Drug and Alcohol Dependence 150 (2015) 38–45

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Risk factors for alcoholism in the Oklahoma Family Health Patterns project: Impact of early life adversity and family history on affect regulation and personality

Kristen H. Sorocco[a,c,*], Nathan C. Carnes[a], Andrew J. Cohoon[a,b], Andrea S. Vincent[d], William R. Lovallo[a,b]

[a] Behavioral Sciences Laboratories, Veterans Affairs Medical Center, Oklahoma City, OK 73104, USA
[b] Department of Psychiatry and Behavioral Sciences, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73190, USA
[c] Donald W. Reynolds Department of Geriatric Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73190, USA
[d] Cognitive Science Research Center, University of Oklahoma, Norman, OK 73072, USA

ARTICLE INFO

Article history:
Received 21 June 2014
Received in revised form 1 February 2015
Accepted 2 February 2015
Available online 11 February 2015

Keywords:
Lifetime adversity
Family history
Alcoholism
Affect regulation
Personality

ABSTRACT

Aim: This study examined the impact of early lifetime adversity (ELA) on affect regulation and personality in persons with family history (FH+) and without (FH−) a family history of alcoholism. We examined the impact of early life adversity in healthy young adults, 18–30 years of age enrolled in a long-term study on risk for alcohol and other substance abuse.
Methods: ELA was assessed by a composite score of low socioeconomic status and personal experience of physical or sexual abuse and/or separation from parents before age 16, resulting in a score of 0, 1–2, or >3 adverse events. Unstable affect regulation and personality variables were obtained via self-report measures.
Results: Higher ELA scores were seen in FH+ ($\chi^2 = 109.2$, $p < 0.0001$) and in women ($\chi^2 = 17.82$, $p = 0.0019$). Although higher ELA predicted less emotional stability and more behavioral undercontrol, further analysis including both FH and ELA showed that FH+ persons are prone to poor affect regulation, negative moods, and have risky drinking and drug abuse tendencies independent of ELA level. ELA predicts reduced stress reactivity and poorer cognitive control over impulsive behaviors as shown elsewhere.
Conclusions: The present work shows that FH+ have poor mood regulation and antisocial characteristics. The greater prevalence of ELA in FH+ persons indicates that life experience and FH+ work in tandem to result in risky patterns of alcohol and drug experimentation to elevate risk for alcoholism. Further studies of genetic and environmental contributions to alcoholism are called for.
Published by Elsevier Ireland Ltd.

1. Introduction

The Oklahoma Family Health Patterns project (OFHP) is dedicated to understanding risk factors for alcoholism by comparing young adults with a family history (FH+) to those with no history (FH−) of the disorder. The premise of the project is that addictions, by definition, represent a failure of brain systems that control motivated behavior, and that increasingly severe loss of behavioral regulation underlies increased severity of addiction (American Psychiatric Association, 1994). This rationale presupposes that even healthy FH+ persons may display poorer regulation of motivated behavior, relative to FH−. Motivation and emotion are regulated by interactions between the brain's prefrontal cortex and limbic system (Damasio, 1994). To operationalize this conceptual model we initially predicted that FH+ persons would show alterations in stress reactivity, affect, cognition, and overt behavior, all of which depend on prefrontal–limbic interactions.

We have recently focused on early life adversity (ELA) as a potential contributor to personal characteristics that may increase risk for alcohol and other substance use disorders and have a differential impact in FH+ persons. ELA is an increasingly well recognized risk factor for a broad range of poor health outcomes (Dube et al., 2003). To guide further studies incorporating ELA, we developed a heuristic model based on brain function as shown in Fig. 1, to describe

* Corresponding author at: Donald W. Reynolds Department of Geriatric Medicine, University of Oklahoma Health Sciences Center, 1122 NE 13th Street, Oklahoma City, OK 73117, USA. Tel.: +1 405 456 1454; fax: +1 405 456 1839.
E-mail address: kristen-sorocco@ouhsc.edu (K.H. Sorocco).

http://dx.doi.org/10.1016/j.drugalcdep.2015.02.001
0376-8716/Published by Elsevier Ireland Ltd.

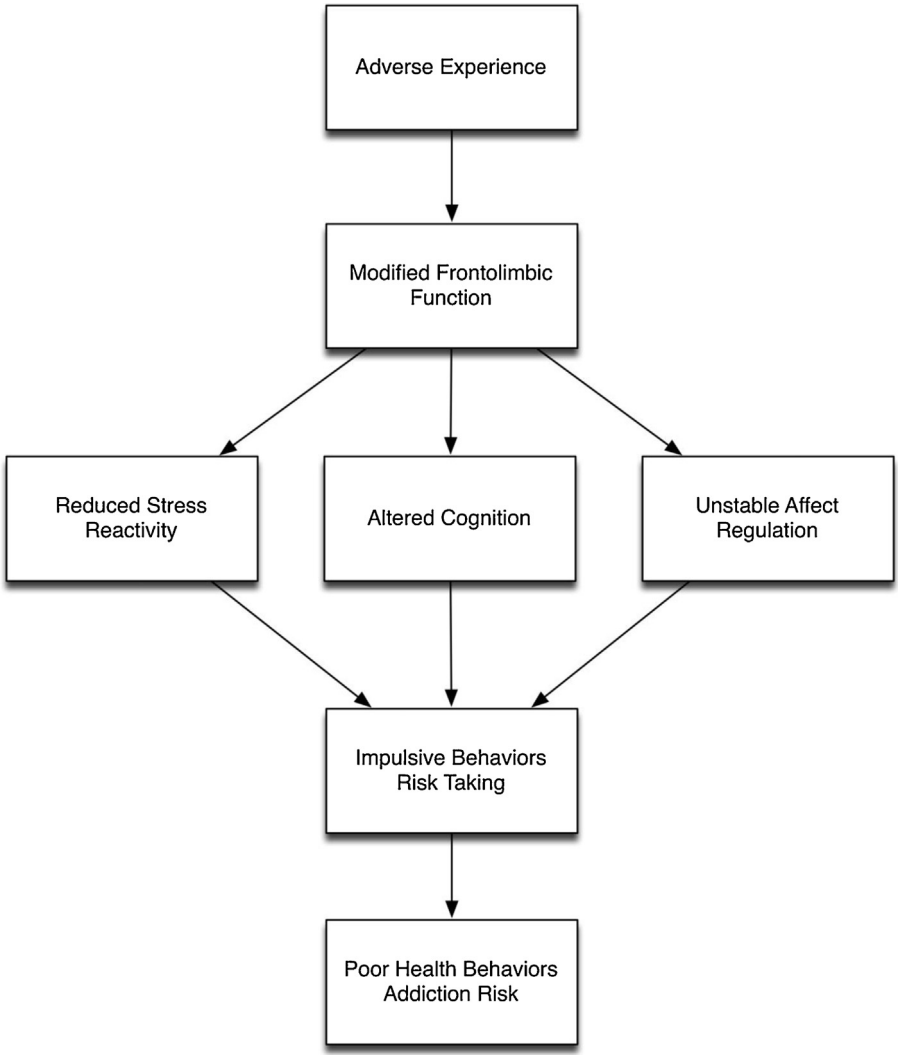

Fig. 1. Model outlining the impact of early adverse experience on stress reactivity, cognition, and affect regulation.

characteristics of ELA-exposed persons in the OFHP cohort that may account for risk for alcohol and other substance use disorders (Lovallo, 2013). The model assumes that ELA during childhood and adolescence alters development of limbic system and prefrontal cortex structures and their connections, with consequences that are seen in three domains: (a) stress reactivity, (b) cognition and behavior, and (c) psychological characteristics.

In the OFHP cohort, persons higher in ELA have blunted cortisol and heart rate reactivity to mental stress (Lovallo et al., 2012b), and they show diminished cognitive capacity and enhanced behavioral impulsivity (Lovallo et al., 2012a). These findings led us to ask whether the effects of ELA extended to the domain of psychological characteristics of the OFHP volunteers and whether these were more strongly represented in FH+ persons who had experienced ELA. Accordingly, the present paper examines personality characteristics and altered regulation of affect in high-ELA persons as a third dimension of increased risk for substance use disorders and the joint impact of ELA and FH+ on these same characteristics.

The current paper examines the relationship between demographic factors, family history, affect regulation, personality, and early life adversity. Participants in the Oklahoma Family Health Patterns (OFHP) project consist of healthy, young FH+ and FH− adults. We predicted that: (1) FH+ participants would report significantly more early life adversity than FH−, and that (2) as the number of adverse life events increased, emotional stability would diminish, and (3) as the number of adverse life events increased, there would be a greater tendency toward poor behavior regulation and a tendency toward norm violation. We propose that FH+ individuals who report experiencing early life adversity are at greater risk for emotional instability and tendency toward behavioral undercontrol, which places them at increased risk for alcoholism.

2. Materials and methods

2.1. Project description

The major hypothesis of the Oklahoma Family Health Patterns project is that alcoholism is most likely to occur in persons with functional alterations in brain systems serving emotion experience and expression. Our goal is to study healthy non-alcohol dependent FH+ and FH− to identify markers of high risk in the domains of psychophysiological function, cognition and behavior, and personality, with an emphasis on probes of emotional response systems. Participants take part in detailed family history and psychological assessments, and undergo behavioral and psychophysiological procedures in the lab.

2.2. Participants

All volunteers who completed screening for the OFHP project were included. These participants ($N = 599$) were 18–30 years of age, in good health, free of prescription medications, and did not meet criteria for a current Axis I mental health disorder as defined by the Diagnostic and Statistical Manual of Mental disorders, 4th ed. (APA, 1994). Subjects were required to pass a urine drug screen and alcohol breath test on each day of testing. All participants signed a consent form approved by the Institutional Review Board of the University of Oklahoma Health Sciences

Center and the Veterans Affairs medical Center in Oklahoma City, OK and were paid for participating.

2.2.1. Inclusion and exclusion criteria. Prospective participants were excluded if they had any of the following: a history of alcohol or drug dependence; diagnosis of substance abuse within the past 2 months; current use of any abused drug; history of any Axis I disorder other than depression assessed by Diagnostic Interview Schedule; depression within the past 2 months; Axis II disorders in clusters A or C assessed by Structured Clinical Interview for Diagnosis-II questionnaire and interview. Axis II, Cluster B disorders were not exclusionary because of the cluster's significant comorbidity with alcohol use disorders.

2.2.2. Screening. An initial telephone screening to ensure general conformity with inclusion and exclusion criteria was followed by a screening at the laboratory conducted by a trained interviewer supervised by a licensed clinical psychologist. Physical health was assessed through obtaining medical history and self-report of current good health.

2.3. Demographics

2.3.1. Family history of alcoholism and other drug problems. Family history classification was established using the Family History Research Diagnostic Criteria (FH-RDC) (Andreasen et al., 1977). The FH-RDC has a high degree of inter-rater reliability (.95) for reports of substance use disorders (Andreasen et al., 1977; Zimmerman et al., 1988). Persons were considered FH+ if either biological parent met criteria for alcohol or substance use by subject report. FH− were those reporting an absence of alcohol or substance use disorders in their biological parents and grandparents. Confirmation of the FH-RDC report by the proband was obtained by parent interview in all possible cases, 79% of the total included sample, and parents confirmed the subject's report of FH status in 89% of these cases. FH status could confidently be reassigned in 3% of the cases and 6% were dropped for inconsistent or insufficient information. Accordingly, for the 21% of participants with no parent interview, we assume that 89% are also correctly classified, leaving an estimated 3% with an unknown classification and a final estimate that 97% of the total included sample is correctly classified. Participants were excluded if either they or the parent reported possible fetal exposure to alcohol or other drugs.

2.3.2. Current substance use. Alcohol and drug use were assessed through the Cahalan Drinking Habits Questionnaire (Cahalan et al., 2004), the Alcohol Use Disorders Identification Test (Babor et al., 1992), and a Drug Use Questionnaire (Cognitive Studies Laboratory, 1994). The Drug Use Questionnaire asks individuals if they have tried a particular drug (e.g., tobacco, alcohol, marijuana, hallucinogens, opiates, stimulants, etc.) and if they have how often they use the substance.

2.4. Negative affect

2.4.1. Affect regulation. Assessed using the negative affect subscale of The Positive Affect and Negative Affect Scale (PANAS; Watson et al., 1988).

2.4.2. Depression. Psychological functioning was assessed using the computerized version of the Diagnostic Interview Schedule-IV (DIS-IV) conducted by a research assistant certified in its administration and through the Beck Depression Inventory II (Beck et al., 1996).

2.4.3. Neuroticism. Emotional stability was assessed using the neuroticism subscale of the Eysenck Personality Inventory (EPI) (Eysenck and Eysenck, 1964, 1968; Meites et al., 1980). The EPI measures also measures extraversion–introversion as described below.

2.5. Behavioral disinhibition

Personality and temperament variables associated with behavioral undercontrol that may be relevant to alcohol and drug abuse risk were assessed through self-report measures.

2.5.1. CPI. The Sociability scale of the California Personality Inventory (CPI-So; Gough, 1994) was administered to assess the degree of a person's conformity to social norms. This measure has a very high degree of agreement with clinical measures of antisocial personality and is useful in studies of offspring (Cooney et al., 1990; Kosson et al., 1994). Gough (1994) pointed out that the score of 30 forms an empirically established cut-off based on a large number of studies. High scores indicate a greater degree of conformity to social norms. Scores of 30–31 suggest normative social compliance. Scores ≥32 suggest above-average rectitude and conformity to social norms, and scores ≤29 suggest problems with social conformity. Other studies have found a similar pattern of scores when examining the relationship between FH of substance use and sociability scores. For example, Searles and Alterman (1994) found that sons of fathers showing one or two DSM-III symptoms of alcoholism had scores of 27, and sons of fathers with three or more symptoms scored 25. Alcoholics score 22 (Cooney et al., 1990; Gough, 1994). In the OFHP, FH+ are more than twice as likely to have low So scores (<30) than the FH−. Among the FH− subjects, 80% scored ≥30. The FH+ were more evenly divided about the cut point, with 51% scoring <30.

2.5.2. Temperament. Other measures of temperament that were administered were the Eysenck Personality Inventory (EPI; Eysenck and Eysenck, 1964, 1968) and the Psychopathic Personality Inventory (PPI; Lilienfeld and Andrews, 1996). The EPI measures both extraversion–introversion and neuroticism–stability. The extroversion–introversion scale consists of items primarily tapping into impulsivity and sociability traits. The PPI is based on Hare's Psychopathic Checklist (Hare and Neumann, 2005) and contains two factors. The PPI Factor I measures fearless dominance, tapping into Hare's core psychopathic personality traits and does not relate with substance use disorders. PPI Factor II score serves an index for poor behavioral regulation and a tendency toward norm violation. PPI Factor II has been found to be positively related to substance use disorders in incarcerated samples (Reardon et al., 2002).

2.6. Adversity

Adversity groups were formed using a composite score that was based on both retrospective reports of early adverse events in combination with Social Economic Status (SES). Retrospective reports of adversity were taken from C-DIS-IV items derived from the posttraumatic stress disorders (PTSD) scale and are closely similar to the life events assessed retrospectively in the studies by Caspi et al. (2002, 2003) as follows: Physical or Sexual Abuse (Have you ever been mugged or threatened with a weapon? Have you ever experienced a break-in or robbery? Have you ever been raped or sexually assaulted by a relative? Have you ever been raped or sexually assaulted by someone not related to you?) and Emotional Adversity (Before you were 16, was there a time when you did not live with your biological mother for at least 6 months? Before you were 16, was there a time when you did not live with your biological father for at least 6 months?). PTSD reports have a very high degree of test–retest reliability and inter-instrument reliability (Foa and Tolin, 2000; Watson et al., 1991). Each person was assigned an adversity score ranging from 0 (no adverse events) to a maximum of 5.

SES was calculated using Hollingshead and Redlich's system and was defined as the highest education and occupational level of the head of household in which the subject grew up, with occupation level categorized from 1 (lowest) to 9 (highest) × 5 plus years of education × 3 (Hollingshead, 1975). For this sample, the scores ranged from 13 (unskilled labor or menial worker) to 68 (professional of major business owner or executive) with a mean of 46 (minor business owner or technical worker). The SES level tended to be lower for subjects experiencing more adversity, with those having 0 adverse events having SES ≥ 56 (major business owner, professional), 1 event 40–55 (medium business, minor professional, technical), and 2 or more events having SES < 40 (ranging from skilled craftsmen to unskilled laborers). The composite adversity score used here was constructed as the sum of adverse events (0–5) and placement in the upper, middle, and lower third of the SES distribution (0, 1, 2) for our subject population, yielding scores that ranged from 0 to 7. For descriptive purposes, composite scores were grouped as 0, 1–2, and 3+.

2.7. Statistical analyses

Demographic and behavioral data were compared across 0, 1–2, or 3+ ELA groups for events experienced prior to the age of 16. ELA classifications were analyzed using one-way ANOVAs, and multiple comparisons were performed with a Tukey–Kramer adjustment. The relationships among ELA, FH, and Sex were analyzed in a second set of ANOVAs based on a model including main effects and all interactions using Type III sums of squares. Hypotheses were two-tailed with a p-value of 0.05 defined as statistically significant. All analyses were performed using statistical software package SAS Version 9.2.

3. Results

3.1. Demographics and substance use

Table 1 outlines relevant demographic characteristics by ELA group. Women ($\chi^2 = 17.82$, $p = .0001$) and non-Caucasians ($\chi^2 = 15.35$, $p = .0005$) comprised a significantly higher percentage of subjects with the highest ELA scores. Similar to what was reported in an earlier publication, groups with high ELA scores also had lower mental age scores on the Shipley Institute of Living Scale ($F = 12.65$, $p < .0001$) (Lovallo et al., 2012a). The relevance of ELA for alcoholism was seen in three measures: (a) FH+ individuals comprised a greater proportion among those with high ELA scores ($\chi^2 = 109.2$, $p < 0.0001$). Drinking scores, as measured by the Alcohol Disorders Use Identification Test (AUDIT), were not significantly different by degree of ELA. However, individuals with higher ELA scores were (b) more likely to report a younger age of first drink

Table 1
Demographic characteristics by adversity.

	Adversity			
	0 (*N* = 81)	1–2 (*N* = 308)	3+ (*N* = 210)	
				p-Value Chi-square (χ^2, df)
FH status (% positive)	16.05	47.88*	80.29*,◊	<0.0001 109.62, 2
Sex (% female)	53.09	53.42	71.15*,◊	<0.0001 17.82, 2
Race (% White)	96.25	87.09	78.82*,◊	0.0005 15.35, 2
Ethnicity (% Hispanic)	2.47	3.91	4.33	0.7609 0.55, 2
				p-Value *F*
Age	23.2 (0.3)	23.4 (0.2)	23.9 (0.2)	0.1505 *F* = 1.90
Shipley mental age	*17.8 (0.1)*	*17.5 (0.1)*	*17.0 (0.1)**,◊	*<0.0001 F = 12.65*
AUDIT	4.3 (0.4)	4.6 (0.2)	4.2 (0.3)	0.4767 *F* = 0.74
Age of first drink	16.6 (0.3) *N* = 58	16.9 (0.2) *N* = 181	15.4 (0.4)*,◊ *N* = 89	0.0005 *F* = 7.82
Drugs used (#)	0.5 (0.056)	0.7 (0.027)*	0.8 (0.028)*,◊	<0.0001 *F* = 10.44
Intent to drink	*2.182 (.757)* *N = 58*	*1.195 (.174)* *N = 181*	*1.376 (.304)* *N = 89*	*.01462 F = 1.94*

Entries show Mean (SEM) unless shown otherwise.
* Statistically different from 0 ELA by $p < 0.05$.
◊ Statistically different from 1 to 2 ELA by $p < 0.05$.
Demographics in italics are ones for which Adversity contributes significantly after controlling for both FH status and sex.

Table 2
Frequency (percentage) of number of drugs used by adversity.

Adversity group	Number of drugs subject reported having used						
	0	1	2	3	4	5	6+
0 (*N* = 81)	38 (46)	22 (27)	11 (14)	4 (5)	1 (1)	2 (3)	3 (4)
1–2 (*N* = 308)	97 (32)	81 (26)	44 (14)	31 (10)	26 (8)	18 (6)	11 (4)
3+ (*N* = 210)	44 (21)	48 (23)	37 (18)	22 (10)	24 (11)	12 (6)	23 (11)

Chi square = 39.14, 12 degrees of freedom.
p-Value < 0.0001.

($F = 7.82$, $p = .0005$) and were (c) reported having tried a greater number of drugs (Tables 1 and 2; $\chi^2 = 39.14$, $p < 0.0001$).

3.2. Negative affect and emotional stability

There was no significant difference between ELA groups on reported experience of negative or positive affect on the PANAS (Table 3). However, groups with higher ELA scores had more symptoms of depression according to the Beck Depression Inventory-II ($F = 14.73$, $p < 0.0001$). Groups with higher ELA scores also had significantly higher scores on the neuroticism scale of the Eysenck Personality Inventory (EPI) compared to the other groups ($F = 10.28$, $p < 0.0001$). Participants did not differ significantly on the EPI extraversion scale.

3.3. Behavioral disinhibition

It is noteworthy that higher ELA scores were strongly related to measures of behavioral disinhibition (Table 3). The group with higher ELA scores has scored significantly lower on the CPI sociability scale ($F = 34.58$, $p < 0.0001$), higher on PPI Factor II ($F = 8.16$, $p = 0.0003$), and lower on PPI Factor I ($F = 3.15$, $p = 0.0434$).

3.4. ELA in relation to family history of alcoholism and sex

The relationships among ELA, FH, and Sex on each of the outcome variables were examined. Several main effects of sex were noted including lower scores among women on: antisocial characteristics (CPI-So, $F = 5.71$, $p = .017$; PPI-II $F = 8.00$, $p = .005$), and the psychopathy scale (PPI-I, $F = 43$, $p < .0001$), along with lower scores on the AUDIT and Cahalan index ($Fs \geq 3.93$, $ps = .05$). There were no interactions between Sex and ELA or Sex and FH or three way interactions for any analysis.

While analyses noted above revealed a number of significant differences among the psychological and temperamental traits examined, inclusion of FH in the analysis resulted in most of the significant effects of ELA dropping out leaving FH as having a significant impact on psychological and temperamental traits and drinking and drug experimentation (Table 4). Notably, there were no significant ELA × FH interactions, indicating a pattern of purely additive relationships. Significant main effects of FH included: CPI-So ($F = 36.15$, $p < .0001$), PPI-I ($F = 12.58$, $p = .0004$) and PPI-II ($F = 14.28$, $p = .0002$), along with indicators of negative and unstable affect seen in PANAS Negative affectivity ($F = 9.85$, $p < .0018$), EPI Neuroticism ($F = 17.62$, $p < .0001$), and BDI scores ($F = 22.38$, $p < .0001$). FH+ exhibited higher levels of risk in drinking and drug use patterns relative to FH, as seen in an earlier Age at First Drink

Table 3
Personality characteristics [mean (SE)] by adversity group.

	0 (*N* = 81)	1–2 (*N* = 308)	3+ (*N* = 210)	*p*-Value	*F*
Negative affect and emotional stability					
Positive affect (PANAS)	33.8 (1.0)	32.3 (0.4)	31.6 (0.6)	0.1137	*F* = 2.18
Negative affect (PANAS)	14.0 (0.6)	14.2 (0.3)	14.3 (0.4)*N* = 184	0.9020	*F* = 0.10
Depression (BDI-II)	3.9 (0.5)	6.3 (0.4)*	8.6 (0.6)*,◊	<0.0001	*F* = 14.73
Neuroticism (EPI)	5.4 (0.4)	6.8 (0.3)*	8.0 (0.3)*,◊	<0.0001	*F* = 10.28
Extraversion (EPI)	*12.9 (0.4)*	*12.2 (0.2)*	*12.7 (0.3)*	*0.1919*	*F = 1.66*
Behavioral disinhibition					
CPI total	*32.9 (0.5)N = 78*	*30.5 (0.3)* N = 296*	*27.3 (0.4)*,◊*	*<0.0001*	*F = 34.58*
PPI Factor 2 (PSI)	12.1 (0.3)	12.7 (0.1)	13.3 (0.2)*,◊	0.0003	*F* = 8.16
PPI Factor 1 (PSI)	18.3 (0.4)	17.8 (0.2)	17.3 (0.2)*	0.0434	*F* = 3.15

* Statistically different from 0 ELA by $p < 0.05$.
◊ Statistically different from 1 to 2 ELA by $p < 0.05$.
Personality characteristics in italics are ones for which Adversity contributes significantly after controlling for both FH status as well as sex.

Table 4
Variable means (SE) by life adversity/SES and family history.

	FH−			FH+		
	0	1–2	3+	0	1–2	3+
PPI Factor 2	11.9 [0.3]	12.1 [0.2]	12.6 [0.3]	12.8 [0.8]	13.2 [0.2]	13.5 [0.2]
PPI Factor 1	18.6 [0.4]	18.1 [0.2]	18.3 [0.5]	16.6 [0.8]	17.5 [0.2]	17.1 [0.2]
Audit	4.3 [0.4]	4.0 [0.3]	4.6 [0.5]	4.5 [1.1]	5.2 [0.3]	4.1 [0.3]
CPI	33.5 [0.6]	32.6 [0.4]	30.3 [1.0]	30.0 [1.5]	28.5 [0.4]	26.5 [0.5]
Positive affect	34.4 [1.1]	32.1 [0.6]	32.6 [1.1]	30.5 [1.9]	32.6 [0.6]	31.3 [0.6]
Negative affect	13.5 [0.6]	13.4 [0.4]	12.8 [0.6]	16.3 [1.6]	15.0 [0.4]	14.6 [0.4]
Neuroticism (EPI)	5.1 [0.4]	5.6 [0.4]	6.4 [0.8]	6.8 [1.3]	8.2 [0.4]	8.5 [0.4]
Beck depression	3.2 [0.4]	4.5 [0.4]	5.5 [1.0]	6.8 [1.7]	8.3 [0.6]	9.4 [0.7]
Cahalan volume	24.1 [0.5]	21.5 [2.3]	28.4 [5.6]	22.0 [6.0]	27.3 [3.2]	20.9 [2.9]
Age of first drink	16.9 [0.6]	17.0 [0.3]	16.9 [0.6]	15.4 [0.5]	16.0 [0.4]	14.9 [0.5]
Intent to drink	1.8 [0.9]	1.2 [0.2]	0.7 [0.2]	4.0 [1.5]	1.2 [0.3]	1.6 [0.4]
Drug use	0.5 [0.06]	0.6 [0.04]	0.7 [0.07]	0.7 [0.13]	0.8 [0.03]	0.8 [0.0]

($F = 6.53$, $p = .0114$), drinking with the explicit Intent to get drunk ($F = 5.31$, $p = .0219$), and in reporting experimenting with a greater number of abused drugs ($F = 12.99$, $p = .0003$).

4. Discussion

The goal of the OFHP is to study healthy non-alcohol dependent FH+ and FH− to identify potential markers of high risk in the domains of psychophysiological function, cognition and behavior, and affect regulation. We recently identified ELA as representing a potentially significant set of events in the individual's development that could affect the same domains of function thought to enhance risk in FH+ persons. This line of reasoning led us to propose an integrative heuristic model outlining the impact of ELA on stress reactivity, cognition and behavior, and affect regulation (Fig. 1).

We have recently tested the first two domains specified in the model and have reported that persons with higher ELA scores have (a) blunted stress reactivity and (b) poorer cognitive function and more signs of impulsive behavior (Lovallo et al., 2012a). (c) In the current analysis, we examined the third domain of functioning thought to be affected by ELA, and we have shown that ELA is associated with more negative affect and more affective instability as shown in the higher scores on the Beck Depression Inventory and the Eysenck Neuroticism scale. In addition, this analysis showed greater behavioral undercontrol seen in lower sociability scores on the California Personality Inventory and higher scores on Factor II of the PPI. The latter score is associated with norm violation and lower behavioral restraint in daily life (Patrick et al., 2006). Scores on Factor I of the PPI, reflecting core psychopathy, characterized by emotional coldness, were somewhat lower in persons with greater degrees of ELA, consistent with the view that ELA contributes to behavioral disinhibition, but not behavioral restraint and emotional coldness. Finally, the present analysis shows that higher levels of ELA are potentially related to risk for alcoholism and other substance use disorders in three measures: (a) higher levels of ELA are highly prevalent in FH+ persons, (b) persons with higher ELA scores report an earlier age at first drink, and (c) they report experimenting with a greater number of drugs.

Although the above relationships suggested a significant impact of ELA on these important risk-related characteristics, examination of a statistical model including both FH and ELA revealed that FH+ accounted for these same personal characteristics. FH+ subjects were different from FH− on important indicators of mood stability and a tendency toward negative affect along with antisocial behaviors and drinking variables. This indicates that the characteristics attributable to ELA alone are attributable to the greater prevalence of FH+ persons in groups having higher levels of ELA. Most importantly, FH+ persons engaged in more risky drinking practices and drug experimentation.

These findings bear interesting implications for the relationships implied in our model in Fig. 1 and they suggest directions for future research. First, our earlier reports of the effects of ELA are consistent with a broad impact of stress in early life. In this case, ELA predicted smaller physiological responses to stress despite the fact that high-ELA groups reported equivalent levels of subjective awareness and experience of the stressors (Lovallo et al., 2012b). It is noteworthy that blunted cortisol and heart rate reactivity to stress are prominent characteristics of abstinent alcohol and substance-abusing patients and heavy social drinkers (Errico et al., 1993; Bernardy et al., 1996; Panknin et al., 2002; King et al., 2009), and stress is a predictor of alcohol relapse (Sinha, 2001; Sinha et al., 2011) and in smoking cessation programs (al'Absi, 2006). In preadolescent FH+ and FH− boys, blunted cortisol reactivity predicted smoking and marijuana experimentation at ages 15–16, and blunted reactivity was a stronger predictor of early experimentation than FH status (Moss et al., 1999, 1995). It appears that blunted

stress reactivity may be a potentially significant predictor of addictive disorders.

In addition, to blunted stress reactivity, we have shown that ELA within the OFHP cohort predicts poorer working memory, lower mental age scores, more rapid delay discounting of monetary rewards, and higher body mass index (Lovallo et al., 2012a; Lovallo, 2013). Impulsive behavioral tendencies and poorer working memory are frequently identified as characteristics of adolescents and young adults with substance use disorders (Verdejo-Garcia et al., 2008) and who are overweight (Verdejo-Garcia et al., 2010). Cocaine and heroin abusers also show poor cognitive and behavioral regulation and rapid delay discounting (Verdejo-Garcia et al., 2006, 2007; Petry and Martin, 2002).

These collective characteristics overlap heavily with characteristics typically identified in earlier studies of FH+ persons. As noted by others, FH+ exhibits a "neurobehavior disinhibition" (Tarter et al., 2004) and "behavioral undercontrol" (Sher et al., 1991). ELA, accordingly provides insight into an environmental risk for enhancing behavioral tendencies that contribute to impulsivity, impaired regulation over emotional responses, and diminished stress reactivity that may reduce the experience of danger in environmentally risky situations. However, it is well established that FH+ have a significantly elevated risk for alcoholism with a genetic basis (Cloninger et al., 1981), and the present results indicate that negative affect, poor mood regulation, and antisocial tendencies relate to this genetically driven characteristic more than to the environment, as measured through ELA. Together, the evidence of a genetic contribution to alcoholism risk in FH+ and the greater degrees of ELA apparently experienced by many FH+ persons raise the possibility of specific vulnerabilities to ELA in FH+ that may greatly increase the potential for addictive behaviors in later life.

There is increasing evidence from animal models that stressful and benign experience during development can affect stress reactivity and behavioral regulation (Liu et al., 1997; Meaney, 2001; Spinelli et al., 2009) in association with prefrontal morphologic changes (Spinelli et al., 2009). In a similar fashion, studies on persons exposed to harsh and stressful conditions during childhood and adolescence can display blunted stress reactivity during adulthood (Carpenter et al., 2007, 2011). In addition, FH+ persons are likely to inherit a tendency to be behaviorally impulsive (King et al., 2009). The above findings therefore suggest a significant overlap in characteristics of FH+ persons and those exposed to ELA. The independent contribution of FH+ to poor prefrontal connectivity to other brain regions, including limbic system and temporoparietal regions associated with cognition, is seen in a series of neuroimaging studies on the OFHP cohort which show: (a) the need for greater recruitment of cognitive resources during work on cognitive tasks (Acheson et al., 2014a), greater activation ventral striatum during tasks assessing response to rewards (Acheson et al., 2009), and diminished white matter integrity in prefrontal regions in healthy FH+ (Acheson et al., 2014b). The possible genetic contribution to the regulation of affect in FH+ individuals is in keeping with a recent report that FH+ persons show a greater impact of specific modification of the serotonin transporter gene while FH− persons show no such impact (Lovallo et al., 2014).

The present findings and those reported earlier from the OFHP suggest that a systematic search for genetic polymorphisms in FH+ with varying degrees of ELA may yield useful insights into environmental contributions to risk for alcohol and other substance use disorders. The present OFHP data set is not sufficiently large to permit this sort of gene by environment analysis. However, a recent examination of the impact of serotonin transporter activity variation in affective regulation in FH+ vs. FH− in this cohort showed that the high gain-of-function allele conferred much greater emotional lability in FH+ persons but with little or no impact in FH− (Lovallo et al., 2014). In a similar fashion, using diffusion tensor imaging to estimate white matter integrity in prefrontal pathways in FH+, we showed poorer white matter integrity to be present in two unrelated samples of FH+ of different ages, a 24 year-old sample from the OFHP and an 11–14 year old sample in a separate study (Acheson et al., 2014c). These findings are compatible with a model of alcoholism risk in which a genetic diathesis present in FH+ may be vulnerable to the effects of ELA. Related studies suggest the potential utility of such further studies (Kreek et al., 2005; Moss et al., 1995; Lovallo, 2013; King et al., 2009). Future analyses on a larger study sample may allow specific tests of this currently speculative hypothesis.

The initial focus of this paper was to examine the impact of ELA on affect regulation and personality in relation to risk for alcoholism. Overall, our hypotheses regarding the impact of adversity among FH+ persons, as well as personality alterations were supported, but with the important modification that FH+ persons have a significant alteration in mood regulation and antisocial characteristics that may contribute to drinking and drug experimentation. A strength of this study is the relatively large sample size of healthy individuals who did not meet criteria for a current mood disorder or substance use disorder. The inclusion criteria for the OFHP were designed to look specifically at psychologically and physically healthy FH+ and FH− individuals in order to reduce the number of confounding variables also associated with risk for alcoholism. It is important to note that just because the OFHP sample was healthy does not mean they are not at risk for alcoholism. Cloninger has noted that "...alcohol abuse itself is not a sensitive criterion of genetic susceptibility" (Cloninger et al., 1981). Falconer has addressed this question at length, noting that complex polygenetic contributions to a given disorder may confer risk-related characteristics at a phenotypic level in the absence of the disorder itself (Falconer, 1965). Although these ELA findings may be generalizable to a broad segment of the population, the results may not be generalizable to individuals who have been severely traumatized and exhibit symptoms of posttraumatic stress disorder or currently meet criteria for another mental health diagnosis (Heim and Nemeroff, 2001; Carpenter et al., 2011). Another limitation of this study, shared by other studies focusing on ELA, is that the adversity data was collected by retrospective self-report. However, the reliability of our family history reports, noted in the methods section here, suggests that participants were reliable informants.

These findings suggest a pattern of relationships between FH+, ELA, unstable affect regulation, and personality traits associated with behavioral undercontrol. This finding is consistent with other domains studied in the OFHP project, including physiological functioning, cognition, and behavior. Collectively, ELA appears to have a disproportionate impact in FH+ persons and FH+ provides independent contributions to poor mood stability, antisocial characteristics, and risky drinking practices. FH+ along with ELA appear to contribute independently to a constellation of affective, personality, and behavioral characteristics that put the FH+ person at risk of alcohol and other substance use disorders.

Role of funding source

Funding for this study was provided by the Department of Veterans Affairs and the National Institutes of Health, NIAAA (R01 AA12207); the sources of funding had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Contributors

Dr. William R. Lovallo designed the study and wrote the protocol. Dr. Sorocco managed the literature searches and summaries of

previous related work. Authors Carnes, Cohoon, and Vincent undertook the statistical analysis, and author Sorocco wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors have no conflict of interest

Acknowledgements

We would like to thank Nancy Simpson who assisted with the formatting and submission of this manuscript.

References

Acheson, A., Robinson, J.L., Glahn, D.C., Lovallo, W.R., Fox, P.T., 2009. Differential activation of the anterior cingulate cortex and caudate nucleus in persons with a family history of alcoholism during a gambling simulation: studies from the Oklahoma Family Health Patterns Project. Drug Alcohol Depend. 100, 17–23.

Acheson, A., Tagamets, M.A., Rowland, L.M., Mathias, C.W., Wright, S.N., Hong, L.E., Kochunov, P., Doughterty, D.M., 2014a. Increased forebrain activations in youths with family histories of alcohol and other substance use disorders performing a go/nogo task. Alcohol. Clin. Exp. Res. 38, 2944–2951.

Acheson, A., Wijtenburg, S.A., Rowland, L.A., Bray, B.C., Gaston, F., Mathias, C.W., Fox, P.T., Lovallo, W.R., Wright, S.N., Hong, L.E., McGuire, S., Kochunov, P., Dougherty, D.M., 2014b. Combining diffusion tensor imaging and magnetic resonance spectroscopy to study reduced frontal white matter integrity in youths with family histories of substance use disorders. Hum. Brain Mapp. 35, 5877–5887.

Acheson, A., Wijtenburg, S.A., Rowland, L.A., Winkler, A.M., Gaston, F., Mathias, C.S., Fox, P.T., Lovallo, W.R., Wright, S.N., Hong, L.E., Dougherty, D.M., Kochunov, P., 2014c. Assessment of whole brain white matter integrity in youths and young adults with a family history of substance-use disorders. Hum. Brain Mapp. 35, 5401–5413.

al'Absi, M., 2006. Hypothalamic–pituitary–adrenocortical responses to psychological stress and risk for smoking relapse. Int. J. Psychophysiol. 59, 218–227.

Andreasen, N.C., Endicott, J., Spitzer, R.L., Winokur, G., 1977. The family history method using diagnostic criteria. Reliability and validity. Arch. Gen. Psychiatry 34, 1229–1235.

American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. American Psychiatric Association, Washington, DC.

Babor, T.F., de la Fuente, J.R., Saunders, J., Grant, M., 1992. AUDIT: The Alcohol Use Disorders Identification Test: Guidelines For Use in Primary Health Care. World Health Organization, Geneva, Switzerland.

Beck, A.T., Steer, R.A., Ball, R., Ranieri, W., 1996. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. J. Pers. Assess. 67, 588–597.

Bernardy, N.C., King, A.C., Parsons, O.A., Lovallo, W.R., 1996. Altered cortisol response in sober alcoholics: an examination of contributing factors. Alcohol 13, 493–498.

Cahalan, D., Cisin, I.H., Crossley, H.M., 2004. American drinking practices. Addiction 99, 1612–1613.

Carpenter, L.L., Carvalho, J.P., Tyrka, A.R., Wier, L.M., Mello, A.F., Anderson, G.M., Wilkinson, C.W., Price, L.H., 2007. Decreased adrenocorticotropic hormone and cortisol responses to stress in healthy adults reporting significant childhood maltreatment. Biol. Psychiatry 62, 1080–1087.

Carpenter, L.L., Shattuck, T.T., Tyrka, A.R., Geracioti, T.D., Price, L.H., 2011. Effect of childhood physical abuse on cortisol stress response. Psychopharmacology (Berl.) 214, 367–375.

Caspi, A., McClay, J., Moffitt, T.E., Mill, J., Martin, J., Craig, I.W., Taylor, A., Poulton, R., 2002. Role of genotype in the cycle of violence in maltreated children. Science 297, 851–854.

Caspi, A., Sugden, K., Moffitt, T.E., Taylor, A., Craig, I.W., Harrington, H., McClay, J., Mill, J., Martin, J., Braithwaite, A., Poulton, R., 2003. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science 301, 386–389.

Cloninger, C.R., Bohman, M., Sigvardsson, S., 1981. Inheritance of alcohol abuse: cross fostering analysis of adopted men. Arch. Gen. Psychiatry 38, 861–868.

Cognitive Studies Laboratory, 1994. The Drug Use Inventory. Center for Alcohol and Drug Related Studies, University of Oklahoma Health Sciences Center.

Cooney, N.L., Kadden, R.M., Litt, M.D., 1990. A comparison of methods for assessing sociopathy in male and female alcoholics. J. Stud. Alcohol 51, 42–48.

Damasio, A.R., 1994. Descartes' Error: Emotion, Reason and the Human Brain. Grosset/Putnam, New York.

Dube, S.R., Felitti, V.J., Dong, M., Giles, W.H., Anda, R.F., 2003. The impact of adverse childhood experiences on health problems: evidence from four birth cohorts dating back to 1900. Prev. Med. 37, 268–277.

Errico, A.L., Parsons, O.A., King, A.C., Lovallo, W.R., 1993. Attenuated cortisol response to biobehavioral stressors in sober alcoholics. J. Stud. Alcohol 54, 393–398.

Eysenck, S.B., Eysenck, H.J., 1964. Eysenck Personality Inventory. Educational and Industrial Testing Service, San Diego, CA.

Eysenck, S.B., Eysenck, H.J., 1968. The measurement of psychoticism: a study of factor stability and reliability. Br. J. Soc. Clin. Psychol. 7, 286–294.

Falconer, D.S., 1965. Inheritance of liability to certain diseases estimated from incidence among relatives. Ann. Hum. Genet. 29, 51–76.

Foa, E.B., Tolin, D.F., 2000. Comparison of the PTSD Symptom Scale-Interview Version and the Clinician-Administered PTSD scale. J. Trauma. Stress 13, 181–191.

Gough, H.G., 1994. Theory, development, and interpretation of the CPI socialization scale. Psychol. Rep. 75, 651–700.

Hare, R.D., Neumann, C.S., 2005. Structural models of psychopathy. Curr. Psychiatry Rep. 7, 57–64.

Heim, C., Nemeroff, C.B., 2001. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. Biol. Psychiatry 49, 1023–1039.

Hollingshead, A.B., 1975. Four Factor Index of Social Status. Yale University, New Haven, CT, pp. 1–22.

King, S.M., Keyes, M., Malone, S.M., Elkins, I., Legrand, L.N., Iacono, W.G., McGue, M., 2009. Parental alcohol dependence and the transmission of adolescent behavioral disinhibition: a study of adoptive and non-adoptive families. Addiction 104, 578–586.

Kosson, D.S., Steuerwald, B.L., Newman, J.P., Widom, C.S., 1994. The relation between socialization and antisocial behavior, substance use, and family conflict in college students. J. Pers. Assess. 63, 473–488.

Kreek, M.J., Nielson, D.A., Butelman, E.R., LaForge, K.S., 2005. Genetic influences on impulsivity, risk taking, stress responsivity and vulnerability to drug abuse and addiction. Nat. Neurosci. 8, 1450–1457.

Lilienfeld, S.O., Andrews, B.P., 1996. Development and preliminary validation of a self-report measure of psychopathic personality traits in noncriminal populations. J. Pers. Assess. 66, 488–524.

Liu, D., Tannenbaum, B., Caldji, C., Francis, D., Freedman, A., Sharma, S., Pearson, D., Plotsky, P.M., Meaney, M.J., 1997. Maternal care, hippocampal glucocorticoid receptor gene expression and hypothalamic–pituitary–adrenal responses to stress. Science 277, 1659–1662.

Lovallo, W.R., Enoch, M.A., Yechiam, E., Glahn, D.C., Acheson, A., Sorocco, K.H., Hodgkinson, C.A., Kim, B., Cohoon, A.J., Vincent, A.S., Goldman, D., 2014. Differential impact of serotonin transporter activity on temperament and behavior in persons with a family history of alcoholism in the Oklahoma Family Health Patterns Project. Alcohol. Clin. Exp. Res. 38, 1575–1581.

Lovallo, W.R., 2013. Early life adversity reduces stress reactivity and enhances impulsive behavior: implications for health behaviors. Int. J. Psychophysiol. 90, 8–16.

Lovallo, W.R., Farag, N.H., Sorocco, K.H., Acheson, A., Cohoon, A.J., Vincent, A.S., 2012a. Early life adversity contributes to impaired cognition and impulsive behavior: studies from the Oklahoma Family Health Patterns Project. Alcohol. Clin. Exp. Res. 37, 616–623.

Lovallo, W.R., Farag, N.H., Sorocco, K.H., Cohoon, A.J., Vincent, A.S., 2012b. Lifetime adversity leads to blunted stress axis reactivity: studies from the Oklahoma Family Health Patterns Project. Biol. Psychiatry 71, 344–349.

Meaney, M., 2001. Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. Annu. Rev. Neurosci. 24, 1161–1192.

Meites, K., Lovallo, W.R., Vladimir, P., 1980. A comparison of four scales for anxiety depression, and neuroticism. J. Clin. Psychol. 36, 427–432.

Moss, H.B., Vanyukov, M., Yao, J.K., Kirillova, G.P., 1999. Salivary cortisol responses in prepubertal boys: the effects of parental substance abuse and association with drug use behavior during adolescence. Biol. Psychiatry 45, 1293–1299.

Moss, H.B., Vanyukov, M.M., Martin, C.S., 1995. Salivary cortisol responses and the risk for substance abuse in prepubertal boys. Biol. Psychiatry 38, 547–555.

Panknin, T.L., Dickensheets, S.L., Nixon, S.J., Lovallo, W.R., 2002. Attenuated heart rate responses to public speaking in individuals with alcohol dependence. Alcohol. Clin. Exp. Res. 26, 841–847.

Patrick, C.J., Edens, J.F., Poythress, N.G., Lilienfeld, S.O., Benning, S.D., 2006. Construct validity of the psychopathic personality inventory two-factor model with offenders. Psychol. Assess. 18, 204–208.

Petry, N.M., Martin, B., 2002. Low-cost contingency management for treating cocaine- and opioid-abusing methoadone patients. J. Consult. Clin. Psychol. 70, 398–405.

Reardon, M.L., Lang, A.R., Patrick, C.J., 2002. An evaluation of relations among antisocial behavior, psychopathic traits, and alcohol problems in incarcerated men. Alcohol. Clin. Exp. Res. 26, 1188–1197.

Searles, J.S., Alterman, A.I., 1994. Environmental differences in young men with and without a family history of alcoholism. Ann. N. Y. Acad. Sci. 708, 147–156.

Sher, K.J., Walitzer, K.S., Wood, P.K., Brent, E.E., 1991. Characteristics of children of alcoholics: putative risk factors, substance use and abuse, and psychopathology. J. Abnorm. Psychol. 100, 427–448.

Sinha, R., 2001. How does stress increase risk of drug abuse and relapse? Psychopharmacology (Berl.) 158, 343–359.

Sinha, R., Fox, H.C., Hong, K.I., Hansen, J., Tuit, K., Kreek, M.J., 2011. Effects of adrenal sensitivity, stress- and cue-induced craving, and anxiety on subsequent alcohol relapse and treatment outcomes. Arch. Gen. Psychol. 68, 942–952.

Spinelli, S., Chefer, S., Suomi, S.J., Higley, J.D., Barr, C.S., Stein, E., 2009. Early-life stress induces long-term morphologic changes in primate brain. Arch. Gen. Psychiatry 66, 658–665.

Tarter, R.E., Kirisci, L., Habeych, M., Reynolds, M., Vanyukov, M., 2004. Neurobehavior disinhibition in childhood predisposes boys to substance use disorder by young adulthood: direct and mediated etiologic pathways. Drug Alcohol Depend. 73, 121–132.

Verdejo-Garcia, A., Bechara, A., Recknor, E.C., Perez-Garcia, M., 2006. Executive dysfunction in substance dependent individuals during drug use and abstinence: an

examination of the behavioral, cognitive and emotional correlates of addiction. J. Int. Neuropsychol. Soc. 12, 405–415.
Verdejo-Garcia, A., Perales, J.C., Perez-Garcia, M., 2007. Cognitive impulsivity in cocaine and heroin polysubstance abusers. Addict. Behav. 32, 950–966.
Verdejo-Garcia, A., Lawrence, A.J., Clark, L., 2008. Impulsivity as a vulnerability marker for substance-use disorders: review of findings from high-risk research, problem gamblers and genetic association studies. Neurosci. Biobehav. Res. 32, 777–810.
Verdejo-Garcia, A., Perez-Exposito, M., Schmidt-Rio-Valle, J., Fernandez-Serrano, M.J., Cruz, F., Perez-Garcia, M., Lopez-Belmonte, G., Martin-Matillas, M., Martin-Lagos, J.A., Marcos, A., Campoy, C., 2010. Selective alterations within executive functions in adolescents with excess weight. Obesity 18, 1572–1578.
Watson, C.G., Juba, M.P., Manifold, V., Kucala, T., Anderson, P.E., 1991. The PTSD interview: rationale, description, reliability, and concurrent validity of a DSM-III-based technique. J. Clin. Psychol. 47, 179–188.
Watson, D., Clark, L.A., Tellegen, A., 1988. Development and validation of brief measures of positive and negative affect: the PANAS scales. J. Pers. Soc. Psychol. 54, 1063–1070.
Zimmerman, M., Coryell, W., Pfohl, B., Stangl, D., 1988. The reliability of the family history method for psychiatric diagnoses. Arch. Gen. Psychiatry 45, 320–322.