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The contribution of digitized electroencephalogram in the clinical and therapeutic monitoring of substance uses disorders

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ABSTRACT

The approaches used in clinical and therapeutic monitoring in addictology are multiple and generally based on subjective instruments such as interviews or observations. However, the lack of frankness can be an obstacle, as the patients monitored may not be entirely honest in their responses, and improvement in symptoms does not always mean continued abstinence. This article proposes a new objective method for monitoring the clinical and therapeutic evolution of addicted patients based on the study of electro-physiological changes collected by digitized electroencephalogram (EEG). The study is a case-control study of 30 hospitalized addicts who met the diagnostic and statistical manual of mental disorders (DSM-V) criteria for substance use disorders substance use disorders (SUD) and who underwent a standard digitized EEG at the end of their hospitalization. A control group of 30 healthy individuals was also included. This research shows a dominance of rapid-frequency beta 2 and hypovolted alpha 2 rhythms in cases with a clear sensitivity to activating maneuvers occasioned by hyperpnoea (HPN) and intermittent light stimulation (ISL) giving either a significant slowing of electrogenesis, bi-occipital entrainment, or an oculo-clonic response signifying a need for further care. However, the major challenge in understanding the EEG signal is that it is not always specific to SUD and suggests the need to consider the trans-diagnostic framework.

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1. INTRODUCTION

Substance use disorders (SUDs) pose a major global public health challenge [1]–[3] and research on associated treatments faces significant obstacles such as the lack of objective brain markers to accurately assess clinical progression and the outcomes of therapeutic interventions. This gap hinders not only an in-depth understanding of the underlying mechanisms of SUD, but also the development of effective, personalized treatments. Identifying reliable brain markers could enable more accurate assessment of the effects of therapeutic interventions, thereby facilitating more effective treatment and better long-term management of SUD.

The tools usually used in clinical monitoring and therapeutic evaluation during the management of addictions are many and are based on interviews, questionnaires, and scales or observations [4]. The use of these evaluation instruments should certainly make it possible to identify qualitatively and/or quantitatively the clinical and therapeutic evolution of addiction [5]. Still, the lack of frankness may establish an obstacle, as it is possible that the patients monitored are not entirely honest in their answers. Thus, the improvement in symptoms does not always mean that abstinence is maintained, hence the need to use more objective and reliable methods. However, truly evaluating the effectiveness of a therapeutic program is rarely an easy task [6].

Electroencephalography (EEG) is emerging as a promising neurophysiological technique, enabling direct measurement of brain activity during these addictions [7], [8]. Although our understanding of EEG activity associated with acute and chronic substance use is relatively well-developed, there are still gaps in our knowledge of EEG about abstinence phases and treatment outcomes [9]–[11]. This lack of information highlights a crucial need for in-depth research aimed at gaining a better understanding of EEG patterns during periods of abstinence and establishing correlations with treatment efficacy [11]. The identification of specific EEG markers could be a major advance, facilitating objective monitoring of progress in SUD treatment and opening up new prospects for more targeted and personalized interventions [12].

EEG rhythms can provide crucial information for the clinical and therapeutic monitoring of addicted patients. The key points on their importance are multiple: i) assessment of the severity of the addiction because studies have shown alterations in alpha and beta rhythms in addicted individuals compared with non-addicts. Reduced amplitudes of alpha waves and increased beta frequencies have been associated with greater severity of addiction [13]; ii) monitoring the effectiveness of treatment because changes in alpha and beta rhythms can be used to assess the effectiveness of therapeutic interventions. For example, studies have shown that reduction in substance use correlates with specific changes in brain activity, such as an increase in alpha waves [14]; iii) predicting treatment outcomes as EEG rhythm characteristics can also be used as biomarkers to predict treatment outcomes. As an example, predictive models based on EEG measurements have shown an ability to distinguish individuals who are successful in recovery from those who relapse [15]; and iv) guiding therapeutic interventions by monitoring alpha and beta rhythms, clinicians can tailor therapeutic interventions more precisely. For example, neurofeedback, a technique aimed at modifying brain activity patterns, can be adjusted according to the specific characteristics of the patient's EEG rhythms [16]. However, to date, there are no truly established brain biomarkers for precise monitoring of SUD treatment and evaluation of results.

It can be concluded that EEG can therefore play an important role in the therapeutic and clinical monitoring of addictions by providing information on neurophysiological alterations associated with addiction, monitoring response to treatment, predicting treatment outcome, and assessing treatment-induced neuroplastic changes. In reality, however, the examination of EEG signals in correlation with clinical and therapeutic evolution is rarely or superficially studied, which is why the present research aims to monitor neurophysiological changes using EEG as an objective method in the hope of contributing to a more personalized and effective approach to the management of addiction. The main contribution of this research work is to establish an informed framework for addictologists to develop pharmacological, psychotherapeutic, and/or neuromodulator interventions based on the objective measurement of brain electrical changes that can enhance the brain's ability to repair itself, restore cognitive function and contribute to positive long-term treatment outcomes in people with addiction.

The rest of the document is organized as follows: section 2 describes the method applied in this research work. Section 3 presents the experimental results and their detailed discussion. Finally, we conclude our overall research work in section 4 with future perspectives.

2. METHOD

This study was carried out on patients with a substance use disorder hospitalized at the national addictology center at the Arrazi Hospital of the CHUIS Rabat-Salé in Morocco. The choice of study site was justified by the availability of the study population in large numbers, as well as the availability of an EEG laboratory with multidisciplinary staff qualified and competent in terms of EEG recording, analysis and interpretation. It should also be noted that this structure devotes a major part of its activities to scientific research and the promotion of innovative methods in the management of SUD.

2.1. Subjects

30 SUD patients who had an EEG at the end of their hospitalization and who are defined according to diagnostic and statistical manual of mental disorders (DSM-V) criteria [17] presenting with a pattern of problematic substance use leading to clinically significant impairment in functioning or suffering, characterized by the presence of at least two of the following manifestations over a 12-month period: i) reduced control, with

persistent desire or unsuccessful efforts to reduce or control use, ii) psychosocial repercussions associated with the user's behavior leading to the inability to fulfil major obligations at work, school or home with reduction or abandonment of important activities, iii) manifestations of risk-taking behavior such as repeated use in situations where it may be physically dangerous despite awareness that a physical or psychological problem is likely to have been caused or exacerbated by the substance, and iv) physiological signs such as tolerance and withdrawal defined by a need for more of the substance to obtain the desired level of intoxication if not the onset of a withdrawal syndrome, characteristic of the substance used.

A group of 30 healthy controls was matched strictly on the basis of sex and age. Inclusion and exclusion criteria were established for these two groups of participants as explained in Table 1. The important consideration was to find participants who were free of any other disorders that might affect the results of our research.

The number of participants was identical in the two groups, fifteen men and fifteen women. The average age was 29 in the SUD group and 28 in the control group. Patients were asked to stop taking any medication the day before the EEG test. The researchers made contact with the study participants (cases and controls). Each participant was contacted in advance to explain the objectives of the research and to arrange an appointment to suit his or her availability. The researchers would explain the location of the examination (EEG laboratory) and the time (from 08:30 in the morning). It should be noted that each participant asked to take part in the study would have to sign a consent form to obtain his or her approval and positive agreement to take part in the study.

Table 1. Inclusion and exclusion criteria for study participants

Participants	Inclusion criteria	Exclusion criteria
Cases (SUD)	- Inpatients meeting DSM-V criteria for substance abuse. - Patients complying with treatment modalities (therapeutic compliance and psychotherapy sessions.)	- psychotic patients; - patients with organic brain pathology (vascular, tumor or degenerative); - patients with a confusional or dementia syndrome; - patients suffering from metabolic disorders or who have had a severe head injury; - Patients receiving thermoregulatory treatment.
Controls (Healthy people)	- Healthy people with similar characteristics to the cases (age, sex)	- Carriers of neurological or chronic diseases. - Previous consultation for addiction problems - Current or past drug users. - Taking any treatment or herbal medicine that could alter the results of the examination.

2.2. EG recording procedure

A standard digital EEG examination at rest was carried out for each participant. The principle of the EEG is to capture, amplify, format, and visualize the activity of several electrodes at the same time to determine the potential changes that may appear in a given part of the scalp. 16 electrodes (Fp1, F7, F3, C3, T3, T5, P3, O1, Fp2, F8, F4, C4, T4, T6, P4 and O2) are placed on the scalp according to the 10-20 international system to be as close as possible to the source generating the electrical activity as shown in Figure 1.

The minimum duration of the examination is 20 minutes, in strict compliance with the technical conditions of the examination and includes at least one or two 3-minutes hyperpnoea (HPN) tests and intermittent light stimulation (ILS). As a general rule, each EEG in the laboratory consists of i) a resting sequence with the eyes closed, ii) brief visual stimulation sequences (opening and closing of the eyes), and iii) activation sequences HPN and ILS Figure 2. At each of these stages, any change in the patient's state of alertness, any movement, and any intercurrent external event must be noted on the trace automatically in the form of annotations.

A bipolar longitudinal, transverse, and referential montage was chosen to display activity across the entire cranium and provide lateralization and localization information in Figures 3(a) to 3(c). Firstly, the longitudinal montage allows us to observe differences in electrical activity between the anterior and posterior regions of the skull. This is essential for understanding how cerebral functions are distributed along the front-back axis of the brain. Secondly, the transverse montage is particularly effective for examining variations in electrical activity between the right and left hemispheres of the brain. This perspective helps to identify potential asymmetries and to assess the functional specialization of different brain regions. Finally, the referential set-up is crucial as it uses a common reference for each recording channel, allowing accurate comparison of electrical signals between different regions of the skull. This helps to minimize artefacts and obtain more accurate electrophysiological measurements.

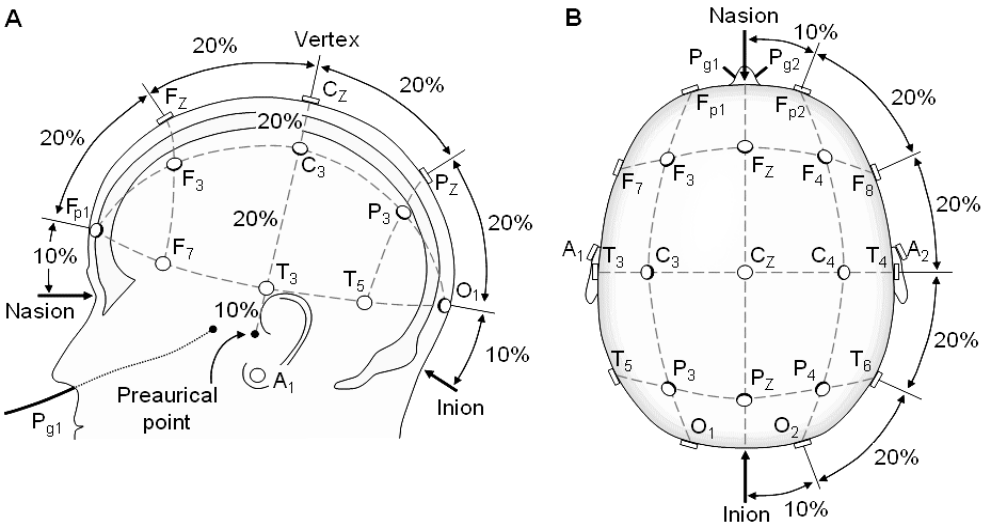

Figure 1. Measurement method for positioning the electrodes in the 10-20 system [18]

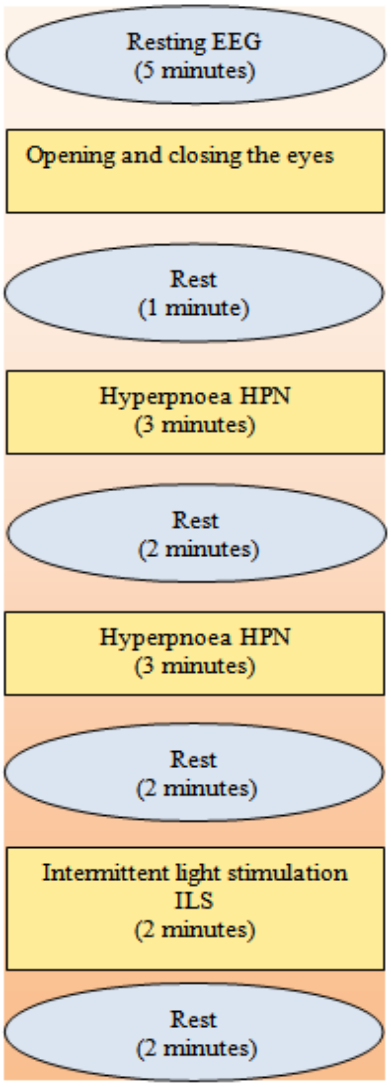

Figure 2. EEG recording sequence

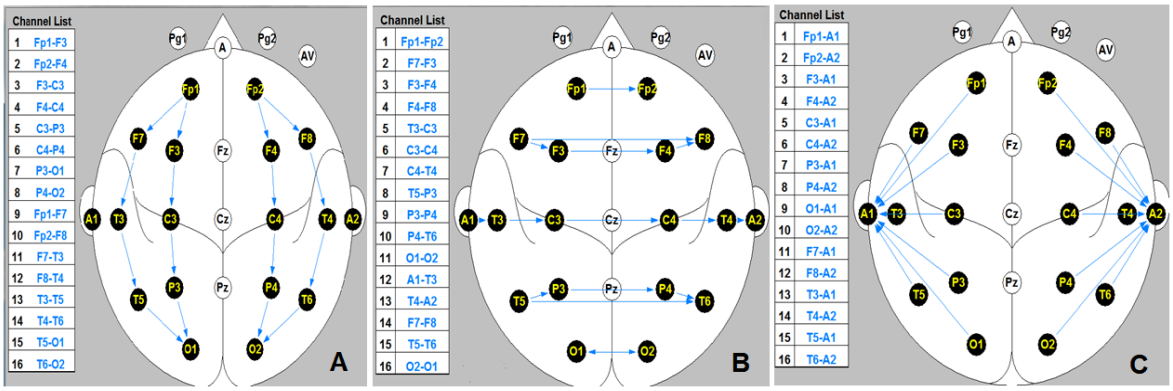

Figure 3. Bipolar montage used (a) longitudinal (b) transverse and (c) referential montage

2.3. Analysis of EEG tracings

Visual analysis of EEGs was the most suitable method for this research, since it avoided the artefacts (eye movements, blinking, cardiac, and muscular activity) and noise that disrupted reading and interpretation, and therefore focused on the so-called "clean" EEG signals [19], [20]. In addition, visual analysis offers the advantage of enabling a qualitative assessment of EEG signal modulations, such as changes in frequency, amplitude and spatial topography. This approach complements the quantitative method, allowing in-depth exploration of the underlying neurophysiological phenomena without the distortions introduced by artefacts.

A tracing analysis grid based on pre-existing data in the literature [21], [22] was designed for this purpose to guide the EEG laboratory team to focus on the research targets by respecting certain characteristics and criteria when reading the EEGs studied. Five reproducible reading criteria were selected to form this analysis grid: i) characteristics of basic physiological rhythms, ii) features of background rhythm, iii) changes caused by hyperpnoea maneuvers HPN, and iv) changes caused by intermittent light stimulation ILS. This structured approach also facilitates the identification of subtle modulations and significant differences in brain activity in response to various stimuli or experimental conditions.

3. RESULTS AND DISCUSSION

In this study, brainwaves are recorded and presented according to several important characteristics: frequency, measured in hertz (HZ), which corresponds to the number of oscillations per second, and each type of brainwave is associated with a specific frequency range; amplitude, determined by the height of the oscillations, which indicates the intensity of brain activity; topography, which refers to the spatial distribution of the waves on the scalp; and reactivity, which refers to brainwaves change in response to stimuli. These features are essential for the in-depth analysis of EEG recordings, providing detailed information about the underlying neurophysiological activity. By incorporating these parameters into our methodology, we were able to systematically explore the complex dynamics of the participants' brains.

Brain waves are classified into different frequency bands: Delta waves (0.5–4 HZ), Theta Waves (4–7 HZ), Alpha waves (8–13 HZ), Beta waves (14–30 HZ) and Gamma waves (30 HZ and above). These activities are described as "rhythms" when they have a relatively constant periodicity and amplitude on the scalp. The EEG activity in the participants consisted mainly of the beta rhythm and the Alpha rhythm. However, Delta and Theta activity are physiologically observed, the extent of which varies according to the hyperpnoea maneuver.

3.1. EEG of basic physiological rhythms

The results show that in-patient addicts exhibit more high-frequency activity than controls, with a predominance of fast basic physiological rhythms, namely Alpha 2 activity at 47% compared with 20% and Beta 2 activity at 60% compared with 30%, as shown in Table 2 and Figure 4. The addicted patients also showed an average hypo voltage amplitude, especially in the Alpha 1 and Alpha 2 background rhythms, with a value of 27 microvolts compared with 47 microvolts in the controls, as shown in Figure 5. Nevertheless, the majority of addicted patients showed a reduction in the alpha 1 and beta 1 reduced-frequency rhythms of 53% and 40% respectively, compared with 80% and 70% in the controls, as exposed in Table 2 and Figure 6.

Comparing them with our work, several studies corroborate perfectly with the results of our research concerning the importance of fast rhythms in the monitoring of addicted patients by explaining that chronic use of psychoactive substances is generally associated with neuronal hyper-activation (i.e., increased power for high frequencies) [23], [24], whereas abstinence and improvement after treatment are generally associated with neuronal hypoactivation (i.e., increased power for low-frequency bands) [24]. Also, groups of patients with a substance use disorder, compared with non-using controls, generally showed greater power in the high-frequency band (i.e., beta), whereas with abstinence there was great power in the lower frequency bands. Thus, decreases in beta or general normalization of EEGs were consistently associated with abstinence-related recovery in SUD [25], [26] and predicted better clinical outcomes and suggesting that increasing and decreasing beta are associated with worse and better outcomes respectively.

Table 2. Physiological EEG rhythms in the participants

Criteria	Elements of the EEG trace	%		Average frequency (in Hertz)		Average amplitude (in µvolt)		Location (F,T,C,P,O)*	
		case	control	case	control	case	control	case	control
Basic physiological rhythms	Alpha 1 (08-10.5 HZ)	53	80	9.5	9	26	49.3	O, P et C	O
	Alpha 2 (10.6-13 HZ)	47	20	11.25	11.50	28.7	45	O, P et C	O
	Beta 1 (14-20 HZ)	40	70	18	16	13	19	F et C	F
	Beta 2 (20.1-30 HZ)	60	30	23	21.5	11	18	F	F
	Gamma (30 HZ et plus)	0	0	0	0	0	0	-	-
	Theta (4 - 7 HZ)	26	6	7	6	16	20	O	O
	Delta (05 - 4 HZ)	0	0	0	0	0	0	-	-

*F= frontal, T= temporal, C= central, p= parietal, O= occipital.

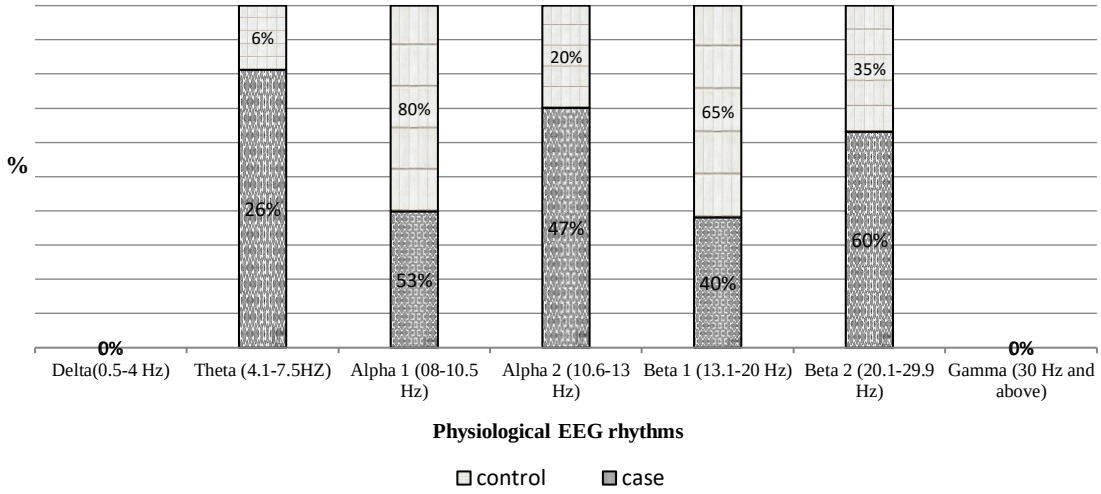

Figure 4. Physiological EEG rhythms in participants

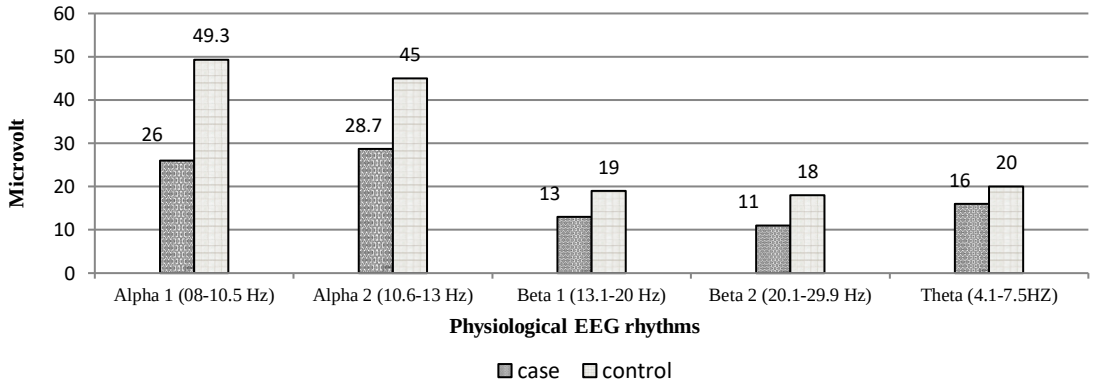

Figure 5. Average amplitude (in microvolt) in the physiological EEG rhythms of the participants

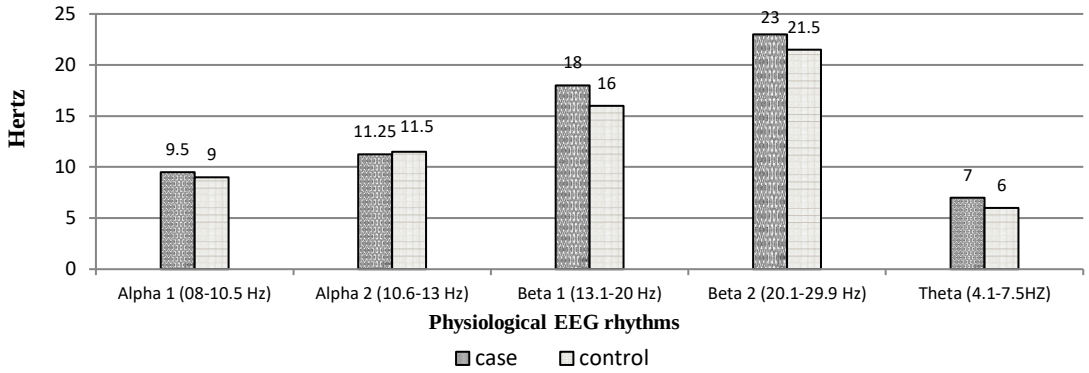

Figure 6. Average frequency (in hertz) in the physiological EEG rhythms of the participants

Overall, we can deduce that the results obtained by the present research on basic physiological rhythms show that addicted participants, even under treatment, still display rapid Beta 2 as shown in Figure 7 and Alpha 2 rhythms. This should draw the attention of therapists to the fact that these addicted patients still require more time and effort, or outright modification of therapeutic interventions, to achieve abstinence and improved treatment.

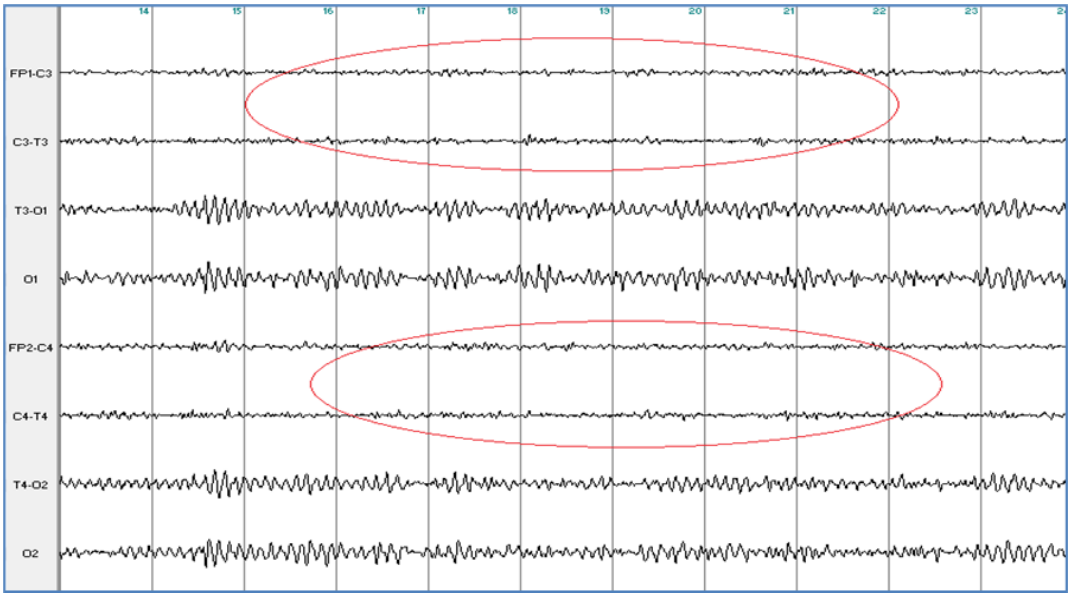

Figure 7. Significant fast beta rhythm activity in the anterior and central regions of addicted inpatients visible on right leads FP2-C4, C4-T4 and left leads FP1-C3, C3-T3

3.2. Background rhythm EEG

Normally in humans, the alpha-band rhythm is characterized by a set of sinusoidal waves with a frequency of between 8 and 13 HZ and amplitude varying from 20 to 100 microvolts. This activity is observed mainly in the posterior regions of the scalp, bilaterally and synchronously. Its amplitude is maximal when the eyes are closed and decreases when the eyes are open or when particular attention is required.

The results in Table 3 show that the background rhythm is marked by the Alpha band, and consists of a train of sinusoidal waves with an average frequency of between 9 and 9.5 HZ that is clearly more reactive to eye-opening in the controls than in the cases, and with an average amplitude of between 27 in the cases and 47 microvolts in the controls, indicating a hypo-voltage in the addicted patients, which is visible in Figure 8, making it difficult to differentiate from the other EEG rhythms. It is distributed synchronously and bilaterally in the posterior regions of the scalp, its amplitude is optimal when the eyes are closed and blocked

when the eyes are opened, as can be seen clearly in Figure 9. It is symmetrical in rhythm and amplitude with an organized topography in the majority of case and control participants.

The work of Vion-Dury *et al.* [21] states that these are rapid, low-amplitude activities that do not allow the presence or absence of reactivity to be observed, with no predominant frequency characterizing an EEG rhythm; these aspects are found in benzodiazepine overload, highly anxious patients and chronic alcoholics. The decrease in Alpha voltage as shown in Figure 10 may therefore be correlated with benzodiazepine overdose, which is frequently used in the treatment of SUDs. This may help addictologists adjust treatment doses, and also assess the chronicity of alcohol addiction.

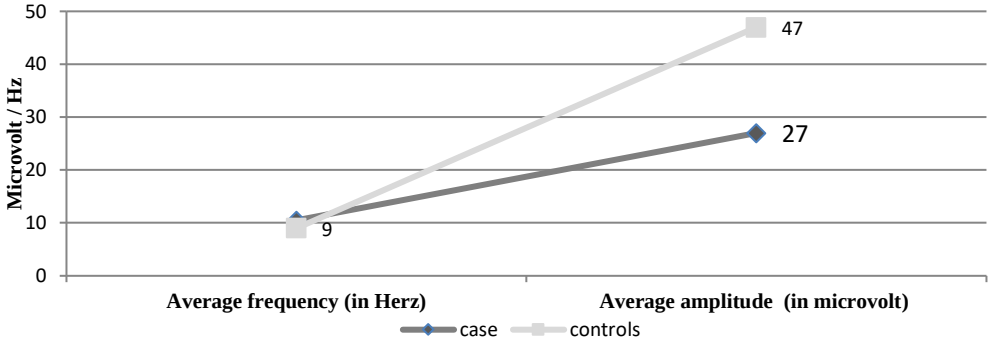

Figure 8. Average amplitude and frequency of background rhythm in participants

Table 3. EEG of background rhythm in participants

Criteria	Elements of the EEG trace	%		Average frequency (in Hertz)		Average amplitude (in µvolt)		Location (F, T, C, P, O)*	
		case	control	case	control	case	control	case	control
Background rhythm	Type alpha	100	100	9.5	9	27	47	O, P	O
	Bilateral and synchronous	94	100	9.5	9	27	47	O, P	O
	Symmetrical in rhythm and amplitude	94	100	9.5	9	27	47	O, P	O
	Reacts to eye opening	90	100	-	-	-	-	O	O
	Organized topography	84	94	-	-	-	-	O	O
	Microvoltage	43	20	10.5	9	27	47	O	O

*F= frontal, T= temporal, C= central, p= parietal, O= occipital.

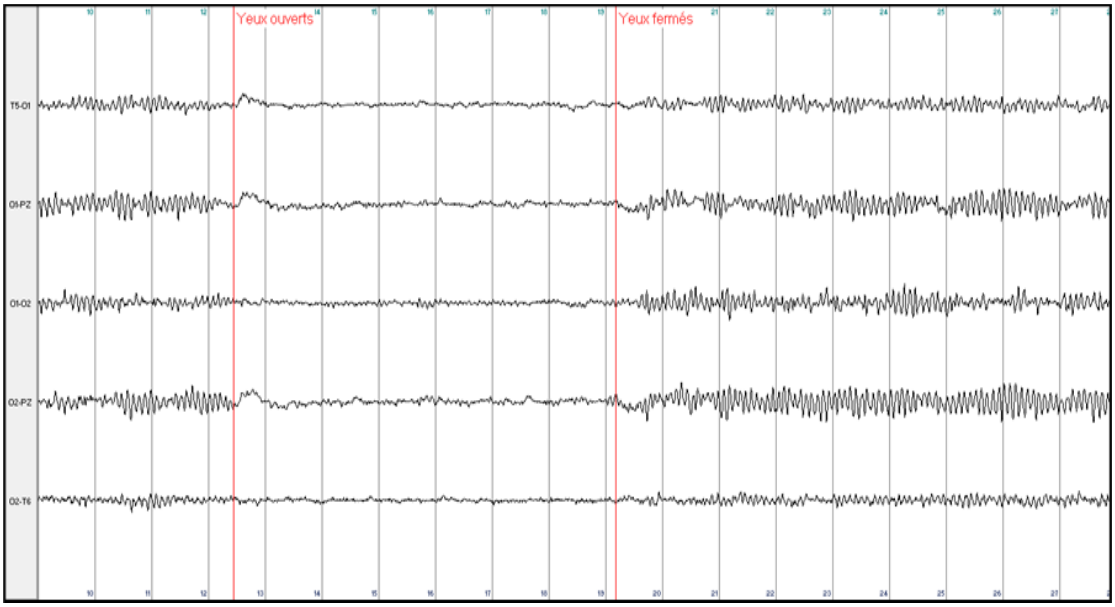

Figure 9. Clear reactivity of the background rhythm to eye opening

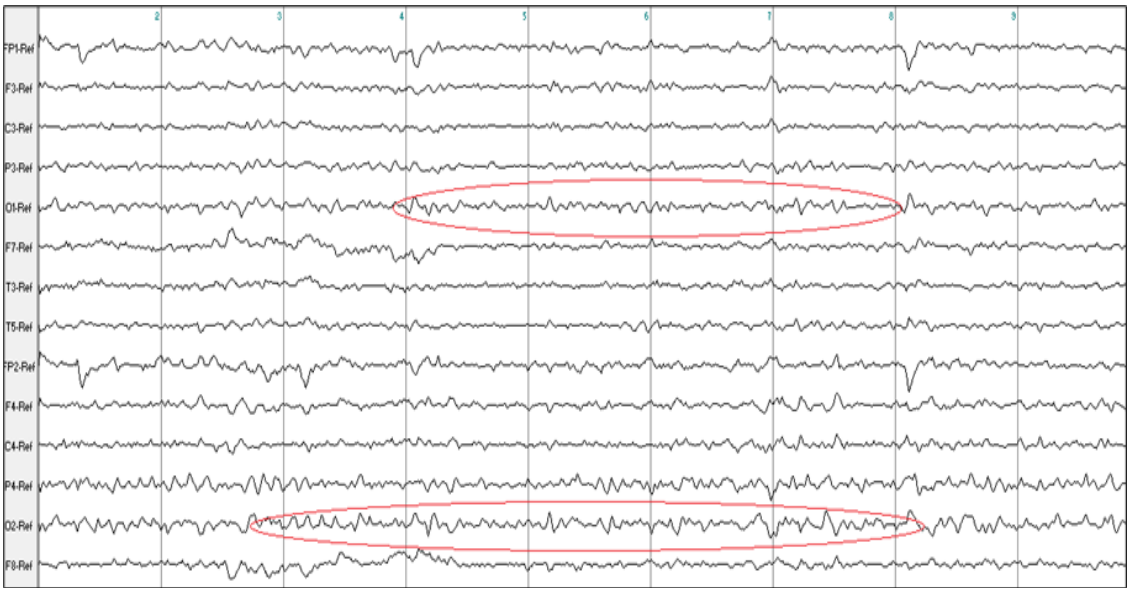

Figure 10. Microvoltage background rhythm on posterior leads O1 and O2 difficult to differentiate from other EEG rhythms in inpatient addicts

3.3. EEG of changes caused by hyperpnoea (HPN)

The results of the hyperpnoea test (HPN) reveal a slowing of electrogenesis visible in Figure 11 and Figure 12 with the appearance of slow Theta-type activity at 28% in the cases compared with 07% in the controls. This activity sometimes modulates the background rhythm 13% in the cases or becomes a diffuse element 17% compared with 03% as observed in Table 4. That significant increase in Theta activity in patients may indicate an abnormal or exacerbated response of the brain to hyperpnoea, a condition often linked to alterations in neuronal and metabolic regulation.

HPN usually has no effect or causes a significant slowing of electrogenesis [27]. The absence of any particular reaction to the test is a normal situation and shows that the individual tolerates it well. However, it is important to note that some people, particularly young people, may be more sensitive to this type of test. This sensitivity is not necessarily negative and may be due to physiological hypersynchrony, which is a natural phenomenon observed in young people. What's more, it's possible to notice significant slowing without there necessarily being any particular cause for it. This may be explained by the high contractibility of the vascular tree, which is a network of blood vessels capable of contracting and dilating to regulate blood flow [21], which confirms that chronic use of addictive substances (specifically marijuana) was also associated with reduced EEG power in the alpha and beta bands [28]. These reductions in EEG power appear to be related to deficits in cerebral perfusion, suggesting alterations in EEG and cerebral blood flow velocity in long-term users [28].

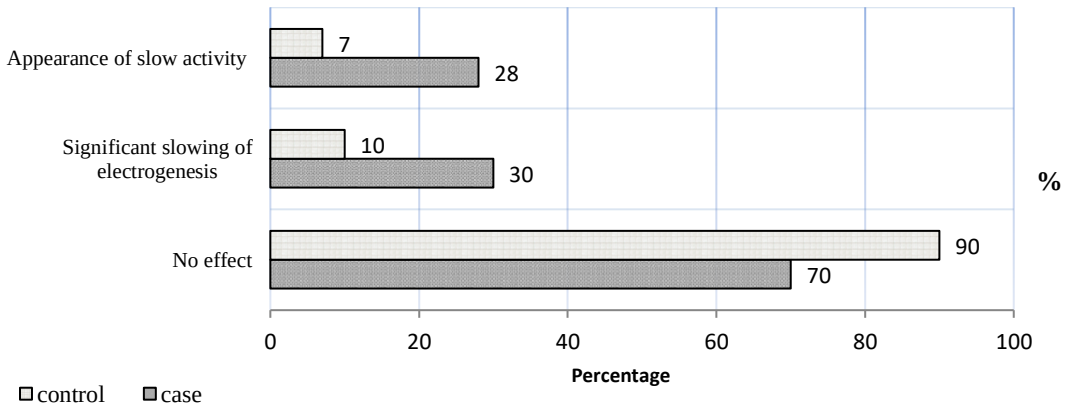

Figure 11. Changes caused by hyperpnoea HPN

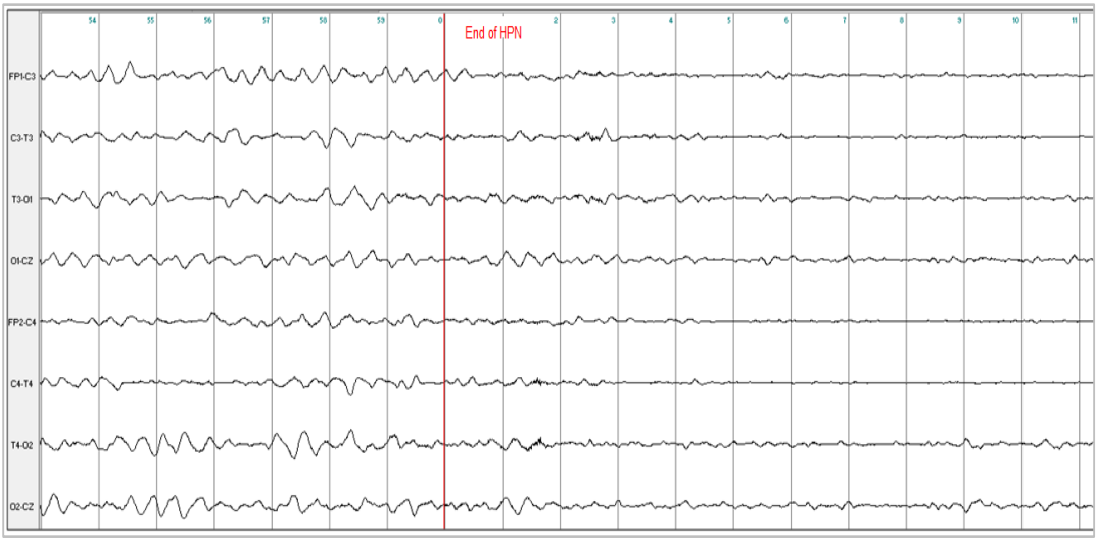

Figure 12. Global slowing during a hyperpnoea session HPN in an addicted patient

Table 4. EEG of changes caused by hyperpnoea (HPN)

Criteria	Elements of the EEG trace	%		Average frequency (in Hertz)		Average amplitude (in µvolt)		Location (F,T,C,P,O)*	
		case	control	case	control	case	control	case	control
Changes caused by hyperpnoea (HPN)	No effect	70	90	-	-	-	-	-	-
	Significant slowing of electrogenesis	30	10	-	-	-	-	diffuse	diffuse
	Appearance of slow activity	28	7	7	6	16	20	O	O
	Slow theta (delta) activity modulating background activity.	13	00	7	00	16	00	O	-
	Slow diffuse theta-type activity or (delta-type)	17	3	7	6	16	20	diffuse	diffuse

*F= frontal, T= temporal, C= central, p= parietal, O= occipital.

3.4. EEG of changes caused by intermittent light stimulation (ILS)

Figure 13 and Table 5 show that intermittent light stimulation (ILS) induced bi-occipital entrainment in 25% of addicted patients compared with 3% of healthy controls clearly observed in Figure 14; with a significantly higher oculo-clonic response in hospitalized addicted patients visible in Figure 15 than in controls, by 30% compared with 10%. These results suggest that addicted patients show increased sensitivity to intermittent light stimulation, manifested by a higher rate of bi-occipital entrainment and a more frequent oculo-clonic response compared with healthy controls.

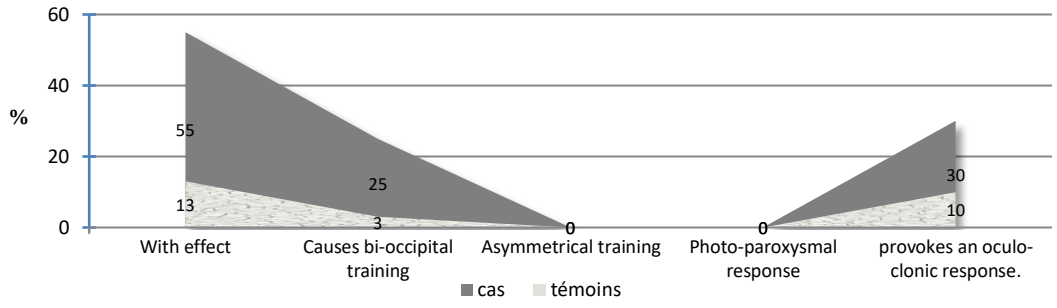

Figure 13. EEG changes caused by intermittent light stimulation (ILS)

ILS provokes bi-occipital entrainment as observed in Figure 14, i.e., large amplitude visual evoked potentials, implying that this entrainment is symmetrical (and therefore that there is no damaged occipital cortex) [21]. It can provoke an oculo-clonic response, which is an involuntary, brief contraction of the eye muscles as noted in Figure 15. It is caused by hyperexcitability of the reflex circuits of the brainstem, in

particular the midbrain, which reflects peripheral (reflex) hyperexcitability rather than pathological susceptibility [21]. Excitability in addicted patients is used to predict relapse to alcohol and drug abuse [14] and also to detect alcoholism [29].

Table 5. EEG of changes caused by intermittent light stimulation (ILS)

Criteria	Elements of the EEG trace	%		Location (F,T,C,P,O)*	
		case	control	case	control
Changes caused by intermittent light stimulation (ILS)	With effect	55	13	O,F	O,F
	Causes bi-occipital training	25	3	O	O
	Asymmetrical training	00	00	-	-
	Photo-paroxysmal response	00	00	-	-
	Provokes an oculo-clonic response.	30	10	F	F

*F= frontal, T= temporal, C= central, p= parietal, O= occipital.

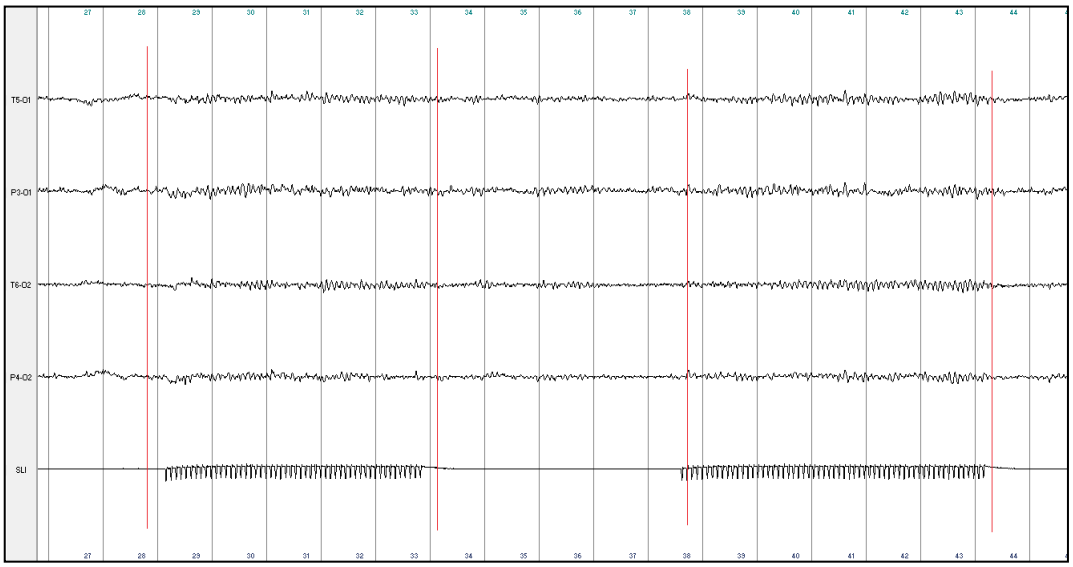

Figure 14. Recording photo-training during an ILS session at 10 HZ in the occipital region on electrodes O1 and O2

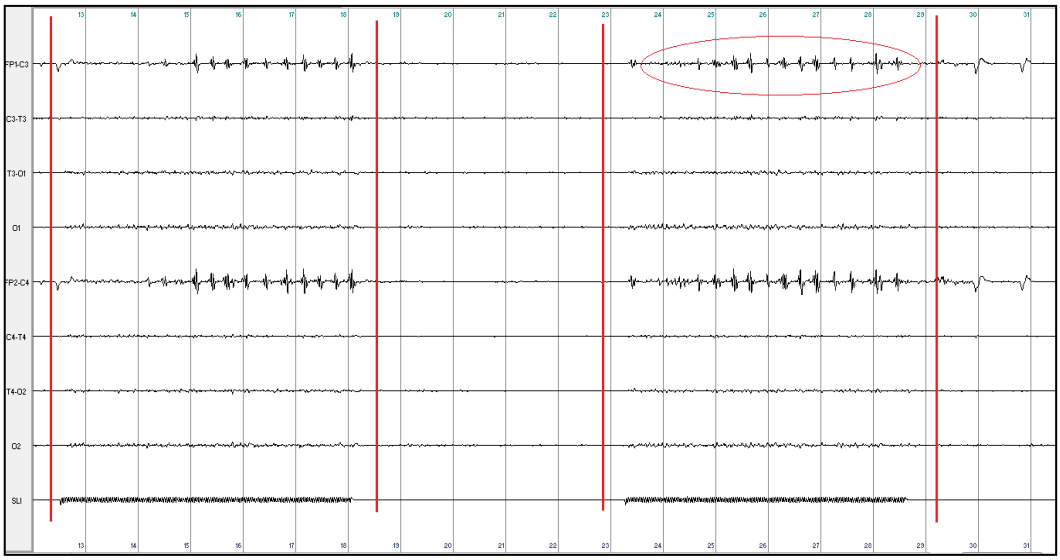

Figure 15. Recording of an oculo-clonic response during an ILS session at 25 HZ in the frontal region on electrodes FP1 and FP2

4. CONCLUSION

Although the use of digitized EEG in addictology remains inconsistent, we have seen the extent to which it can provide clinicians with strong neurophysiological arguments for monitoring the clinical and therapeutic progress of addicted patients. Consequently, we strongly recommend close collaboration between addictologists and neurophysiologists, as well as the development of skills in neurophysiology applied to addictology among clinicians, because the digitized EEG is all the more important if it is interpreted by the person who prescribed it. The major challenge of knowledge about digitized EEG activity is that it is not always specific to SUD and suggests the need to consider the trans-diagnostic framework.

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