Research article

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Physiological Responses to Induced Stress in Individuals Affected by Alcohol Use Disorder with Dual Diagnosis and Alexithymia

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Abstract

Alcohol use disorders (AUD) are among the most common and undertreated mental disorders in developed countries. The co-occurrence of psychiatric comorbidity and AUD has already been well documented. Moreover, alexithymia was found associated with heavy drinking and alcohol dependence. A large part of AUD individuals, between 45 and 67%, have been identified as alexithymics. Both psychiatric comorbidity and alexithymia can negatively impact the course of recovery from alcohol. Alcohol consumption has also been shown to significantly influence autonomic responses. Chronic use of alcohol may induce significant changes in heart rate variability, respiratory frequency, electrodermal activity and skin temperature. To date, only a few studies have comprehensively investigated the comorbidity of alexithymia in AUD individuals with dual diagnosis. Thus, the aim and also the novelty of the present investigation were to disclose in individuals with AUD the emotional and cognitive stress responses to selected physiological parameters measured by ProComp5 Infiniti™ encoder in AUD patients suffering alexithymia with or without concomitant dual diagnosis. Quite interestingly, in AUD subjects with concomitant dual diagnosis we found that the alexithymia elevated skin temperature, heart rate variability and decreased respiratory frequency. Alexithymia, if associated with the dual diagnosis condition in AUD individuals, can be considered as a further vulnerability factor to stressing factors, impacting psychosomatic processing and inducing alterations in physiological parameters. In this paper, we discuss the implications of these findings in the early treatment of alexithymic AUD individuals. ***Clin Ter 2020; 171 (2):e120-129. doi: 10.7417/CT.2020.2201***

Key words: *Alcohol use disorders, Dual Diagnosis, Alexithymia, Biofeedback, Autonomic Responses, Stress disorder*

Introduction

Alcohol Use Disorder (AUD) is one of the most prevalent mental disorder worldwide. AUD is a complex and heterogeneous condition (1–3), defined as a chronic and relapsing disease characterized by compulsive alcohol use, loss of control over alcohol intake, and a negative emotional state when not using substance (4). AUD may lead to or exacerbate in various clinical manifestations, mental (5,6) and behavioral disorders (7–13), internal medicine diseases or neurological problems (9,13–15).

AUD individuals frequently show related psychiatric disruptions (16–19) although alcohol consumption may reduce stress evidencing a strong relationship between emotion dysregulation and drinking including Alexithymia, a personality construct characterized by the subclinical inability to identify and describe emotions in the self (20–23). To date, many researchers still argue the importance of negative reinforcement as a motivator for alcohol use (24,25). Further evidences in alcohol addiction studies have shown comorbidities between AUD, depressive and anxiety disorders displaying a more severe course of dependence than AUD individuals without dual diagnosis (11,26–28). Kessler found that from 50 to 70 % of AUD individuals suffered during their life from a comorbid psychiatric disorder where the term comorbidity describes the simultaneous co-occurrence of two different behavioral health diagnoses in the same individual (27). The prognosis for comorbid patients is more negative compared with that for non-comorbid patients. Indeed, the co-occurrence of alcohol (or drug) dependence with other psychiatric disorders alters psychiatric symptoms, increases their frequency, potentiates the number of days of hospitalization, and reduces life expectancy (29–33).

Emotional disturbances are a central characteristic of many mental disorders, including AUD. In particular, AUD has been associated with difficulties with identifying emotions in self that is the central characteristic of Alexithymia (34,35). Quite interestingly, a study reported unusual presence of alexithymia among AUD individuals (45–67%) (20). The core characteristics of alexithymia are marked dysfunctions in emotional awareness, social attachment, and interpersonal relating (36). Furthermore, individuals with Alexithymia have difficulty in distinguishing and appreciating the emotions of others, which is thought to lead to a non-empathic and ineffective emotional responding (36–41).

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Alcohol consumption has also been shown to impact autonomic responses (42–44). Heart Rate Variability (HRV) and specific respiratory rates are considered objective and sensitive measures of physiological functioning of heart rhythm in response to internal and external demands (45). While Heart Rate (HR) focuses on the average beats per minute, HRV measures the specific changes in time (variability) between successive heart beats. A low HR indicates rest, while a high HR corresponds with exercise or exertion. Conversely, a low HRV at rest or during activity indicates that the body is under stress from exercise, psychological events, or other internal or external stressors. By contrast, higher HRV usually means that the body has a strong ability to tolerate stress or is strongly recovering from prior accumulated stress (46–52). It was found that individuals with high HRV reported more empathy and less alexithymia than individuals with low HRV (53). Moreover, individuals with higher HRV have been found to be more sensitive to specific aspects of social cognition (54). Studies have shown that reduced HRV is associated with vulnerability to stress and deterioration of medical and/or psychiatric conditions, while increased HRV is associated with a favorable treatment response and to a positive recovery (55,56). HRV is toughly influenced by gender and age, factors that should be considered when performing HRV studies (57). Chronic abuse of alcohol may induce changes in HRV (55,58–60). Respiration (Respiratory Frequency – RF) is an automatic function of the body controlled by the respiratory center of the brain and by a voluntary or behavioral control system in higher neural centers and is enormously influenced by the emotional state (61). Indeed, emotions importantly influence respiration, and vice versa, respiration affects emotional state. Generally, anxiety elicits a rapid shallow breathing; shorter inspiratory and expiratory time and increased breathing frequency, due to and while breathing volume decreases; this resulting in a potentiated minute ventilation and in a decreased in end-tidal carbon dioxide (62,63). Electrodermal activity (EDA) is an additional parameter associated with substance use disorders (60,64,65) including AUD (60). EDA is the property of the human body that causes continuous variation in the electrical characteristics of the skin since skin resistance varies with the state of sweat glands in the skin. Sweating is controlled by the sympathetic nervous system and skin conductance is an indication of psychological or physiological arousal (66). If the sympathetic branch of the autonomic nervous system is highly aroused, then sweat glands activity also increases, which in turn increases skin conductance. In this way, skin conductance can be a measure of emotional and sympathetic responses (67,68). Alcohol drinking at any level may play also a key role in the fine thermoregulation of the body affecting under pathological conditions the body temperature, as an adjunctive index of autonomic response changes (69). Under acute stress, sympathetically-mediated vasoconstriction causes a rapid drop in skin temperature (ST) and this influx of peripheral blood, along with stress-induced thermogenesis, simultaneously increases the core temperature (70,71). The core temperature elevation, termed 'stress-induced hyperthermia', is proportional to stressor intensity (72).

To date, only a few studies have comprehensively investigated in AUD individuals with dual diagnosis and Alexithymia, a subclinical condition indicating subtle changes in the autonomic nervous system dysfunctions (43,60). Thus, the aim and also the novelty of the present investigation were to disclose in AUD individuals the emotional and cognitive stress responses to selected physiological parameters (HRV, EDA, RF and ST) assessed by ProComp5 Infiniti™ encoder in AUD patients suffering alexithymia with or without dual diagnosis. We predicted that in AUD individuals exposed to emotional and cognitive stress the disrupted sensorial responses to external cues caused by both alexithymia and dual diagnosis may reveal changes in HRV and EDA autonomic responses subtly affected by alcohol addiction.

Methods

Participant Recruitment

Adult male AUD individuals were recruited in the "Centro di Riferimento Alcologico della Regione Lazio (CRARL)" of Policlinico Umberto I, Sapienza University Hospital, in Rome, Italy attending the 15-days long Day-Hospital period of the standard treatment for alcohol dependence in the Sapienza University Hospital. All participants (see Table 1) met the DSM-5 criteria for AUD (73). According to the indications of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) we considered "at-risk" people those drinking up to 4 drinks per day or 14 per week for men (in Italy 1 drink = 12 g), more than 3 drinks per day or 7 drinks per week for women. NIAAA defines heavy drinking as 5 or more standard drinks in a day for a man and 4 or more standard drinks in a day for a woman. AUD individuals enrolled in the study were 91 but after the exclusion criteria described below, 50 AUD patients were included in the final sample (Table 1). Indeed, the exclusion criteria for the recruitment included history of head injury, loss of consciousness, history of organic mental disorder, present assumption of psychoactive drugs (as cocaine, opioids, amphetamine, other recreational drugs, anxiolytics, euphoriants, antipsychotics, barbiturates, antidepressants, hallucinogens-data based on urine toxicology), seizure disorder or central nervous system diseases, no sign of hypertension at the time of recruitment, no complete abstinence by alcohol to avoid any interference with the testing (74,75). Breath alcohol level was measured by using Alcoscan AL7000 to evaluate abstinence. Symptom checklist 90-R (SCL-90-R) questionnaire was used to screen psychological suffering (76) and a psychiatric examination by a specialist was used to confirm the presence of dual diagnosis based on DSM-5 criteria (73). The Toronto AlexithymiaScale-20 (TAS-20) was used to measure Alexithymia. Patients were assigned to 6 groups on the bases of the clinical diagnoses: AUD patients with dual diagnosis and positive Alexithymia, n=6; AUD patients with dual diagnosis and negative Alexithymia, n=15; AUD patients with dual diagnosis and borderline Alexithymia, n=10; AUD patients without dual diagnosis and positive Alexithymia, n=8; AUD patients without dual diagnosis and negative Alexithymia, n=14; AUD patients without dual diagnosis and borderline Alexithymia, n=9. After the end of the 15-day long hospitalization period, participants were subjected to the ProComp5 Infiniti evaluation and at

Table 1. AUD people characteristics. Data are expressed as percentage or SEM

	Study Sample (n=61)
Age in years	45.50 ± 1.32
Ethnic Origin (%)	
Caucasian	90.3
African	6.1
Asian	1.9
Hispanics	1.7
Marital Status (%)	
Single	37.1
Married	37.1
Separated/Divorced	24.2
Widowed	1.6
Qualifications (%)	
Primary School	0
Middle School	41.9
High School	45.2
University Degree	12.9
Employment Status (%)	
Workers	64.5
Unemployed	27.4
Retired	8.1
Smokers (%)	79
Daily cigarettes' numbers	17.52 ± 1.61
Family History of Alcoholism (%)	80.6
From both parents	11.3
From father	33.9
Alcohol Related Variables	
Age of onset of at risk drinking	28.18 ± 1.47
Years of at risk drinking	16.44 ± 1.48
Alcohol units' intake per die 30 days before Day Hospital admission	18.99 ± 2.93
Alcohol preference	
Wine (%)	48.8
Beer (%)	37.6
Spirit (%)	13.6

least after 10 days the end of any pharmacological treatment. The study was approved by the Sapienza University Hospital ethical committee; an informed consent was signed by each participant and all the study procedures were in accordance with the Helsinki Declaration of 1975, as revised in 1983, for human experimentation.

Psychological Assessment

SCL-90-R

The SCL-90-R (77) is a 90-items self-report symptom inventory designed to reflect psychological symptom patterns of psychiatric and medical patients. Each item of the questionnaire is rated on a 5-point scale of distress from 0 (none) to 4 (extreme). The SCL-90-R used in the present investigation consists of the following nine primary symptom dimensions: Somatization (SOM, which reflects distress arising from bodily perceptions), Obsessions-Compulsions (OC, which reflects obsessions-compulsions symptoms) Interpersonal Sensitivity (IS, which reflects feelings of personal inadequacy and inferiority in comparison with others), Depression (DEP, which reflects depressive symptoms, as well as lack of motivation), anxiety (ANX, which reflects anxiety symptoms and tension), Hostility (HOS, which reflects thoughts, feelings, or actions that are characteristic of negative affective states of anger, aggression, irritability, rage, and resentment), Phobic Anxiety (PHO, which reflects symptoms of persistent fears as responses to specific conditions), Paranoid Ideation (PAR, which reflects symptoms of projective thinking, hostility, suspiciousness, and fear of loss of autonomy), and Psychoticism (PSY, which reflects a broad range of symptoms from mild interpersonal alienation to dramatic evidence of psychosis) (30,54,55).

There are three suggested global indices for the SCL-90: 1) Global Severity Index (GSI), which is the average score of the 90 items of the questionnaire, 2) Positive Symptom Distress Index (PSDI), which is the average score of the items scored above zero, and 3) Positive Symptoms Total (PST), which is the number of items scored above zero (78). However, the GSI is the best indicator of the current level or depth of an individual's disorder (79,80). It combines information concerning the number of symptoms reported with the intensity of perceived distress. The SCL-90-R takes between 12 and 20 min to complete. The internal consistency coefficient α values for the nine symptom dimensions ranged from a low of 0.77 for psychoticism to a high of 0.90 for depression. In an Italian study, the internal coherence for all subscales showed alpha values ranging between 0.70 and 0.96 (80) and the T cut-off level used to discriminate AUD individuals with dual diagnosis vs AUD without dual diagnosis individuals was set to $T \geq 55$ in the GSI score. The SCL-90-R was completed in the presence of a psychologist who provided clarifications when necessary. In the present study, we report the SCL 90-R self-report total score (global severity index, GSI) to detect the psychological suffering (30).

TAS-20

The TAS-20 (44) is a 20-item self-report that assesses Alexithymia. The TAS-20 has a three-factor structure, as follows: Difficulty Identifying Feelings (DIF; e.g., "when I am upset, I don't know if I am sad, frightened, or angry"); Difficulty Describing Feelings (DDF; e.g., "I find it hard to describe how I feel about people"); and Externally Oriented Thinking (EOT; e.g., "I prefer talking to people about their daily activities rather than their feelings") (81). Cut-off scores have been established to categorize individuals as alexithymic (≥61), borderline (52–60), and non-alexithymic (≤51) (81).

The test–retest reliability of the TAS-20 in English (82) German (83), Italian (84) and Hindi (85) has been established. The test validity ranges from α=0.79 to α=0.82 (86).

Physiological Assessment

Based on previous investigations with minor modifications (87,88) in the present testing we measured 4 physiological variables measured by ProComp5 Infiniti™ encoder:

i) Inter-beat heart rate intervals – heart rate variability (HRV - expressed in milliseconds) measured by a pulse detection sensor housed in a middle finger to measure heart rate.

ii) Respiration frequency (RF – expressed as number of chest expansions) measured by a respiration sensor, a sensitive girth sensor worn using an easy fitting and high durability woven elastic band fixed with a length adjustable webbing belt that detects chest or abdominal expansion/contraction and outputs the respiration waveform;

iii) Electrodermal activity (EDA – expressed in microSiemens) or skin conductance across the skin was measured by a sensor connected to the index finger and ring finger;

iv) Skin Temperature (ST – expressed as Celsius degrees) measured by a sensor connected to the right thumb to measure skin surface temperature.

ProComp5 Infiniti™ encoder and software by Thought Technology were used to measure the above described physiological variables (http://thoughttechnology.com/index.php/hardware/procomp5-infiniti-5-channel-biofeedback-neurofeedback-system-w-biograph-infiniti-software.html). ProComp5 Infiniti™ is a 5 channel, multi-modality device for real-time computerized biofeedback and data acquisition. The apparatus has five protected pin sensor inputs with two channels sampled at 2048 samples per seconds and three channels sampled at 256 samples per seconds. All sensors are completely non-invasive and require little or no preparation for use. Just before the beginning of each session, participants were seated in a comfortable chair, and sensors were pasted to their wrists. Data acquisition was divided in 7 phases of 2 minutes each according to ProComp5 Infiniti™ manufacturer instructions (See Table 2 for details).

Data Analysis

Alcohol-related and clinical data were analyzed by two-way ANOVAs with dual diagnosis (with or without) and alexithymia (negative, borderline and positive) as main factors also according to methods previously described (89–91). Respiratory frequency, skin conductance, heart rate and body temperature were analyzed by repeated measures ANOVAs (the 7 steps of the ProComp5 Infiniti™ apparatus, see methods) with dual diagnosis (with or without) and alexithymia (negative, borderline and positive) as main factors. Post-hoc comparisons within logical sets of means were performed by the Tukey's HSD test, the use of which is permissible or even recommended in the absence of significant main or interaction effects in the ANOVA to minimize frequency errors of both type I and type II (92).

Results

Descriptive statistics

Socio-demographic, alcohol-related and clinical data of AUD patients are summarized in Table 1. The AUD men enrolled in the study were 50. The youngest was 29 and the oldest was 71 years old. The 90.3% of AUD individuals examined were Italian, the 37.1% were married, the 24.2% were divorced and the 37.1% were single, only the 1.6% were widowers. The mean age of onset of alcohol problems was 28.18±11.58 years. The AUD individuals reported an average of 16.44±11.67 years of problem drinking and an average of 18.99±23.06 drinks per day during the month prior to admission to the treatment unit. The 91.9% of the cases had completed at least 8 years of schooling. No other effects or correlations were found concerning the socio-demographic, alcohol-related and clinical data of AUD patients investigated.

Heart Rate Variability (HRV)

Figure 1 shows the HRV results. ANOVAs data evidenced a main effect of the alexithymic condition ($F(2,56)=5.94$, $p=0.05$). As disclosed by post-hoc comparisons, AUD individuals with positive alexithymia had potentiated HRV throughout the 7 steps of the ProComp5 Infiniti™ apparatus mainly compared to borderline or negative alexithymics (see Fig. 1).

Respiratory Frequency (RF)

ANOVA data for the RF (Figure 2) show an interaction between alexithymic condition and dual diagnosis presence in AUD subjects ($F(2,56)=4.55$, $p=0.01$ in the ANOVA for dual diagnosis x alexithymia). Indeed, as clearly evidenced by the panels of Fig. 2 *i)* AUD individuals with both dual diagnosis and positive alexithymia show lower RF if compared to AUD individuals with dual diagnosis but with negative alexithymia throughout the 7 phases of the physiological assessment: *ii)* AUD individuals without dual diagnosis with positive alexithymia had higher RF compared to AUD individuals without dual diagnosis but with negative alexithymia throughout the 7 phases of the physiological assessment.

Table 2. Description of the 7 sessions for the physiological data acquisition by ProComp5 Infiniti™ encoder according to the manufacturer instructions.

Phase 1	Baseline data Recording 2-min long	This preliminary phase was conducted without any external stimuli; participants were asked to relax and watch at the computer screen.
		30 sec Pause - no recording
Phase 2	Color-blindness test Recording 2-min long	Participants were asked to quickly respond specifying the color of the word of the Stroop color-word task (J.R. Stroop, Studies of interference in serial verbal reactions., J. Exp. Psychol. 1935;18:643). It is commonly used as laboratory stress tool for studying human psychophysiological response to stress. This test induces subjective stress with concomitant increasing of autonomic reactivity. The Stroop color-word task evaluates the ability of a person to inhibit automatic verbal responses: the different word denotes the names of some colors displayed in an unlike manner (e.g., the word "blue" is written in "red" instead of "blue").
Phase 3	First period of resting Recording 2-min long	Participants were asked to rest returning at the arousal value registered in the baseline data phase.
		30 sec Pause - no recording
Phase 4	Mathematic task Recording 2-min long	The math task consists in a progressive mental subtraction of the number seven starting from the number "1081" similarly at Mini-Mental State Examination Calculation subtest (Folstein MF, Folstein SE, McHugh PR. 'Mini-mental State'. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.).
Phase 5	Second period of resting Recording 2-min long	Participants were asked to rest returning at the arousal value registered in the baseline data phase.
		30 sec Pause - no recording
Phase 6	Emotional Task Recording 2-min long	The emotional task consists in imaginary task in which participants were asked to finish incomplete sentences, according to their life experience. Sentences concern different functioning areas: family, work, habits, affective relations. Participants had to think how integrate sentences according to their emotion states, meanwhile sensors were registering physiological parameters, without verbal contact with the operator.
Phase 7	Third period of resting Recording 2-min long	Participants were asked to rest returning at the arousal value registered in the baseline data phase.

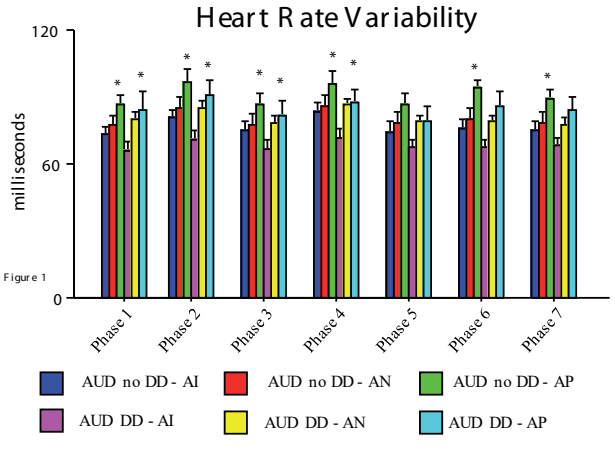

Fig. 1. ANOVA data of the heart rate variability expressed in milliseconds in AUD people with or without dual diagnosis (DD) with comorbidity for positive Alexithymia (AP), no Alexithymia (AN) and borderline Alexithymia (AI) (see methods) during the 7 steps of the physiological assessment. The error bars indicate pooled standard error means derived from appropriate error mean square in the ANOVA. Asterisks indicate significant differences between groups (*, $p < 0.05$).

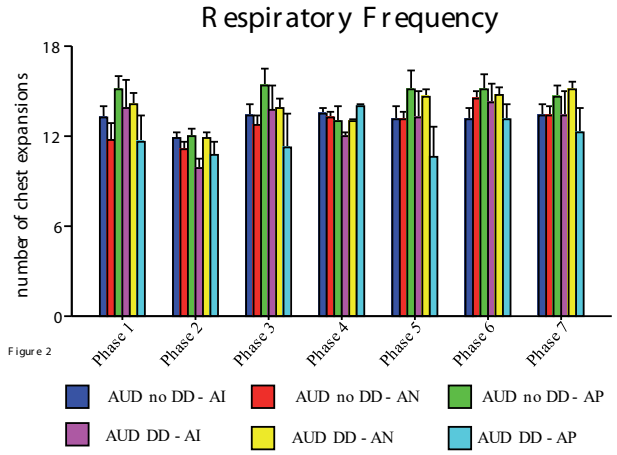

Fig. 2. ANOVA data of the respiratory frequency expressed in numbers of chest expansion in AUD people with or without dual diagnosis (DD) with comorbidity for positive Alexithymia (AP), no Alexithymia (AN) and borderline Alexithymia (AI) (see methods) during the 7 steps of the physiological assessment. The error bars indicate pooled standard error means derived from appropriate error mean square in the ANOVA.

Electrodermal Activity (EDA)

Statistical analysis of the EDA data clearly disclose a main effect of dual diagnosis associated with an interaction between dual diagnosis x alexithymia ($F(1,56)=5.80$; $F(2,56)=5.25$, $ps=0.05$ respectively). Actually, as shown in Fig. 3, although data evidences high variability between subjects, mainly in AUD individuals with dual diagnosis with positive Alexithymia, the same patients had greater values of EDA throughout the 7 steps of the ProComp5 Infiniti™ apparatus mainly compared to AUD without dual diagnosis but with positive Alexithymia.

Skin Temperature (ST)

As for ST (Fig. 4), Quite interestingly ANOVA failed to disclose a main effect of alexithymia due to the higher values shown by positive alexithymics compared to negative alexithymics.

Discussion

The main aim of this study was to investigate the relationship between emotional and cognitive stress responses to selected tasks in AUD patients suffering alexithymia with or without concomitant dual diagnosis through the measurement of some autonomic arousal responses.

In the present cohort of AUD patients, the condition of alexithymia in AUD subjects elevates RF, ST and HRV. Indeed, alexithymia can be considered as a stress vulnerability factor, impairing psychosomatic processing and inducing alterations in physiological parameters (93). It has been hypothesized that the limited emotional awareness and cognitive processing extend and amplify the physiological arousal and neuro-vegetative reactivity to stress. This idea was described as the "Alexithymia-stress hypothesis" (94). On the other hand, Papciak et al. proposed the "decoupling hypothesis", which states a mismatch between physiological arousal and emotional awareness in alexithymic individuals under stressful situation (95). However, Martin & Pihl argued that alexithymics are not necessarily more physiologically reactive to stress *per se*, but their subjective stress responses tend to be «decoupled» from their autonomic responses (96). The findings of our study are in line with the Martin and Pihl model strengthening the hypothesis that alexithymia results in higher levels of baseline physiological arousal even strongly associated with AUD.

Interestingly, in AUD subjects with concomitant dual diagnosis, the condition of alexithymia alters some autonomic responses showing with an elevation of ST and a decrease in RF. Several studies found high prevalence of comorbid mental disorders among AUD individuals (97–100). Recent works have suggested also that alexithymia is closely related to psychiatric symptoms including AUD and may be a measure of distress and an indicator of negative outcomes in psychiatric populations (101). Data from the present study in AUD individuals with dual diagnosis and concomitant alexithymia reveal disrupted levels of physiological parameters making them highly vulnerable to stressful situations. Indeed, stress is strongly connected to alcohol abuse emphasizing coping behavior to manage conditions of emotional suffering and struggles (102). Certainly, Koob (103) defined AUD a disorder that includes a progression from impulsivity (positive reinforcement) to compulsivity (negative reinforcement) where negative reinforcement is considered as a drug taking that alleviates a negative emotional state derived from dysregulation of specific neurochemical elements involved in reward and stress within the basal forebrain structures involving the ventral striatum and extended amygdala, respectively. Specific neurochemical signals in these structures include not only alterations in neurotransmission regulating

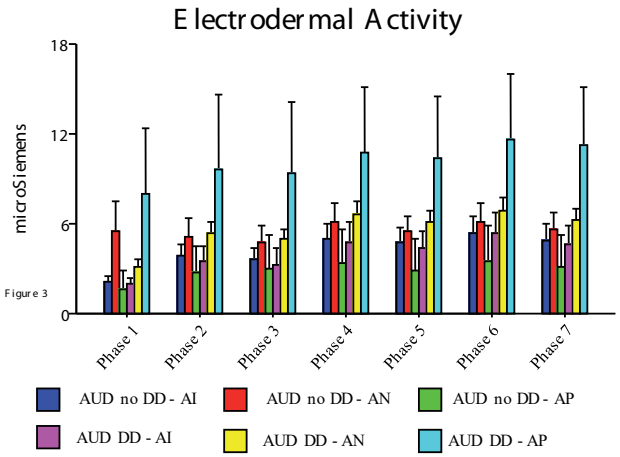

Fig. 3. ANOVA data of the electrodermal activity expressed in microSiemens in AUD people with or without dual diagnosis (DD) with comorbidity for positive Alexithymia (AP), no Alexithymia (AN) and borderline Alexithymia (AI) (see methods) during the 7 steps of the physiological assessment. The error bars indicate pooled standard error means derived from appropriate error mean square in the ANOVA.

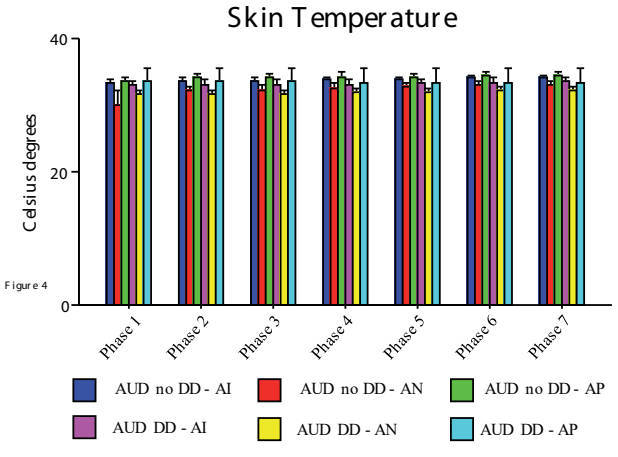

Fig. 4. ANOVA data of the skin temperature expressed in Celsius degrees in AUD people with or without dual diagnosis (DD) with comorbidity for positive Alexithymia (AP), no Alexithymia (AN) and borderline Alexithymia (AI) (see methods) during the 7 steps of the physiological assessment. The error bars indicate pooled standard error means derived from appropriate error mean square in the ANOVA.

reward, such as decreased dopamine and γ-aminobutyric acid function in the ventral striatum, but also the recruitment of brain stress systems, such as corticotropin-releasing factor, in the extended amygdala (103). According to the Koob's postulation, we do speculate that AUD patients with dual diagnosis and alexithymia perceiving a greater amount of stress due to their personal psychopathology and to the alexithymia induced emotional dysregulation may display disrupted psycho-emotional conditions associated with altered autonomic responses. However, other studies support the existence of higher sympathetic activation in Alexithymia. Indeed, it has been demonstrated in alexithymics a higher tonic heart rate (HR) (95,96,104), while others have shown higher EDA (105). In particular, some studies reported increased HR and EDA but others reported elevated EDA (105), without tonic differences between alexithymic and nonalexithymic participants (106).

Lauren McGillivray, pointed out the importance of identifying first the alexithymic condition to start afterwards specific therapeutic interventions on AUD individuals with dual diagnosis since high levels of alexithymia before treatment may lead to poorer therapeutic outcomes, particularly in patients diagnosed with addictive disorders (102). Thus, to early discovery of alexithymia in AUD individuals, by the Biofeedback therapy could be a quite useful method of intervention. Indeed, the Biofeedback involves the reading of certain signals from the autonomic nervous system (107,108). Biofeedback is the process of gaining greater awareness of many physiological functions primarily using instruments that provide information on the activity of those same systems, with a goal of being able to manipulate them at will (107). Some of the processes that can be controlled may include ST, HRV, EDA and RF (87). Indeed, in the Biofeedback therapy the patients are connected to electrical sensors that help into receive information (feedback) about body patients (bio). Previous data have shown in a follow-up study an increase in long-term abstinence after HRV-biofeedback for alcohol dependence in addition to rehabilitation (109,110). Further, other works have used biofeedback therapy in AUD individuals with positive outcomes. (108,111). However, based on our knowledge, no works have been published about the use of biofeedback in alexithymic individuals.

External stimuli can interfere with the processes that regulate synapse neurodevelopment, causing alteration in the development, maintenance, and plasticity of neuronal network connectivity (112,113). The stressful stimuli can determine some adverse effects on these processes, mainly if they occur during the neurodevelopment phase. The consequences are represented by the pathophysiology of various developmental brain disorders. It has been also demonstrated that stimuli intrinsic or extrinsic can modify the circuitries of the brain (113). Indeed, stimuli with positive impact help in strengthening and stabilize the synaptic connectivity. Stimuli with the negative effect may result in alterations of the synaptic efficacy causing abnormalities in the formation of synapse or its connectivity during development leading to a number of neurodevelopmental disorders.

In conclusion, although further investigations are necessary mainly for the low number of positive and borderline alexithymics recruited for study (aspect that could be considered as a study limit), we may draw some conclusions: 1) AUD individuals with dual diagnosis and alexithymia perceive a greater amount of stress due to their personal psychopathology and to the Alexithymia; 2) an early diagnosis of alexithymia in AUD individuals with dual diagnosis may allow an early intervention for the specific symptoms of alexithymia to improve the AUD treatment and outcomes (aspect that we do consider a strength of the study). Furthermore, since alcohol abuse is a devastating problem in Western countries, the present study may represent a step forward in the attempt to disclose other biological processes and behavioral responses underlying the dark side of addiction (Koob 2015). These results may also be of interest for specialists in the field of human dependencies.

Declaration of Interest

The authors report no conflicts of interest

Conflict of interest: all authors do inform that they have not any kind of financial relationships directly related to the subject of this paper.

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