# Leo Sher Alexander Vilens

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Editors

Suicidal Behavior in Alcohol and Drug Abuse and Dependence

Psychiatry - Theory, Applications, and Treatments

## SUICIDAL BEHAVIOR IN ALCOHOL AND DRUG ABUSE AND DEPENDENCE

# LEO SHER AND ALEXANDER VILENS EDITORS

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Chapter 4

## PSYCHOPHYSIOLOGICAL ASPECTS OF ALCOHOL EPILEPTIC SYNDROME

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#### **ABSTRACT**

Alcohol epileptic syndrome is one of the most frequent neurologic manifestations of alcohol dependence occurring during withdrawal. The goal of the study was to investigate psychophysiological peculiarities of patients with alcohol epileptic syndrome in order to develop special diagnostic algorithms for its detection and selection of correct treatment and management approaches. The main methods of the study were screening, a clinical method, electroencephalopraphy, computerized tomography, a laboratory method. As part of the study, frequency of occurrence of separate clinical, psychophysiological and laboratory indexes was compared in patients with idiopathic, symptomatic epilepsy, alcohol epileptic syndrome.

#### INTRODUCTION

Among patients with alcohol withdrawal syndrome (AWS) a tendency takes place for growth of the number of critical, life threatening states requiring urgent intensive care hose states include alcohol epileptic syndrome (AES), which is one of the most frequent disorders among patients suffering from chronic alcoholic intoxication (CAI) 90% of cases, epileptic attacks develop in 7-48 hours after the last alcohol taking to other manifestations of alcohol withdrawal syndrome and don't require any

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on NMDA-receptors, that inhibits the excitation system and causes abnormal excitation processes, as well as increases brain concentration of adenosine, an inhibitory neurotransmitter. Abnormal regulation of GABA-mediated inhibition and activation of NMDA-receptors account for excitation effect in dramatic alcohol withdrawal [4,5,6].

However, references do not give clear criteria of AES, and the psychophysiological aspects of patients with AES are described insufficiently. Both reasons cause difficulties in ES differential diagnostics, during making expert decisions about patients' working abilities and vocational aptitude, as well as in searching for ways of adequate therapy and prevention. As a result, analysis of psychophysiological status of patients with AES acquires great practical importance for specification of AES mechanisms' development and working out of diagnostic principles of the pathology in question.

The goal of our study was to detect specific neurophysiological peculiarities of patients with AES for working out of their diagnostic algorithms.

There have been examined 251 Caucasian persons, their average age was 42.3±0.89. At the time of the study, they stayed at the Neurological Department of the Severodvinsk City Hospital, the Arkhangelsk region, Russia. In the course of the study, three groups of patients have been distinguished.

I group patients with ES and CAI without brain localized organic damages in anamnesis (89 persons), average age 41.66±1.15: of them, 16 persons - under 30, 67 persons – at the age 31-55, 6 persons - over 55.

II group patients with ES without CAI (78 persons), of them 26 persons - under 30, 29 persons - at the age 31-55, 23 persons - over 55.

II-a group patients with ES and brain localized organic damages (craniocerebral injuries, insults, tumors) in anamnesis (22 persons), the average age 54.23 ± 3.04; of them, 2 persons - under 30, 7 persons - at the age 31-55, 13 persons - over 55.

II-b group patients with ES and without brain localized organic damages (56 persons), the average age  $36.98 \pm 1.86$ ; of them, 24 persons - under 30, 22 persons - at the age 31-55, 10 persons - over 55.

(comparison group) – patients with lumbar osteochondrosis, disciliculatory encephalopathy I and II stage secondary to arterial hypertension and cerebral atherosclerosis, migraine and vegetative-vascular dystonia, not suffering from ES and CAI (84 persons), the average age 43.40 ± 1.66; of them, 25 persons - under 30, 39 persons – at the age 31-55, 20 persons - over 55.

The age difference among the patients with ES was statistically significant in I and II-a groups (p < 0.001), in I and II-b groups (p < 0.05), what confirmed the fact that ES of various genesis occurred frequently in different age groups. So, attacks manifested in childhood and at a young age, were more often caused by hereditary factors, perinatal pathologies, abnormal development, at a middle and late age – by tumors, vascular diseases, brain injuries, alcoholism. AES occurred more frequently in persons at a middle age. The age difference among the patients was insignificant in the I and III groups.

The following methods were applied during the study of frequency of occurrence of different neurophysiological characteristics:

- 1. Screening detection of sings of alcohol dependence and a high risk of its emergence with the help of the methods "Self-reporting card PAS", AUDIT test [7].
  - 2. Clinical method neurological examination of the patients, detection of typical symptoms of the studied pathology: withdrawal signs, polyneuropathy of lower extremities [8,9], disorders in intellectual, motion activity, perception and vegetative spheres that was carried out every day during the patients' stay at the Neurological Department.
  - 3. ECG recording was made on a 19-ported computer electro encephalograph "Neuron-Spectrum" with the use of the international lead system «10-20» with application of 19 active electrodes on the 1<sup>st</sup>-2<sup>nd</sup> day of a patient's admission to the Hospital, reexamination of some patients on the 3<sup>rd</sup>-7<sup>th</sup> day.
  - 4. For CT test on the 1<sup>st</sup>-3<sup>rd</sup> day of hospital admission, a computer tomograph with technology of helical scanning «High Speed Dxi General Electric» (US) was used. In the course of implementation of a layer-specific axial section test according to the international testing standards, brain sub- and supratentorial structures were analyzed. The width of scans (Tomograph step) was 1 cm, on brain base, it was 0.5 cm. If a mass brain lesion or any other local pathology was suspected, a contrast agent was administered for verification of obtained results.
  - 5. Laboratory method for study of blood serum biochemical indices alanine aminotransferases (ALT), aspartate aminotransferases (AST), gamma-glutamyl transpeptidases (GGTP), alkaline phosphatases (APh), creatine phosphokinase (CPh) a biochemical autoanalyzer «Vitalab Flexor E» was used. The study was conducted on the 2<sup>nd</sup> day of hospital admission. If enzymes' indexes were high, the study was repeated in 3-5 days.

In the neurological status of the patients from the I group, focal symptoms were not revealed, however in 68.5% of cases, polyneuropathy of lower extremities has been detected. In 100% of cases, EEG of the patients from the I group had the following features: lowamplitude type, absence of zonal differences and alpha-rhythm modulations, dysrhythmia, Eacht diffuse changes in the form of slow waves, multiple artifacts of recording; epileptic and local slow wave activity was not detected on the EEG. 82.0% of the patients form the I group of them, 10.1% were under 30, 67.4% - under 55, 22.5% - over 55) had diffuse hypotrophic hydrocephaly on brain CT. In 94.3% of the patients from the I group, high activity of blood serum ALT, AST, GGTP was registered. GGTP was most active, its activity was tens times higher and in 3-5% of cases - a hundred times higher. The level of ALT activity rated second, mexceeded the maximum allowable level 10-30 times, AST activity in 7-10% of cases was 2-3 times higher. Almost in 90% of cases on the 5<sup>th</sup>-6<sup>th</sup> day of hospitalization, GGTP and ALT indexes were 2-3 times lower with further reduction in a week period of time to normal ar slightly higher than normal indexes. The characteristic feature was that the normal level of blood serum bilirubin was accompanied by extremely high GGTP and ALT indexes what wed to distinguish between hepatitis of different actiology and alcoholic hepatitis.

In the neurological status of all the patients from the II-a group, focal symptoms of pramidal insufficiency type were detected in 72.7% of cases; hemiparesis of I - IV degree - 27.3% of cases. In this group, polyneuropathy of lower extremities was detected in 36% of the patients, on EEG in 77.1% of the patients, low-wave activity in brain injured hemispheres determined, in 9.1% of cases - low electrobiological activity of the brain, in 3.6% -

dysfunction of medial-stem brain structures. On CT in 100% of cases, cystic-gliostic brain changes were detected. 77.3% of the patients had higher indexes of blood serum transferases, the GGTP level was maximally high, ALT – to a lesser degree, AST - 2-4 times higher.

During collection of anamnestic data of the patients from the II-b group, it was detected that 73.2% of them had epiphenomena, 7.1% - CI in anamnesis, 3.6% - brain tumor after surgery in anamnesis, 19.4% - hereditary tainted epilepsy. During the clinical examination of 17.9% of the patients, focal symptoms were determined. Polyneuropathy of lower extremities was detected in 17.9% of the patients. On EEG of 44.6% of the patients, epileptic activity was detected in the form of commissures, discharges «peak – sharp wave», «sharp wave – slow wave»; in 25.0% - dysfunction of medial-stem structures, in 19.4% of the patients - high paroxysmal brain readiness in the form of hypersynchronous sharp alpha-rhythm, discharges of bilateral synchronous sharp alpha-rhythm polyphase alpha-kin waves with an amplitude twice as high as the background, in 10.7% - low-amplitude type and slight diffuse changes were recorded. On repeated EEG, epileptic activity was lower in 20% of cases owing to medical treatment.

On CT of the brain, 25% of the patients had indexes within the norm, 10.7% of the patients had cystic-gliostic brain changes of posttraumatic nature, 64.3% of the patients had mixed hypotrophical hydrocephaly. 3-4 times higher activity of blood serum transferases (GGTP, ALT, AST) was registered in 10.7% of the patients.

In the III group, epileptic phenomena were detected in 23.8% of the patients, anamnestic record in epilepsy among 7.1% of the patients, craniocerebral injuries in anamnesis of 4.8% of the patients. During the clinical examination, focal neurological symptoms were detected in 4.8% of the patients, and nontoxic polyneuropathy of lower extremities - in 11.9% of them. On EEG of the patients from the III group in 23.8% of cases, there was revealed a dysfunction of medial-stem structures in the form of single discharges of bilateral synchronous polyphase alpha-kin waves with the amplitude up-to-background, flatness of zonal differences; in 17.9% heightened paroxysmal brain readiness (frontier EEG type) was detected; in 4.8% of cases focal slow wave activity was registered; in 23.8% there was no pathology detected. On CT of the brain in 31.0% of cases, there were no changes registered, in 64.3% - there were signs of mixed hypotrophic hydrocephaly, in 4.7% - cystic-gliostic brain changes were registered. Higher activity of hepatic enzymes was detected in 10.7% of the patients, mostly ALT and AST indexes were higher, GGTP activity was within the norm in 30% of cases.

A comparison of indexes detected in each group is shown in Table 1 and Diagrams 1,2.

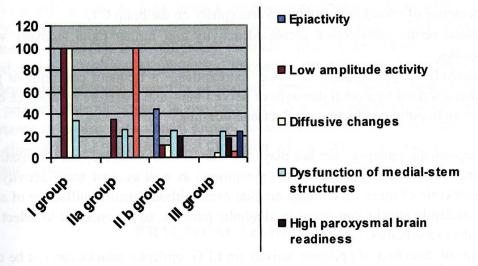
A strong direct correlation relationship between the patients' age and polyneuropathy presence was established (R= 0.45, P < 0.001), and a relationship between age and low electrobiological activity on EEG (R=0.21, P<0.001), mixed hypotrophic hydrocephaly (R=0.29, P<0.001), cystic-gliostic brain changes (R=0.27, P<0.001), high levels of blood serum transferases (R=0.27, P<0.001) as well as an inverse relationship of age and absence of traumatological anamnesis (R=-0.27, P<0.001), focal symptoms (R=-0.28, P<0.001) and epileptic activity on EEG (R=-0.34, P<0.001). There was a statistically reliable connection between the CAI sings and the absence of epiphenomena (R=0.5,P<0.001), epileptic heredity (R=0.22, P<0.001), traumatological anamnesis and the presence of focal neurological symptoms (R=0.9, P<0.001), and a correlation relationship between alcoholic withdrawal and epileptic activity on EEG (R=-0.3, P<0.001) and transferases blood serum indexes within the

norm (R=-0.8, P<0.001) has been detected. Statistically more often, EAS was detected among middle-aged men (P<0.001).

At the same time, epileptic activity on EEG typical for the patients with idiopathic ES had an inverse correlation relationship with age (R=-0.34, P<0.01), with the presence of alcohol anamnesis and withdrawal syndrome (R=-0.3, P<0.001), polyneuropathy (R=-0.24, P<0.001), the presence of low electrobiological activity on EEG (R=-0.32, P<0.001), cystic-gliostic brain changes on CT (R=-0.13, P<0.05) and high blood serum transferases' levels (R=-0.24, P<0.01). Statistically more often, it occurred in patients with hereditary tainted epilepsy (R=0.13, P<0.01), as well as the level of GGTP content in blood was insignificantly higher (R=0.14, P<0.05), probably, due to toxic influence of anti-epileptic medicines.

Table 1. The frequency of anamnestic and neurophysiological indexes detected by screening, use of clinical and laboratory methods in the groups of the studied patients (%)

Indexes	I group	II group		III group
1 The second of		IIa	IIb	Long Transition
epiphenomena	0	50	73.5	23.8
hereditary tainted epilepsy	0	81.8	19.4	7.1
CI, brain tumor after surgery in anamnesis	0	100	7.1	4.8
polyneuropathy of lower extremities	68.5	36.4	17.9	11.9
focal and meningeal symptoms	0	100	17.9	4.8
AWS	100	100	0	0
increased GGTP indexes more than 10 times	78.5	70.0	0	0
increased GGTP indexes 2-10 times	15.8	7.3	10.7	5.6
increased AST indexes more than 10 times	65.3	68.3	0	3.4
increased AST indexes 2-10 times	29.0	9.0	5.3	9.0
increased ALT indexes more than 10 times	5.3	4.0	0	0
increased ALT indexes 2-10 times	89.7	73.3	2.3	0



1. The frequency of neurophysiological indexes detected by use of electroencephalographic method in the studied group and the comparison groups (%).

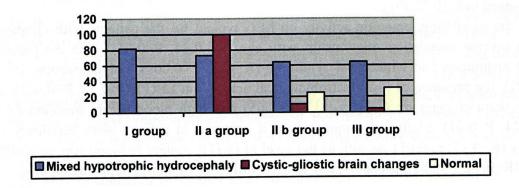


Diagram 2. The frequency of psychophysiological indexes detected by use of computerized tomography method in the studied group and the comparison groups (%).

#### **CONCLUSION**

On the basis of the study conducted, it has been concluded that the patients suffering from AES had the following significant anamnestic and neurophysiological characteristics:

- alcohol anamnesis, primary generalization of paroxysms, attacks of wakefulness,
- absence of epiphenomena, personality disorders of epileptoid type, hereditary tainted epilepsy, craniocerebral injuries and insults in anamnesis; focal and general brain symptoms during clinical examinations,
- absence of epileptic and focal activity on EEG,
- presence of low electrobiological activity, diffuse changes of the brain, superposition of muscular tremor on EEG,
- presence of mixed hypotrophic hydrocephaly on the brain CT,
- blood serum transferases' increased activity and further rapid recovery within 2-3 weeks,
- alcoholic polyneuropathy of lower extremities a frequent concomitant pathology characterized by axonal damages of nerve fibers, and therefore by absence of delayed nerve impulse conduction on electroneurogram.

In symptomatic epilepsy, alcohol plays the role of a provocative, not a causative factor. Fixed changes in a clinical picture (focal symptoms) as well as slow wave activity on EEG, and cystic-gliostic changes on CT indicate that even without harmful influence of alcohol on the brain, epileptic attacks can occur in alcoholic patients, so it is needed to select adequate anti-convulsion medicines.

In cases of detection of epileptic activity on EEG, epileptic attacks can not be caused by alcohol. In those cases, alcohol was only an initiating agent.

Epileptic phenomena occur more often in patients with idiopathic epilepsy, who suffer neither from ES nor from CAI (P< 0.001).

EEG changes typical of patients with AES practically do not occur in patients with idiopathic or symptomatic epilepsy, as well as in persons who do not suffer from CAI or epileptic attacks (P<0.001).

A common feature for the patients with nonalcoholic ES was typical changes on EEG in the form of epileptic or slow-wave activity (P < 0.001).

Beside epileptic activity in the groups of the patients with nonalcoholic ES and without alcoholic ES and CAI, there were often observed changes on EEG like conditional-epileptic activity and dysfunction of medial-stem structures, that is not typical for the patients with AES [10].

Mixed hypotrophic hydrocephaly is a general sign indicating brain diffuse lesion, however in cases of CAI absence, it occurs in health only in elderly patients. Brain lesions caused by CAI result in CT – pattern of hypotrophic hydrocephaly in patients at the middle and even young age. For reference – in the age groups of the patients who suffer from interpathic epilepsy, CT is more often within the standard (P<0.01). In symptomatic epilepsy, pathological focus in brain tissue is a precondition.

A correct classification of attacks and accurate detection of ES types will provide rational and individual basis for therapy, allow to improve prognosis and quality of life of patients suffering from different epileptic attacks.

Diagnostics of AES should include a total of anamnestic, clinical, laboratory and instrumental data. So, sings of «alcohol anamnesis», screening tests positive to alcohol dependence, absence of hereditary tainted epilepsy in anamnesis, epiphenomena and epileptic personality features do not mean that attacks can be only of alcohol origin. Focal or total and meningeal symptoms within the clinical pattern are typical for symptomatic embersy, and alcohol is often an initiating agent, but not a causative factor. Absence of those symptoms presupposes a possibility of intoxication or idiopathic attacks. Polyneuropathy of lower extremities as another significant sign of CAI is typical of patients with alcoholic expleptic attacks, but its occurrence together with a high level of blood serum transferases can and give a decisive answer about the reason of the epileptic attack. Immunological investigations will help to exclude another genesis of polyneuropathy of lower extremities thereditary, autoimmunological, paraneoplastic, toxic). High activity of ALT, AST, GGTP is a biomarker of CAI [11]. It is obligatory to study brain electrobiological activity during diagnosis between alcoholic and idiopathic attack genesis. Detection of epileptic means that the attack cannot be of alcoholic genesis. CT brain testing of patients who have had primary epileptic attacks is also necessary as a final link in the diagnostic process. emportance is in early detection of tumors, localized hematomas, cysts, which can not be development of epileptic foci and development of matic epilepsy.

#### PRACTICAL GUIDELINES

it is reasonable to use diagnostic algorithms for detection of polyneuropathy and the epileptic syndrome during differential diagnostics of epileptic attacks.

Amiconvulsants are not indicated for patients with AES because they do not develop seemes if they do not use alcohol.

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