluation.

METHOD

Subjects

Sixteen depressive patients (8 men and 8 women; 47 ± 16 years; 8 endogenous melancholics and 8 neurotic depressives) were selected according to the medical diagnosis, the Wittenborn Psychiatric Rating Scales and the Stroop Color Word Stress Test. The results to the Wittenborn PRS for the endogenous patients were: 5.7 to scale 1 (anxiety), 5.3 to scale 4 (depression), and 4.8 to scale 9 (anankasty). For the neurotic patients the results were: 5.75 to scale 1, 5.5 to scale 4, and 5.25 to scale 9. A control group was composed of 16 healthy subjects (9 men and 7 women; 46.8 ± 12 years).

Procedure

The potentials were recorded at Fz, Cz, Pz, P1 and P2 with linked earlobe reference and amplified (AC) with a long time constant (6 sec). The data were then automatically computerized with artifact rejection (EOG, EMG, *etc.*).

Stimuli (S_1 and S_2) were emitted at 2 second intervals. The warning (S_1) was a

filtered click of 1200 Hz and 70 dB. The conditional signal (S_2) was a sequence of flashes of light of 10 Wh and 5 μ s which the subject was instructed to interrupt. A reaction time was measured in this way. Averaging was calculated on 10 trials.

The protocol and the experimental situation have been described in other papers (Paty *et al.*, this volume). Five conditions were sequentially presented to the subjects.

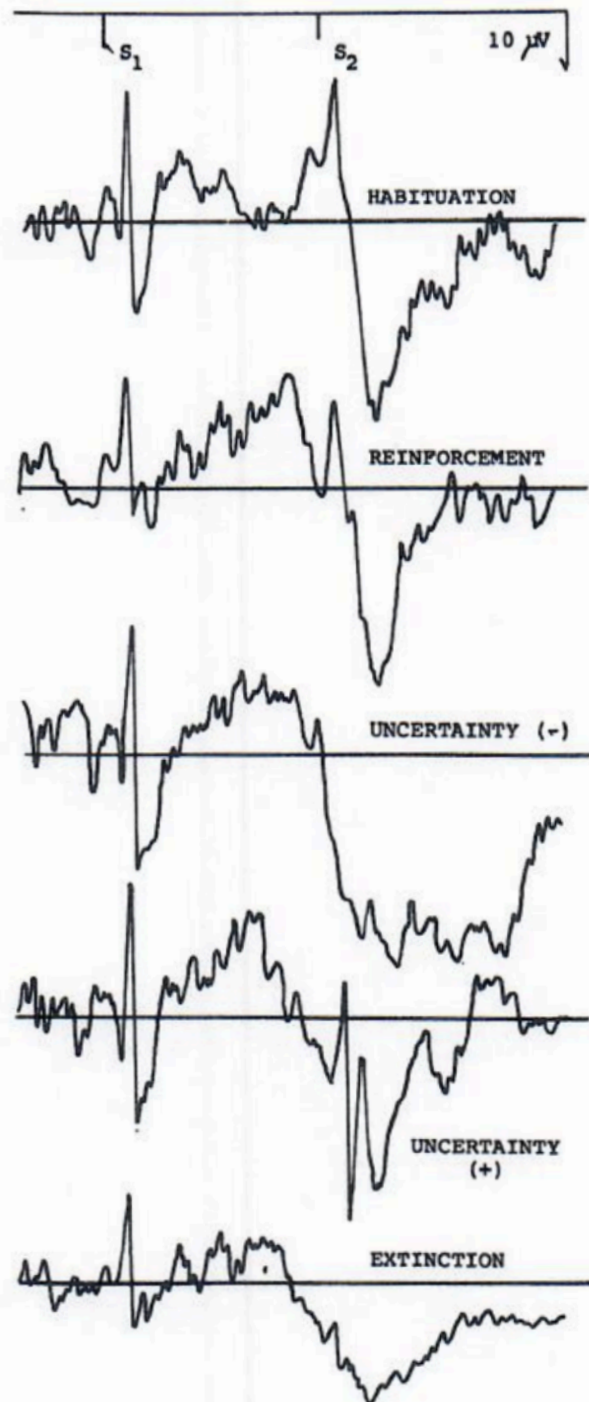


FIGURE 1. The paradigm with five conditions (habituation, reinforcement, uncertainty (-), uncertainty (+), extinction) tested in a depressive subject.

Habituation (1) was a random presentation of S_1 - S_2 stimulations every 20 or 25 seconds. Reinforcement (2) was the same presentation with positive reinforcement by announcing the reaction time. Uncertainty plus (3) and minus (4) were two situations of presentation of S_1 - S_2 with random suppression of S_2 without previous warning to the

subject; the averaging was made separately according to the presence (uncertainty +) or absence (uncertainty -) of S_2 . Extinction (5) was obtained by systematic suppression of S_2 .

The average reaction time and its standard deviation were calculated for each condition. The average amplitude of the CNV was calculated by means and standard scores in five time bands: Na and Nb (between 500 and 800 ms, and 1500 and 1800 ms after S_1), Pa, Pb and Pc (between 200 and 700 ms, 1500 and 1800 ms, and 2400 and 2600 ms after S_2). These measures are shown in FIGURE 3. The following wave features were distinguished: normal ascending CNV and normal descending CNV, positive CNV, prolonged CNV or flat CNV. (See Paty *et al.*, this volume.)

Data Analysis

In considering the amplitudes, our analysis was not based upon the direct measures Na, Nb, Pa, Pb, and Pc, but upon a parameter describing the initial amplitude Na and upon an exhaustive system describing the rest of the signal by the amplitudes relative to Na: Nb/Na, Pa/Na, Pb/Na, Pc/Na. The choice of these parameters rests on a theoretical consideration of signal time series analysis. The CNV can be considered to be a signal $f(t)$ sampled at the n times (i) and entirely defined by the $n(n-1)/2$ quantities:

$$\begin{aligned} &f(t_1)/f(t_2); \quad f(t_1)/f(t_3); \quad f(t_1)/f(t_4); \quad \dots\dots\dots; \quad f(t_1)/f(t_n); \\ &f(t_2)/f(t_1); \quad f(t_2)/f(t_3); \quad \dots\dots\dots; \quad f(t_2)/f(t_n); \\ &\dots\dots\dots; \quad \dots\dots\dots; \quad \dots\dots\dots; \\ &f(t_{n-1})/f(t_n); \quad f(t_1). \end{aligned}$$

However, the careful study of this system shows that all the quantities, $f(t_2)/f(t_1)$, $f(t_3)/f(t_1)$, $f(t_4)/f(t_1)$, $\dots\dots\dots$, $f(t_n)/f(t_1)$ form an exhaustive system (S), that is to say, all the other quantities $f(t_i)/f(t_j)$ can be a simple combination of two elements of the system (S), so $f(t_i)/f(t_j) = f(t_i)/f(t_1) \times f(t_1)/f(t_j)$.

We chose $(t_1) = \text{Na}$ as Na is always far enough before the baseline so that the division of this quantity can be carried out in the most discriminatory manner. Out of all the exhaustive systems, we decided to use the first one as S.

In considering the effect of condition, the quotient is σ/m for every index taken into account for each subject, m being the mean of the values of the index in the 5 conditions, σ being the standard score in these conditions. For instance, $\text{SI}(\text{Na}) = \sigma/m(\text{Na})$ in habituation, reinforcement, uncertainty (+) and uncertainty (-), and extinction conditions.

Comparisons were interpreted with the aid of analysis of variance and student's t -test. We also looked for CNV correlates of the results of the Wittenborn and Stroop tests.

RESULTS

TABLE 1 shows a condition effect for reaction time. For the control group, reaction time (RT) was significantly shorter for the reinforcement condition than for the habituation condition and longer in the uncertainty condition. RT was generally longer

TABLE 1. Depressive Disorders: Significant Parameters ($p < 0.1$) in Depressive Patients and Control Group

Parameters	Condition	Control Subjects ($n = 16$)	Depressive Patients ($n = 16$)	F Statistic	Probability
Performance					
RT	Habituation	120.7 ms	182.1 ms	7.24	0.012
SRT	Habituation	23.9 ms	72.6 ms	16.73	0.0003
RT	Reinforcement	118.8 ms	171.1 ms	4.51	0.043
SRT	Reinforcement	23.1 ms	63.0 ms	14.16	0.0008
RT	Uncertainty	136.6 ms	215.6 ms	6.44	0.017
CNV Index					
Nb/Na	Habituation	0.94	0.15	3.32	0.078
Nb/Na	Uncertainty +	0.97	0.31	6.49	0.016
Pa/Na	Reinforcement	-0.51	0.46	2.88	0.10
Pb/Na	Reinforcement	-0.64	0.38	5.11	0.032
Pc/Na	Extinction	-0.12	2.11	3.40	0.076
1s Pc	Extinction	0.99	1.87	4.05	0.053

in depressive patients, and the variability was significantly augmented, but the condition effect was still present.

The amplitudes of the CNV were always smaller in the depressives than in the control subjects. This difference was more or less marked according to the condition. The Na amplitude was smaller in the depressive in the habituation condition, but this difference increased in the other conditions.

Moreover, there exist differences between endogenous and neurotic depressives. In the habituation condition, the neurotics differed little from the control subjects when the mean Na amplitudes were much smaller. In conditions of interference (reinforcement and uncertainty), the Na amplitude has diminished the maximal preimperative indices (Nb/Na) and the condition of reinforcement altered the maximal post-imperative indices (Pa/Na, Pb/Na) in the depressives. The Pc postimperative index was significantly altered in the depressives only in the extinction condition.

The condition effect has to be appreciated in every subject by the index of the variability of the amplitudes of the CNV according to the conditions defined. Standard

TABLE 2. Depressive Disorders: Condition Effect (Calculated on Reaction Time and Amplitude Indices: Mean Values in the Two Nosological Classes)

Situations	Control Subject (<i>n</i> = 16)	Depressive Patients (<i>n</i> = 16)	Depressives	
			Neurotic (<i>n</i> = 8)	Endogenous (<i>n</i> = 8)
Performance				
RT	0.142	0.182	0.215	0.142
SRT	0.355	0.425	0.482	0.370
CNV Index				
Na	0.335	0.732	0.657	0.782
Nb	4.242	3.747	2.715	4.972
Pa	1.637	1.257	2.492	0.847
Pb	1.520	0.695	1.637	0.365
Pc	0.990	1.875	3.680	0.678

score/means were calculated for each of the parameters, RT, SRT and amplitude indices. TABLE 2 shows the condition effect differences between the neurotic group and the endogenous group, in the preimperative and the postimperative part of the CNV. The index decreased in the preimperative part in the neurotics but not in the endogenous. It decreased greatly in the postimperative part in the endogenous compared with the control subjects.

The abnormal CNV waveshape was more frequent in the patients than in the control subjects. The existence of these form anomalies were more frequent in emotional interference situations (reinforcement and uncertainty). Thus, 100% of abnormal forms could be observed in situations of uncertainty, 88% in situations of reinforcement and habituation in endogenous patients, more than 75% in situations of interference, more than 50% in situations of habituation in neurosis, and less than 40% in control subjects. Positive CNV was never observed in the control group, but was frequently observed in the endogenous group, particularly in the reinforcement condition.

Multiparametric Outlines

A synthetic representation using individual profiles enables us to visualize the data of the test as a whole (amplitudes, synthetic forms, types of CNV, variation according to the conditions). FIGURE 2 represents four individual outlines. For the control subject with CNV or normal features, and normal amplitudes, the condition effect is noticeable. The neurotic patient has a CNV with abnormal features in the habituation condition and shows a discreet, postimperative negativity. The situation effect is clearly marked. Two endogenous patients are shown in the figure. The first shows a CNV with a positive polarity in all the conditions; the second shows a smaller amplitude in all the conditions.

The significant correlations of amplitude measures with clinical traits shown in FIGURE 3 indicate the relevance of test situations. A high level of anxiety, of anankasty and of compulsive character (Wittenborn) correlates with a poorer habituation of the CNV and a later extinction (larger amplitudes). General or specific speed to the test of stress (Stroop) correlates with a larger amplitude of the postimperative components in situations of uncertainty. The level of depression (Wittenborn) and the sensitivity to interference (Stroop) correlates mainly with the amplitude of Na (preimperative) in the conditions of reinforcement and uncertainty.

DISCUSSION

The comparison between depressive and health subjects using a dynamic approach to the CNV allows us to demonstrate a methodology of evaluation of behavior in psychopathology and psychiatry. The results pose three types of issues: (1) the neurobiological significance of the CNV, (2) an appreciation of behavior in psychiatry, (3) the notion of the depressive state.

Neurobiological Significance of the CNV

The CNV is a composite potential which corresponds to a DC shift. According to Wilder's law (1957), the variation would depend on the initial level relating to the

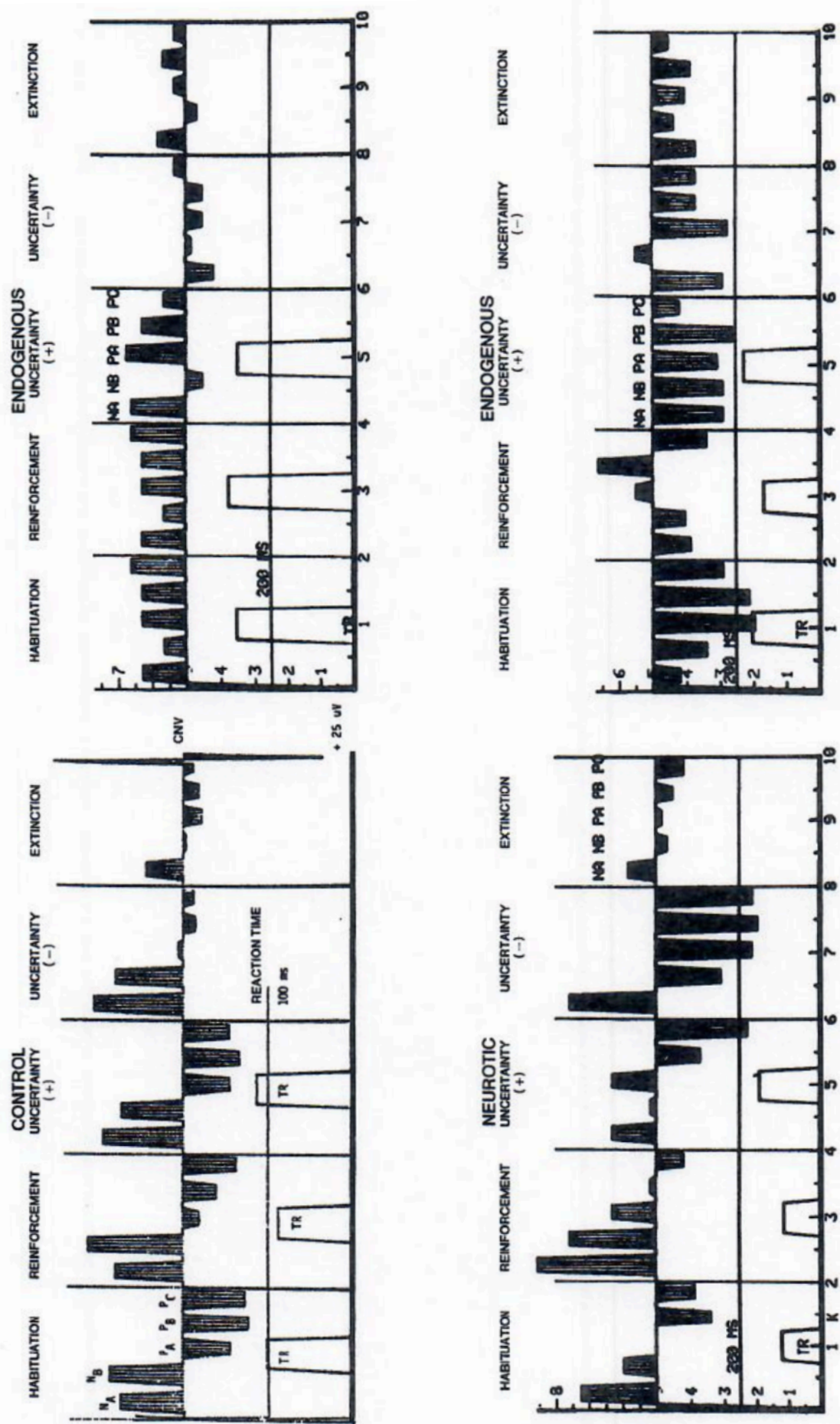


FIGURE 2. Multiparametric profiles with the five measures of amplitude and the reaction times.

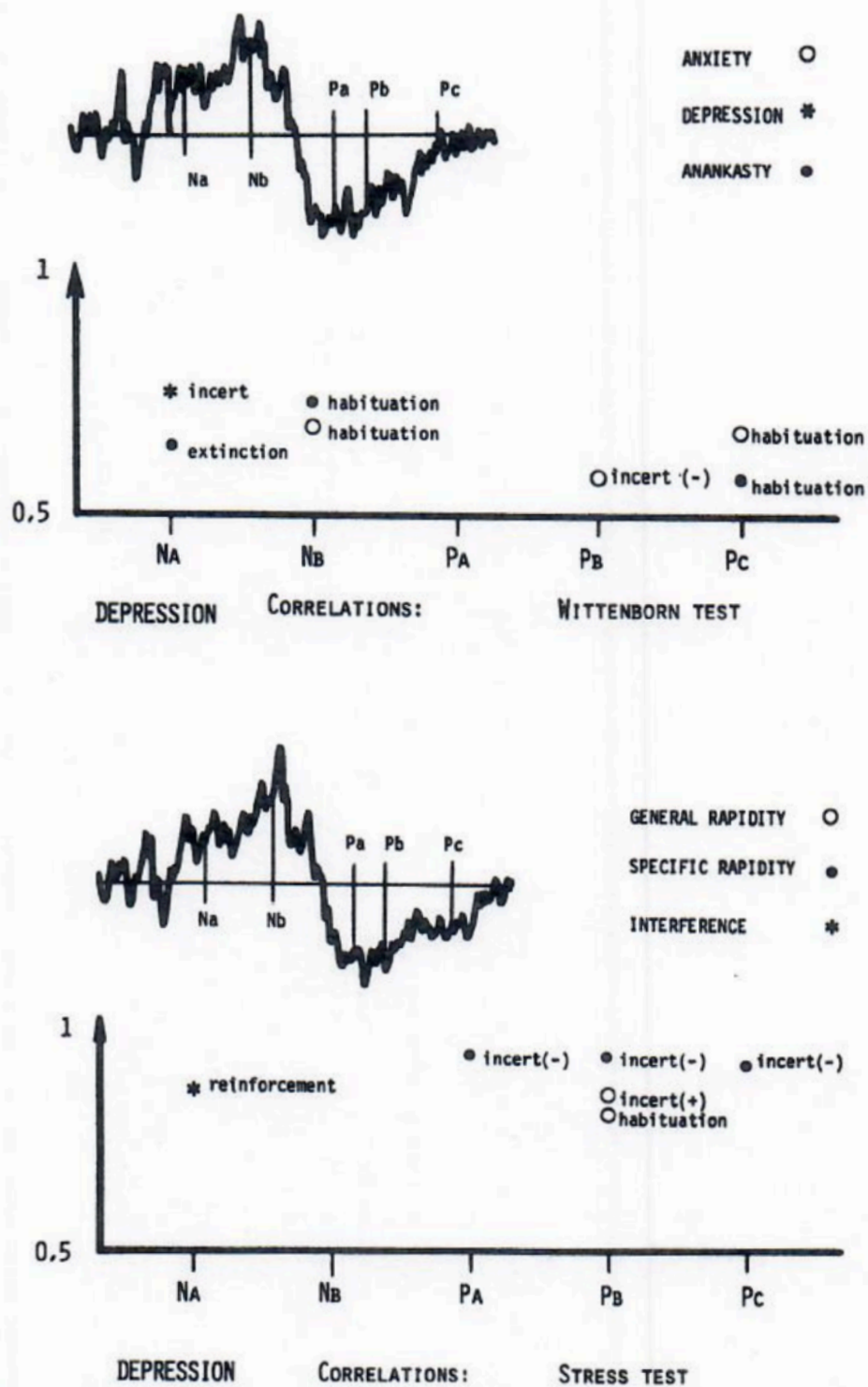


FIGURE 3. Correlation coefficients: psychological features (Wittenborn scale and Stroop test) and CNV indices.

general degree of cerebral activation (Requin, 1969; Picton and Stuss, 1980). It is not easy to assess the initial level by traditional methods. However, this evaluation can be approximated thanks to margins of variation related to the psychological task and to our protocol using different conditions.

The preimperative period corresponds to two strategies of different features. For some subjects, the response to the second stimulation is prepared for only after a certain delay from the alarm signal. Here the CNV appears late (type 1) and the reaction time is unstable. For others, the preparation begins with first stimulation and the reaction times are longer but more stable (type 2).

In the case of the neurotics, the decreasing CNV could represent a diminishing level of attention in the preimperative periods. Usually, the amplitude is smaller in the depressives, which could represent a lower activation from the initial level. Therefore, the positive CNV (type 3) in endogenous depressives could correspond to a very high initial level of activation and to a relaxation of the initial level. Most anomalies appear in the postimperative period, especially in the endogenous group. This time is one of self-evaluation of performance and then relaxation of the initial level.

Thus, it is necessary to note the importance of abnormal waveforms in situations of emotional interference, when standard situations do not identify them. These anomalies seem to be linked to variations of test situation.

CNV and Behavior

In the neurotics, large modifications appear in interference situations of reinforcement and uncertainty. In the endogenous group, extinction seems slower. We devised a situation index which takes into account the plasticity of the attention of the subject.

The neurotics have large variability and the endogenous group has small variability compared to the control subjects. The evaluation of the reaction times allows us to relate habituation and performance of the subject during the task.

Psychopathological Interpretation

The correlations with psychopathological features point in the favor of a pattern corresponding more to psychological elements—*cognitive strategies, selective attention, resistance to stress, habituation, perseverances, etc.*—than to classical nosographic categories that appear to be too global. These results allow us to stress the interest of behavioral studies using the CNV, and to illustrate the importance of studies using a more dynamic approach to the CNV wave in the evaluation of psychopathological disorder.

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