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OBM Neurobiology

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Original Research

Clinical-Neurological Features and Cognitive Deficit in Chronic Alcoholic Encephalopathies

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Academic Editor: Giuseppe Biagini

OBM Neurobiology
2026, volume 10, issue 3
doi:10.21926/obm.neurobiol.2603340

Received: March 09, 2026
Accepted: June 25, 2026
Published: July 06, 2026

Abstract

The article presents a comprehensive clinical, neurological, and neuropsychological analysis of chronic alcoholic encephalopathy (CAE) as a systemic toxic-metabolic lesion of the central nervous system, characterized by a stage-dependent progressive course that is not a direct equivalent of the stages of alcohol dependence. Based on the examination of 66 patients with CAE of varying severity, the disease is shown to involve a combination of diffuse neurological symptoms (cerebellar, vestibular, pyramidal, sensorimotor, and autonomic disorders, among others) and a systemic cognitive deficit. It has been established that cognitive impairment is one of the early and pathogenetically significant manifestations of CAE and demonstrates a fronto-subcortical regulatory pattern. In the compensated stage, impairments of voluntary attention, neurodynamics, and executive control are already present, with relative preservation of global cognitive status (MMSE). As CAE progresses, cognitive deficits become

persistent and multicomponent, involving executive functions, cognitive flexibility, behavioral regulation, and memory, reaching a dementia level in the decompensated stage. The results of specialized neuropsychological methods (FAB, Schulte-Gorbov tables, Pieron-Ruzer test, Clock Drawing Test, 10-word memory test, and "Exclusion of the Superfluous" test) demonstrated high sensitivity to early regulatory disturbances. They allowed for objective assessment of the staged progression of fronto-subcortical dysfunction. It was shown that impairments in memory and constructive activity in CAE are secondary and regulatory, resulting from deficits in programming and control rather than primary amnestic or apraxic disorders. The obtained data support the concept of CAE as a progressive disorder of integrative brain regulatory mechanisms and justify the use of a comprehensive neuropsychological approach for early diagnosis, staging, and prognosis of alcohol-related CNS damage.

Keywords
Chronic alcoholic encephalopathy; cognitive impairment; neuropsychological techniques; psychometric testing

1. Introduction

Although neurological manifestations occur throughout the clinical course of alcohol dependence, they are most pronounced in the second and third stages (from 5 to 20 or more years of abuse), accompanied by comorbid somatic and psychiatric pathology, as well as cognitive and behavioral disorders [1].

From the point of view of a neurologist, who relies on clinical and neurological symptoms, hardware and laboratory methods, it is more expedient to distinguish three relatively clearly defined stages of damage to the nervous system in alcohol dependence [1-5]. Terminologically, they can be described within the structure of chronic alcoholic encephalopathy (CAE) as manifestations of organic brain damage. The staging of CAE reflects the depth of organic damage to the CNS and is not a direct equivalent of the stages of alcohol dependence. The term CAE most accurately reflects the entire pathological complex that occurs in the CNS, mainly characterized by diffuse neurological symptoms, psychovegetative disorders, and cognitive deficits, which are the result of the direct effects of ethanol and its metabolic products, frequently combined with traumatic brain injury, liver failure, and, first of all, vascular disorders [3, 6-10]. The latter are of primary importance, and in our opinion, it is advisable to use the well-known classical concept of chronic ischemic damage to the CNS, for which effective diagnostic approaches have already been developed.

The diagnosis of CAE is established based on patient complaints, anamnestic data, clinical and neurological status, psychometric studies, consultations with a neurologist, narcologist, and other specialists, laboratory data, as well as hardware diagnostic studies and other methods necessary in each specific case [11].

It should be noted that CAE has a multifactorial mechanism of CNS damage, but the clinical picture is not limited to structural changes with characteristic neurological symptoms. Cognitive

impairment (CI) is an integral part of the symptom complex and often precedes the development of neurological syndromes, often being masked by age-related and vascular changes, etc.

Cognitive functions are among the basic integrative activities of the CNS, providing purposeful behavior, adaptation to changing environmental conditions, and control of voluntary activity. In this context, the study of the cognitive sphere becomes a universal indicator of the functional state of the brain across various forms of chronic cerebral pathology. Its assessment allows the detection of even minimal changes in neuroregulation, which may subsequently be accompanied by pronounced neurological symptoms. CI in the early stages of alcohol dependence is detected in 50-70% of cases, and in 10% of patients reaches the stage of dementia [12, 13]. Alcoholic dementia accounts for 7% of all cases of severe cognitive impairment worldwide (third place after neurodegenerative and vascular dementia) [14, 15].

The above defines the clinical need to study CI in CAE to consider it not as a secondary or concomitant manifestation of alcoholism, but as a systemic marker of damage to the regulatory mechanisms of the brain for diagnostic and prognostic purposes.

1.1 Purpose of the Work

To study the clinical and neurological features of the course and neurocognitive disorders in patients with chronic alcoholic encephalopathy and their dependence on disease severity.

1.2 Study Limitations

The sample included only men, limiting the ability to extrapolate the results to the general population of patients with CAE. Neuroimaging examination was not performed in all patients, mainly in decompensated stages of CAE.

In addition, despite taking into account the duration of alcoholism in the clinical and demographic characteristics of the groups, a separate analysis of its impact on the severity of cognitive impairment was not conducted. The study was mainly clinical and psychometric and cross-sectional, which limits the ability to assess the dynamics of cognitive changes over time and to establish cause-and-effect relationships.

Statistical analysis focused primarily on assessing between-group differences and did not include the calculation of effect sizes, which may limit the accuracy of assessing the clinical significance of the results. Further studies require larger samples, prospective designs, and comprehensive neuroimaging and neurophysiological support.

2. Materials and Methods of the Study

Sixty-six patients with CAE were examined, all men aged 26 to 55 years (mean age 43.8 ± 3.9 years) with a duration of alcohol abuse ranging from 5 to 19 years. Patients were divided into compensated (group I, n = 13; 19.6%), subcompensated (group II, n = 24; 36.4%), and decompensated (group III, n = 29; 43.9%) stages. The control group (CG) consisted of 10 practically healthy individuals aged 25 to 59 years. The clinical and demographic characteristics of the examined groups are presented in Table 1.

Table 1 Clinical and demographic characteristics of the subjects group.

Alcoholic encephalopathy	Light (compensated)	Average (sub-compensated)	Heavy (decompensated)	Control group
Quantity (n)	13	24	29	10
Avg. age (years)	39.2 ± 3.2	44.3 ± 3.9	45.8 ± 4.1	43.2 ± 2.8
AUDIT (points)	More than 7 points	From 16 to 19 points	More than 20 points	Up to 4 points
Experience of alcoholism	5.7 ± 2.1 years	12.5 ± 3.3 years	16.3 ± 4.2 years	-
Comorbid pathology	2 (15.4%)	5 (20.8%)	17 (58.6%)	-

The groups were comparable in age. At the same time, with increasing severity of CAE, an increase in the duration of alcoholism and the frequency of comorbid pathology was noted. The examination was conducted in a hospital setting against the background of stabilization of the somatic state and standardized nutrition. All participants had at least completed secondary education (grades 10-11); secondary specialized education prevailed, while individuals with higher education were observed only occasionally.

A neurologist, narcologist, and other specialists consulted and examined all patients. Instrumental diagnostic studies were also performed, including ultrasound, duplex scanning of the main head arteries, and electrophysiological methods, as required in each specific case. MRI was performed in 20 patients, mainly in those with decompensated CAE (69.2%).

Inclusion criteria were: presence of alcohol dependence; age 26-55 years; abstinence from alcohol consumption for at least 1 month; clinical signs of CNS damage; a probable causal relationship between alcohol intoxication and the identified disorders; verification of CAE stage based on clinical and anamnestic data; stable somatic condition at the time of examination; possibility of performing neuropsychological testing; and informed consent to participate in the study.

Exclusion criteria were: acute alcoholic conditions (intoxication, delirium); severe mental disorders (psychotic, severe affective disorders); use of high doses of sedatives, antipsychotics, or other psychotropic drugs that may affect cognitive functions; history of severe traumatic brain injury; neurodegenerative diseases; and severe liver failure with signs of hepatic encephalopathy.

The diagnosis of CAE was established in the presence of the following conditions: (1) presence of alcohol dependence; (2) clinical signs of brain damage, including neurological, cognitive, and emotional-affective disorders confirmed by clinical and psychodiagnostic examination; (3) a probable cause-and-effect relationship between chronic alcohol intoxication and the detected disorders; (4) absence of other diseases capable of explaining the observed changes; (5) signs of structural brain changes according to neuroimaging data (CT/MRI), if available; (6) additional findings from examination methods (electroencephalography, electrocardiography, ophthalmoscopy, laboratory indicators) confirming the systemic nature of the lesion; (7) presence of concomitant alcohol-associated lesions (polyneuropathy, autonomic dysfunction, etc.).

Staging of CAE was performed based on aggregate clinical, cognitive, neurological, and functional impairments.

2.1 Stage I (Compensated)

Characterized by a predominance of subjective complaints (main pain, dizziness, fatigue), mild cognitive impairment (decreased attention, slowing of mental processes), and emotional-affective disorders (asthenic and anxiety syndromes). Neurological examination reveals minimal scattered microsymptoms. Social adaptation is preserved. Neuroimaging may show single foci of leukoaraiosis (if present). Laboratory findings may reveal some vascular risk factors without significant metabolic disturbances.

2.2 Stage II (Subcompensated)

Marked by pronounced cognitive impairment (memory and executive dysfunction, reduced critical thinking), with the formation of a fronto-subcortical syndrome. Emotional changes include apathy and depressive manifestations. Neurologically, pyramidal, extrapyramidal, and initial pseudobulbar symptoms are observed. Social and occupational adaptation is reduced. Neuroimaging reveals multiple foci of leukoaraiosis, lacunar lesions, and moderate cerebral atrophy. Laboratory data demonstrate more pronounced vascular and metabolic disturbances.

2.3 Stage III (Decompensated)

Characterized by severe cognitive deficit (dementia), pronounced fronto-subcortical dysfunction (apathetic-abulic syndrome, loss of self-control). Neurological examination reveals pseudobulbar, parkinsonian, and cerebellar syndromes, as well as gait and balance disturbances. Independence is lost.

Assignment of patients to the appropriate stage of CAE was based on the dominant clinical syndrome, with consideration of combined cognitive, neurological, and functional impairments.

Psychometric testing included concept exclusion tests [16], Pieron-Ruzer test [17], Gorbov-Schulte test [18], Mini-Mental State Examination (MMSE) [19], Frontal Assessment Battery (FAB) [20], 10-word memory test according to A.R. Luria [21], and the Clock Drawing Test [22, 23].

Data are presented as mean (M) ± standard error of the mean (m). In tables, data are presented as relative values with 95% confidence intervals (CI). The χ^2 test or Fisher's exact test was used for statistical analysis. Differences were considered statistically significant at $p < 0.05$.

2.4 Compliance with Ethical Standards

The authors certify that the study was conducted using data from primary medical records and included clinical observations of patients. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki of the World Medical Association on the ethical principles of conducting scientific medical research involving human subjects, the European Society Directive 86/609 on the participation of humans in biomedical research, as well as the Order of the Ministry of Health of Ukraine No 690 of September 23, 2009. Informed consent to participate in the study was obtained from all participants after providing them with clear, complete and accessible information about the purpose, design and methodology of the study, its potential risks, expected benefits and possible alternatives. All participants confirmed their voluntary participation by signing an informed consent document. Participants had the right to withdraw at any time without giving a reason. In accordance with confidentiality regulations, all data was collected anonymously and

processed in compliance with applicable data protection legislation. All information was used exclusively for this study and was summarized for further analysis of the results. The study complied with ethical standards and was approved by the Bioethics Commission of Odessa National Medical University at its meeting on November 12, 2025, protocol No. 09.

3. Research Results

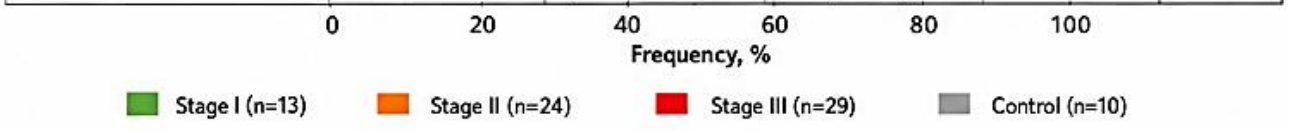
According to the obtained data, 80.3% of CAE cases were observed in the final phase of stage II and in stage III of alcohol dependence. In the early (compensated) stage of alcohol dependence, CAE was diagnosed in 13 patients (19.7%), $p < 0.05$.

Psychoemotional disorders were more prevalent in patients with CAE compared to controls ($p < 0.05$). Irritability in the decompensated stage of CAE, compared to the compensated stage, decreased almost twofold ($p < 0.05$). Sleep disturbances were observed at all stages of CAE, whereas they were completely absent in the control group. Sleep disorders (present in 50.0% of all examined patients) were more prevalent in groups II and III ($p < 0.05$). Complaints of gait instability and imbalance significantly increased in groups II and III compared to group I (almost ninefold, $p < 0.05$). Sensations of weakness in the limbs predominated in groups II and III (58.3% and 68.1%, respectively) and were absent in group I ($p < 0.05$). Complaints of dizziness increased with the severity of CNS damage: group I (7.7%), group II (54.2%), and group III (62.1%), $p < 0.05$.

Severe withdrawal syndrome was observed in 43.9% of cases (7.7% in group I; 37.5% in group II ($p < 0.05$); and 65.5% in group III ($p < 0.05$)). Sensory disturbances were present in groups II and III (41.7% and 68.9%, respectively) and absent in group I ($p < 0.05$). Pain in the extremities increased progressively (7.7%, 20.8%, and 72.4% in groups I-III, respectively; $p < 0.05$).

Headache was reported in 54.2% of cases during the subcompensated stage (group II) and decreased in group III (34.5%). Complaints of hearing loss, cramps, falls, speech disturbances, and seizures increased significantly in group III ($p < 0.05$) and were absent in group I ($p < 0.05$). Reduced attention, distractibility, and inability to perform tasks were observed in group III (75.9%, $p < 0.05$) and were rare in group I. Memory impairment progressively increased and reached a maximum in group III ($p < 0.05$). Memory palimpsests were 2.7 and 4.5 times more frequent in groups II (41.7%) and III (68.9%), respectively ($p < 0.05$) (Figure 1, Figure 2).

Complaint	Frequency, % (95% CI)				p
	Stage I n=13	Stage II n=24	Stage III n=29	Control n=10	
Fear, anxiety, depression	76.9 (46–95)	79.2 (58–93)	65.5 (45–82)	10.0 (0–45)	<0.001
Irritability	84.6 (55–98)	75.0 (53–90)	48.3 (30–67)	10.0 (0–45)	<0.001
Early awakenings	46.1 (19–75)	66.7 (45–84)	55.2 (36–73)	–	0.002
Imbalance	7.7 (0–36)	62.5 (41–81)	68.9 (49–84)	–	<0.001
Easy fatigability	46.1 (19–75)	54.2 (33–74)	44.8 (27–64)	–	0.018
Memory impairment	7.7 (0–36)	50.0 (29–71)	72.4 (52–87)	–	<0.001
Anxious sleep	15.4 (2–45)	66.7 (45–84)	55.2 (36–73)	–	<0.001
Palinpsest	15.4 (2–45)	41.7 (22–63)	68.9 (49–84)	–	<0.001
Weakness in the limbs	–	58.3 (37–78)	62.1 (42–79)	–	<0.001
Dizziness	7.7 (0–36)	54.2 (33–74)	62.1 (42–79)	10.0 (0–45)	<0.001
Trembling	15.4 (2–45)	50.0 (29–71)	58.6 (39–76)	–	<0.001
Numbness	–	41.7 (22–63)	68.9 (49–84)	–	<0.001
Abstinence syndrome	7.7 (0–36)	37.5 (19–59)	65.5 (45–82)	–	<0.001
Decreased attention	7.7 (0–36)	25.0 (10–47)	75.9 (56–89)	–	<0.001
Pain in the limbs	7.7 (0–36)	20.8 (7–42)	72.4 (52–87)	–	<0.001
Headache	7.7 (0–36)	54.2 (33–74)	34.5 (18–54)	10.0 (0–45)	0.004
Muscle pain	–	37.5 (19–59)	51.7 (33–70)	–	<0.001
Hearing loss	–	29.2 (13–51)	66.7 (47–82)	–	<0.001
Cramps	–	37.5 (19–59)	41.4 (24–61)	–	0.002
Falls	–	12.5 (3–32)	44.8 (27–64)	–	0.001
Speech disturbances	–	12.5 (3–32)	41.3 (24–61)	–	0.002
Seizures	–	4.2 (0–21)	24.1 (11–43)	–	0.041



Notes: data are presented as % (95% confidence interval); *p* – level of significance between groups (χ^2 test or Fisher's exact test for small expected frequencies).
Control group (n=10) – frequency of complaints was 10% (0–45) for the indicators for which it was defined.

Figure 1 Frequency of complaints in patients with CAE depending on stage (with 95% confidence interval).

Symptom	Frequency, % (95% CI)				p
	Stage I n=13	Stage II n=24	Stage III n=29	Control n=10	
Tremor	23.1 (5–54)	72.4 (52–87)	79.3 (60–92)	–	<0.001
Ataxia	7.7 (0–36)	79.2 (58–93)	89.6 (72–98)	–	<0.001
Autonomic dysfunction	69.2 (39–91)	75.0 (53–90)	62.1 (42–79)	10.0 (0–45)	<0.001
Hyperhidrosis	23.1 (5–54)	41.7 (22–63)	75.9 (56–89)	–	<0.001
Trophic disorders	–	50.0 (29–71)	75.9 (56–89)	–	<0.001
Pathological reflexes	–	50.0 (29–71)	62.1 (42–79)	–	<0.001
Flaccid paresis of the legs	–	25.0 (10–47)	82.8 (64–94)	–	<0.001
Coordination disorders	15.4 (2–45)	37.9 (20–58)	58.6 (39–76)	–	<0.001
Muscle tenderness	7.7 (0–36)	16.6 (5–36)	82.8 (64–94)	–	<0.001
Sensory disorders	7.7 (0–36)	33.3 (16–55)	66.7 (47–82)	–	<0.001
Deep sensitivity disorders	–	29.2 (13–51)	62.1 (42–79)	–	<0.001
Oral automatism symptoms	–	37.5 (19–59)	51.7 (33–70)	–	<0.001
Cyanosis	–	16.6 (5–36)	65.5 (45–82)	–	<0.001
Decreased muscle tone	–	41.7 (22–63)	37.9 (20–58)	–	<0.001
Nasolabial fold flattening	7.7 (0–36)	29.2 (13–51)	37.9 (20–58)	–	<0.001
Decreased tendon reflexes	–	25.0 (10–47)	37.9 (20–58)	–	<0.001
Dysarthria	–	12.5 (3–32)	44.8 (27–64)	–	<0.001
Muscle atrophy	–	8.3 (1–27)	48.3 (30–67)	–	<0.001
Nystagmus	–	20.8 (7–42)	37.9 (20–58)	–	<0.001
Oculomotor disorders	7.7 (0–36)	16.6 (5–36)	34.5 (18–54)	–	<0.001
Increased tendon reflexes	7.7 (0–36)	29.2 (13–51)	24.1 (11–43)	–	<0.001
Increased muscle tone	–	8.3 (1–27)	31.0 (15–51)	–	<0.001
Central paresis	–	–	27.6 (13–47)	–	<0.001

Notes: data are presented as % (95% confidence interval); *p* – level of significance between groups (χ^2 test or Fisher's exact test for small expected frequencies).
Control group (n=10) – frequency of autonomic dysfunction was 10% (0–45).

Figure 2 Clinical and neurological symptoms in patients with CAE depending on the stage (with 95% confidence interval).

Tremor had different characteristics: large-scale tremor (74.5%), intention tremor (19.1%), and, in some cases in group III patients, “clapping” tremor. It mainly accompanied the subcompensated and decompensated stages of CAE (group II: 72.4% and group III: 79.3%).

Coordination disorders (45.4% of all examined patients) increased across groups, peaking in group III (58.6%, $p < 0.05$). Ataxia (69.7% of cases) was associated with cerebellar lesions (54.3%) or proprioceptive disturbances (45.7%) and was predominantly observed in group III (89.6%, $p < 0.05$). Nystagmus and oculomotor disorders were present in groups II and III (100.0% and 93.3%, respectively, $p < 0.05$).

Similar findings were obtained for oral automatism (100.0%), flattened nasolabial fold (94.7%), and dysarthria (100.0%), with maximal representation in group III ($p < 0.05$). Signs of autonomic-vascular dysfunction (68.2%) were distributed across patient groups (69.2%, 75.0%, and 62.1%, respectively, for groups I-III), with a predominance of trophic disorders, skin cyanosis, and atrophy in group III ($p < 0.05$).

Increased tendon reflexes (22.7%) were recorded in groups II and III (93.3%, $p < 0.05$). Decreased reflexes (25.7%) were also observed in patients with polyneuropathy in groups II and III (100.0%). Sensory-motor polyneuropathy predominated in stage III CAE ($p < 0.05$).

A tendency toward decreased muscle tone in groups II and III (47.6% and 52.4%, respectively; $p < 0.05$) was also noted. Alcoholic myopathy was observed in groups II (8.3%) and III (48.3%).

Increased muscle tone (16.7%) with a pyramidal pattern (72.7%) was observed in group III patients (88.9%, $p < 0.05$). Pyramidal-type movement disorders (12.1%) were registered only in group III patients (27.6%, $p < 0.05$).

In the early stages of the CI, symptoms may be subclinical and manifest mainly as reduced voluntary attention, asthenia, and impaired regulation of activity. As alcohol dependence progresses and CAE develops, these disturbances become persistent and progressively worsen, involving executive functions, cognitive flexibility, and mechanisms of behavioral control. Thus, analysis of cognitive status allows not only the detection of early signs of central nervous system dysfunction, but also the objectification of the severity and extent of organic brain damage. In this regard, the study of cognitive functions in CAE requires the use of methods that are sensitive to impairments of regulatory and executive control [18-23].

The psychological test “Exclusion of the Superfluous” detects impairments in categorization, abstraction, and critical thinking. The method is sensitive to toxic-metabolic damage to frontal-subcortical neuronal systems and reflects the degree of disintegration of higher regulatory (executive) functions [24-26].

After testing, the mean score in group I was within the high range of logical-conceptual thinking (51.5 ± 3.9 points). Tasks were performed correctly; generalizations were mostly appropriate but less abstract than in the control group. Mild slowing of performance, fluctuations in selecting generalizing features, and simplification of formulations were noted. Functional compensation of frontal dysregulation was preserved, possibly due to intact cognitive reserves.

In groups II and III, performance significantly decreased due to organic CNS damage, corresponding to involvement of frontal and fronto-subcortical functional circuits (42.2 ± 4.1 and 31.3 ± 3.4 points, respectively; $p < 0.05$). In group II, difficulties in generalizing remaining concepts were observed; classification strategies changed depending on specific stimuli, and pseudo-generalizations and perseverations were recorded. These findings indicate reduced abstraction efficiency and executive control, reflecting dysfunction of frontal-subcortical systems.

In group III, impairments were evident at all stages of the test: during initial classification, errors in selecting the "extra" word, inability to form generalizing concepts, impulsive and fragmented responses, as well as perseverations, lack of self-correction, and mental fatigue by the end of the task. This corresponds to a severe disintegration of logical, conceptual, and regulatory components of thinking, consistent with a developed frontal syndrome in CAE.

No impairments were observed in the control group compared to the CAE groups ($p < 0.05$).

Attention is one of the key cognitive domains, and its impairment in alcohol dependence supports executive dysfunction [27]. According to the Pieron-Ruzer method, stage-dependent, statistically significant differences in attention profiles were found in patients with CAE compared to the control group (very high level in 90.0% of cases, $p < 0.05$).

Stage I is characterized by a relatively even distribution of performance levels, with the presence of high values (very high level - 19.2%, high - 23.1%), as well as moderate (19.2%) and low levels (30.8%), which may reflect compensatory activation of regulatory mechanisms against the background of initial decompensation in some patients.

In Stage II, a polarization of indicators is observed, with a predominance of the medium level (37.5%) and the emergence of very low values (16.7%, $p < 0.05$), likely reflecting instability and fluctuating attention due to depletion of compensatory mechanisms.

In Stage III, low and very low levels predominate (34.5% and 27.6%, respectively; $p < 0.05$), with almost complete absence of high-performance indicators ($p < 0.05$), reflecting a persistent organically determined attentional deficit.

Overall, a stage-dependent impairment of attention was identified in CAE: from a pseudo-normal or slightly elevated level in Stage I, through polarization in Stage II, to a profound deficit in Stage III. The obtained data confirm the systemic nature of attentional disturbances in CAE and the high sensitivity of the Pieron-Ruzer test as a clinical marker of disease progression.

Impairments in voluntary attention and regulation of mental activity are early and persistent cognitive disturbances in CAE, reflecting dysfunction of frontal regulatory systems. The Schulte-Gorbov tables represent a valid method for assessing concentration, visual search speed, and cognitive flexibility, thereby justifying their use for stage differentiation in CAE [28].

The T1 indicator (first series) demonstrated a progressive increase in task completion time with advancing stages of CAE: from mild regulatory impairment in stage I (52.1 ± 12.1 s), through moderate fronto-subcortical dysfunction in stage II (75.1 ± 18.1 s), to severe impairment of voluntary attentional control in stage III (112.4 ± 24.3 s), while the control group demonstrated age-appropriate normative values (39.8 ± 14.3 s). Intergroup differences were highly significant ($F = 41.72$; $p < 0.000001$).

Analysis of attention switching time (T3) showed a more pronounced stage-wise increase in cognitive flexibility deficit: from moderate slowing in stage I (107.0 ± 15.3 s) to marked regulatory insufficiency in stages II (188.8 ± 25.2 s) and III of CAE (210.5 ± 35.3 s), with normative values observed in the control group (51.0 ± 3.8 s). Highly significant between-group differences were found ($F = 126.87$; $p < 0.001$), along with a strong positive association between CAE stage and attention switching time ($\rho = 1.00$; $p < 0.001$).

The obtained data confirm a progressive decline in concentration, slowing of information processing, and increasing fronto-subcortical dysfunction in CAE, with attention switching time representing one of the most sensitive markers of disease progression.

The Clock Drawing Test (CDT) is a valid tool for assessing executive functions, visuoconstructive abilities, and spatial planning. It is sensitive to frontal-prefrontal regulatory deficits characteristic of alcohol-related brain damage [29-31]. The assessment was performed using the 10-point Sunderland scale, which provides a quantitative measure of visuospatial and executive impairment [32].

In patients with CAE, a stage-dependent progression of CDT performance impairment was observed: in stage I, the mean score was 8.4 ± 0.8, indicating minimal and largely reversible regulatory difficulties; in stage II, 6.3 ± 1.3 points with pronounced constructive errors and limited self-correction; in stage III, 4.5 ± 1.7 points with severe disruption of global task organization and occasional refusal to perform the test. In the control group, results were within normal limits (9.7 ± 0.7 points, $p < 0.05$).

The quantitative CDT scores differed significantly among groups according to CAE severity: group I (8.4 ± 0.8; $p < 0.05$ vs. control group), group II (6.3 ± 1.3; $p < 0.01$), and group III (4.5 ± 1.7; $p < 0.001$).

Dyspraxia was primarily related to impaired clock-face construction and reflects dysfunction of frontal regulatory systems. Gnostic disturbances were systemic in nature and were not limited to isolated parietal dysfunction, consistent with the concept of distributed neural organization of gnostic functions [33-35].

The 10-word recall test assesses acquisition of new verbal material, delayed recall, and memory organization strategies [36-38]. According to the A.R. Luria method, a stage-dependent decline in test performance was observed in patients with CAE ($p < 0.05$).

In stage I, performance was relatively preserved, with a typical learning curve and effective use of cues (6.3, 7.3, 7.9 words across the first three presentations, and 7.6 words in delayed recall). In stages II-III, a marked reduction in delayed recall (5.1 and 3.7 words, respectively), absence of a learning effect, and a flattened learning curve were observed (group II: 4.8, 5.7, 5.9 words across three presentations; group III: 4.2, 4.4, 4.6 words). These findings reflect impaired encoding, fixation, and consolidation of information.

The error profile included perseverations, impaired sequencing during recall, and reduced cue effectiveness, indicating fronto-subcortical dysregulation of memory processes. The observed memory pattern in CAE may reflect a systemic disintegration of mnemonic functions associated with toxic-metabolic brain injury and hippocampal-frontal disconnection characteristic of chronic alcohol exposure.

The standardized MMSE screening test was used to assess global cognitive status and its stage dynamics in CAE [39]. A progressive decline in total MMSE scores with increasing disease stage was observed: in stage I, 26.9 ± 0.8 points (mild cognitive impairment); in stage II, 24.3 ± 0.5 points (moderate impairment); in stage III, 20.1 ± 0.9 points (mild dementia range), while in the control group, the values corresponded to normal cognitive performance (29.2 ± 0.4 points). All intergroup differences were statistically significant ($p < 0.05$).

The obtained data reflect a stage-dependent decline in cognitive functions in CAE and are consistent with progressive organic CNS damage. At the same time, a dissociation was observed between MMSE scores and specialized attention tests: even in the early stages, relatively preserved MMSE scores coexisted with pronounced attentional regulatory disturbances, confirming a fronto-subcortical pattern of cognitive impairment. This is likely due to the limited sensitivity of the MMSE

to executive dysfunction and supports the need for comprehensive neuropsychological assessment in alcohol-related brain damage.

The Frontal Assessment Battery (FAB) was used to quantify frontal (executive) dysfunction rapidly and is sensitive to early prefrontal and fronto-subcortical impairments in alcohol dependence [40-42]. The FAB demonstrated a progressive decline in executive functions in CAE: in stage I, mild frontal dysfunction (14.8 ± 0.8 points); in stage II, moderate dysfunction (12.3 ± 0.4 points); and in stage III, severe fronto-subcortical executive impairment (10.1 ± 0.9 points), while in the control group values were within the normal range. Intergroup differences were statistically significant ($p < 0.05$-0.001).

The obtained data indicate a progressive involvement of the prefrontal regions and fronto-subcortical regulatory circuits in CAE, with clinically significant executive dysfunction already evident in the early stages and reaching a dementia-level pattern in advanced disease stages.

4. Discussions and Results

Complaints of early awakenings were common in patients across all CAE groups, which may indicate complex neurohumoral and neurotransmitter dysregulation and correlate with disturbances of circadian rhythms, the sleep-wake cycle, and alterations in hormone synthesis, primarily melatonin, as well as anxiety disorders. In addition, early awakenings are considered an early and clinically significant marker of alcohol withdrawal, even in the absence of pronounced somatic symptoms.

Gait instability primarily indicates organic damage to central nervous system structures with predominant involvement of the cerebellum, its conduction pathways, and structures responsible for proprioception. The occurrence of this symptom reflects disruption of pathways involved in cortical control, integration of sensory information, and postural regulation, which is characteristic of CAE.

Fatigue, in our opinion, has a multifactorial and systemic nature, reflecting both peripheral (polyneuropathies, myopathies, decreased muscle strength, impaired neuromuscular transmission) and central (asthenia, autonomic dysfunction, energy deficiency, and impaired central regulatory control) mechanisms.

Nystagmus and oculomotor disorders are typical manifestations of disease progression involving the vestibular structures, the oculomotor nuclei of the brainstem, and their conduction pathways. These symptoms are usually combined with other manifestations of CAE and reflect impaired integrative activity of cerebellar-brainstem systems, as observed in most examined patients.

Autonomic and autonomic-vascular disorders are manifested by lability and dysfunction at multiple levels of the autonomic nervous system, with a wide range of symptoms affecting multiple organ systems. Within the vascular system, these disturbances reflect impaired neurohumoral regulation of vascular tone, which is part of the systemic multifactorial mechanism of damage. Autonomic nervous system dysfunction is significantly exacerbated during withdrawal syndrome, highlighting its pathogenetic association with alcohol dependence.

Analysis of the study results indicates that limb weakness and muscle atrophy (predominantly in proximal segments), as well as other trophic disorders, represent manifestations of CNS damage with predominant involvement of sensorimotor and vegetative-trophic systems. This is associated

with toxic-metabolic injury to nerve fibers, impaired axonal transport, reduced neurotrophic support of muscle tissue, and dysregulation of central control mechanisms.

Dizziness in the examined patients is predominantly of mixed origin and is caused by lesions of vestibular structures at both central and peripheral levels. It may reflect impaired integration of visual, proprioceptive, and vestibular afferents, which is characteristic of chronic alcohol intoxication. Dizziness may also be associated with vascular dysregulation and hypoxic-metabolic changes in brainstem structures, which may explain its frequent association with nystagmus and gait instability.

Signs of pyramidal insufficiency may reflect involvement of corticospinal tracts. These signs are usually moderate and diffuse in nature and are associated with chronic toxic-metabolic CNS damage without a clearly localized lesion. This emphasizes the combined involvement of cerebellar and extrapyramidal systems in the pathological process.

Withdrawal syndrome is a clinical manifestation of neuroadaptive changes resulting from prolonged alcohol abuse. Its symptoms reflect an imbalance between excitatory and inhibitory neurotransmitter systems (primarily glutamatergic and GABAergic) and activation of the sympathoadrenal system.

Cephalgic syndrome has a polyetiological nature and may result from a combination of vascular, cerebrospinal fluid, and toxic-metabolic factors. Headache was accompanied by a feeling of heaviness in the head, aggravated in the morning and after sleep disturbances, suggesting a role of venous stasis and autonomic dysregulation.

Tremor, primarily postural and intentional, is a consequence of impaired regulatory interactions among the cerebellum, brainstem structures, and the extrapyramidal system. Its severity was often increased during abstinence or emotional stress, likely due to involvement of central neurotransmitter mechanisms and autonomic dysregulation.

Memory palimpsests represent a manifestation of alcohol-related memory impairment with disrupted encoding and consolidation processes and relatively preserved retrieval. They are caused by dysfunction of the mediobasal temporal lobes and limbic structures combined with impaired neurotransmitter support of memory processes. Their presence in CAE may indicate early fronto-limbic disintegration and disruption of memory regulatory mechanisms and may serve as a preclinical or prodromal marker of amnestic progression.

The results of the comprehensive psychometric assessment indicate that cognitive impairment in CAE is systemic, multicomponent, and stage-progressive, with predominant involvement of regulatory, neurodynamic, and mnemonic mechanisms of mental activity.

Early involvement of frontal regulatory mechanisms in CAE was demonstrated, particularly impairment of programming, control, and voluntary regulation of actions. The obtained results support the leading role of fronto-subcortical dysfunction in the development of alcohol-related cognitive deficits.

MMSE scores remained within the normal or subnormal range in the early stages, which may reflect relative preservation of global cognitive function and the limited sensitivity of the scale to early fronto-subcortical dysfunction. As CAE progressed, a consistent increase in overall cognitive decline was observed.

Using the FAB, a progressive decline in executive functions was demonstrated, with predominant impairment of programming, cognitive flexibility, and inhibitory control, suggesting early and progressive damage to prefrontal and fronto-subcortical regulatory circuits.

The results of the CDT revealed impaired holistic organization of activity, visuospatial planning, and self-control, especially in the subcompensated and decompensated stages. Disorganization of the drawing with partial preservation of individual operations may indicate early and progressive damage to prefrontal and fronto-subcortical regulatory circuits, with predominantly regulatory rather than primary apraxic errors.

Schulte table performance demonstrated a gradual increase in task completion time and greater inter-series variability, reflecting reduced concentration, decreased attentional stability and switching ability, and depletion of neurodynamic resources, indicating impaired frontal mechanisms of attentional regulation. These disturbances form the basic background of alcohol-related cognitive deficits and reduce the efficiency of other cognitive functions.

A decrease in accuracy and speed in the Pieron-Ruzer test, along with the emergence of errors, indicates impaired selective attention and sensorimotor control, correlating with deficits in regulatory mechanisms and neurodynamic instability. Thus, attentional impairments in CAE are both quantitative and qualitative in nature.

Memory disorders were characterized by impaired encoding and organization of material with relative preservation of immediate memory span, along with the presence of palimpsests and contaminations, and a strong dependence on regulatory support. This suggests a secondary, regulatory-limbic nature of mnestic impairment.

The results of the "Exclusion of the Superfluous" test indicated reduced abstraction and generalization with a tendency toward concretization of thinking. Errors were impulsive or formal, reflecting deficits in executive control rather than primary intellectual decline.

Thus, the obtained psychometric data confirm that cognitive impairment in CAE follows a fronto-subcortical pattern with early involvement of regulatory and neurodynamic mechanisms and secondary disruption of memory and thinking processes. The progressive worsening of deficits is associated with a gradual loss of compensatory cerebral capacity and has important diagnostic and prognostic significance.

5. Conclusions

1. Chronic alcoholic encephalopathy is characterized by diffuse clinical and neurological manifestations of both the central and peripheral nervous systems, including cerebellar, vestibular, pyramidal, extrapyramidal, sensorimotor, and autonomic symptoms, in the absence of clearly localized focal neurological deficits.
2. Clinical and neurological manifestations of CAE are associated with impaired regulatory mechanisms, manifested by disturbances of the sleep-wake cycle, withdrawal symptoms, tremor, autonomic lability, and anxiety-affective disorders.
3. Cognitive impairment in CAE is stage-dependent, ranging from mild cognitive impairment to dementia (according to the MMSE scale), and corresponds to a predominantly fronto-subcortical pattern of dysfunction. This is confirmed by FAB results and is manifested by reduced attention, impaired programming, and deficits in behavioral control, with relative preservation of visuospatial and constructive functions.
4. Memory impairments in CAE are predominantly regulatory in nature and are associated with deficits in executive functions, which may indicate predominant involvement of fronto-subcortical mechanisms.

5. The use of a comprehensive neuropsychological assessment battery is clinically justified, as its combination allows for the detection of early cognitive impairment, clarification of its structure, and assessment of the severity of cognitive deficits at different stages of CAE.
6. An association was observed between the severity of clinical and neurological symptoms and the degree of impairment of regulatory and executive functions.
7. The obtained results support the view of CAE as a progressive clinical, neurological, and cognitive disorder, in which executive dysfunction is one of the earliest and most sensitive clinical manifestations.

Author Contributions

Oleksandr M. Stoyanov - research design, work with literature, editing of the article, final preparation for publication. Valeriy Y. Kalashnikov - research design, work with literature, editing of the article, final preparation for publication. Rooslan S. Vastyanov - interpretation of results, writing of conclusions, editing of the article. Yevgen V. Oprya - writing of conclusions, editing of the article. Yuriy V. Melnyk - participation in the interpretation of results, editing of conclusions, preparation of the article for publication. Yana I. Kuhel - work with literature, participation in the interpretation of results, preparing the article for publication. Tamara O. Andreeva - editing of conclusions, preparation of the article for publication.

Funding

The research was carried out without financial support.

Competing Interests

The authors of the manuscript consciously declare that there is no actual or potential conflict of interest regarding the results of this work with pharmaceutical companies, biomedical device manufacturers, other organizations whose products, services, financial support may be related to the subject of the materials provided, or who sponsored the research conducted.

Data Availability Statement

The authors of the manuscript consciously declare that the work uses the results of their own clinical studies, which were systematized and analyzed by the authors. Primary data include generalized patient indicators, laboratory results, protocols and obtained quantitative characteristics. All materials are stored in the archive of the research group and can be provided upon reasonable request to the corresponding author, taking into account the requirements of confidentiality and ethical norms.

AI-Assisted Technologies Statement

The authors of the manuscript hereby declare that no generative artificial intelligence tools or services were used in the research and preparation of this manuscript to perform any tasks listed in the Taxonomy of Generative Artificial Intelligence Delegation of Tasks (GAIDeT, 2025). All stages of

the work - from conceptualization to final editing - were performed without the involvement of generative artificial intelligence, exclusively by the authors.

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