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Craving and Indicators of Depression and Anxiety Levels in Different Time Points of Intensive Alcohol Dependence Treatment

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1. Introduction

Addiction/dependence is a chronically relapsing disorder that is characterized by a compulsion to take drugs and loss of control in limiting intake; brain stress systems can contribute to the compulsivity of drug-taking and therefore participate in the development and persistence of dependence (Koob, 2008). The concept of craving for alcohol can be recognized as a central component of the alcohol dependence syndrome together with the loss of control over and relapse to alcohol use (Anton, 1999). Gradual adaptation of brain function (neuroadaptation) to the presence of alcohol seems to be a central feature in the development of alcohol dependence (Koob & Le Moal, 2008). The neuroadaptation is not a conscious process and many alcohol dependent persons are likely to deny any craving for alcohol. Craving seems to emerge fully only when a person is prevented from access to alcohol or consciously attempts to quit alcohol use (Tiffany, 1990). Certain similarities exist between obsessive-compulsive disorder (OCD) and some aspects of craving (Anton et al., 1996) in form of recurrent and irresistible thoughts about alcohol during early recovery and during later recovery when experiencing stimulus clues or stressful states. Several scales have been developed to assess certain specific aspects of the craving phenomenon as a multidimensional and temporary phenomenon; the Obsessive Compulsive Drinking Scale (OCDS) (Anton et al., 1996) is suitable for determining the amount of craving experienced over a longer time interval (e.g. one week) and not only as a momentary urge to drink.

Concurrent depression and anxiety symptoms are among the most common problems in alcohol dependent patients: heavy drinkers with co-occurring depressive and anxiety symptoms evidence heavier alcohol use and increased risk of relapse (Hasin et al., 2007). In detoxified alcoholics, in early abstinence, overall dopaminergic neurotransmission in the ventral striatum of alcohol dependent patient is reduced. Brain studies with positron emission tomography revealed a reduction of availability and sensitivity of central dopamine D2-receptors in alcohol dependent patients, which may reflect a compensatory down-regulation after chronic alcohol intake and was associated with the subsequent relapse risk (Heinz et al., 2009). Dysfunction of dopaminergic, glutamatergic, and opioidergic neurotransmission in the brain reward system can be associated with alcohol craving. In early abstinence state of higher levels of glutamate and noradrenergic activity

with lower GABA, dopaminergic and serotonergic activity is achieved (Koob & Le Moal, 2008).

Alcohol use to relieve different affective states leads to encoded memory through the amygdale's connections with the dorsolateral prefrontal cortex and the basal ganglia; this reinforcement could support the addiction cycle. Affective stimuli, contrary to depression and anxiety, commonly associated with drinking situations can induce craving in the absence of alcohol cues, thus underlining the importance of addressing the association of (perceived) depression and anxiety with relapse (Mason et al., 2008). Craving has also been defined as the memory of the pleasant rewarding effects of drugs of abuse superimposed on a negative emotional state (Koob, 2000).

Laboratory studies of cue-elicited craving are used to evaluate the relationship between alcohol cues, behavioural responses (e.g., subjective craving ratings) and physiological responses. Regarding the association with alcohol cue reactivity most studies have found a strong relationship between craving, depressive symptoms, and anxiety symptoms among heavy drinkers (Fox et al., 2007). The study of Feldstein Ewing et al. (2010) found that cooccurring depressive and anxiety symptoms are associated with significant differential activation in key neurobiological regions in response to alcohol versus appetitive control cues with heavy drinking adults. It indicates that depressive or anxiety symptoms may increase the salience of alcohol cues, increase the perception of the positive aspect of alcohol consumption and reduce attention to the negative consequences of alcohol use (Monti et al., 2000).

Alcohol-induced depression and anxiety may be improved significantly with a sustained period of abstinence (four weeks is suggested), however they can have nature of relatively independent mental disorders' symptoms and persist beyond remission of dependent behaviour (Liappas et al., 2002). To reduce craving and improve outcome (i.e., decrease risk of relapse), treatment of depressed or anxious alcohol dependent patients therefore should address both the anxiety-depressive symptoms and the craving for alcohol, because both phenomena appear to be intertwined.

Different instruments are available to identify and/or measure the degree of alcohol dependence, among them AUDIT (Alcohol Use Disorders Identification Test) (Reinert & Allen, 2002) with summative score as a result. Instrument AUDIT detected a high prevalence of potential alcohol use disorders (Mendoza-Sassi & Beria, 2003), especially in primary care, but it lacks assessment of personality, relational and behavioural aspects. One of the very opportune measures of psychosocial implications of addictive behaviour could be subscores of SASSI instrument (The Substance Abuse Subtle Screening Inventory), declared to be the instrument, which breaks through denial (Miller et al., 1994). The SASSI outcome is conceptualised in ten subscores, allowing different dimensions of addictive behaviour to be identified. The following sub scores are obtained: FVA = face valid alcohol (acknowledged use of alcohol); FVOD = face valid other drugs (acknowledged use of other drugs); SYM = symptoms (true/false items that relate directly to substance misuse); OAT = obvious attributes (characteristics commonly associated with substance misuse); SAT = subtle attributes (basic personal style similar to substance dependent people); DEF = defensiveness (DEF tries to determine, if the client denies the existence of a substance abuse problem. DEF may or may not be related to substance abuse and that may reflect either an enduring character trait or a temporary reaction to a current situation. Low DEF score is also indicative of emotional pain.); SAM = supplemental addiction measure; FAM = family vs. controls (adult scale is based on the responses of the enabling spouses of the chemically

dependent people; the FAM measures the extent to which the client may be codependent); COR = correctional (similarity to people with extensive legal difficulties); RAP = random answering pattern (assesses whether or not responses are meaningful).

The treatment program at Centre for Alcohol Dependence Treatment of the University Psychiatric Hospital Ljubljana is abstinence-based, applying a biopsychosocial paradigm and providing integrated care for concurrent mental disorders. Treatment orientation has been based on attempt of synthesis of different therapeutic approaches, including principles of group, motivational enhancement therapy and (behavioural) marital and family therapy. The intensive treatment programme has two consecutive parts: the first is inpatient treatment, lasting about four to five weeks and the second part is provided in an every-day outpatient setting (about six to eight weeks, depending on patients' goals and needs). The patients' change of intensity of craving and negative affect during intensive dependence treatment is one of the important focuses of therapists' interest. However, in reality of every day clinical practice, patients have difficulties to identify their affect. If therapists want to offer the personally-tailored programme of treatment, the vulnerable patients (relapse-prone) could be better identified through understanding of interaction of craving and negative affect (in psychiatric terms as higher levels of depression and anxiety).

1.1 The purpose of the study

In the actual research, different indicators were chosen as criterion of therapeutic effect, among them intensity of »craving« as the most central dependent variable. The main purpose of the actual contribution is to analyze effect of therapy from the aspect of craving as central criterion-dependent variable, comparing three phases (time points) of therapy in Centre for Alcohol Dependence Treatment of the University Psychiatric Hospital Ljubljana (in the beginning; in the middle and at the end). Chosen variables, which are otherwise treated as partial personality indicators of multiple criterion therapeutic success, are taken into account as covariates: readiness for change in the beginning of therapy, so as perceived levels of depression and anxiety from each of three time points of therapeutic procedure. The intention was also to identify the structure of all just mentioned variables together.

1.2 Hypotheses

The following hypotheses were formulated:

H1: Significant differences in craving regarding different time points (therapeutic phases, when testing occurred) exist so in the case H1a. without covariates included, as H1b. in the case when age and degree of education, together with perceived levels of depression and anxiety from each time point are included as covariates; H1c. no significant covariate effects are expected.

H2: SASSI subscores, obtained at the end of therapy, H2a. mostly significantly correlate with craving, levels of depression and anxiety from the end, but they H2b. mostly do not correlate with levels of depression, anxiety and craving from the beginning of therapy, and, yet H2c. SASSI subscores at the end of therapy significantly correlate with readiness for change from the beginning of therapy.

H3: There are significant differences in chosen variables (in readiness for change, in perceived levels of depression and anxiety, and in craving) between the groups of tested and non tested participants, so in time point 2 (middle of the therapy), as in the time point 3

(end of therapy). Or: chosen variables from the beginning of therapy significantly discriminate between four level criterion, formed by groups of (non)tested participants in time point 2 and time point 3, on the level of at least one significant discriminate function (from three possible significant ones).

H4: Patients, who participated and who did not participate in testing in time point 3 do not differ in readiness for change and in any chosen variable from time point 1 and time point 2.

H5: Patients in different therapeutical time points significantly differ in perceived degree of own depression.

H6: Patients in different therapeutical time points significantly differ in perceived degree of their own anxiety.

Two general expectations, which could not be defined in terminology of univariate and bivariate relations, were additionally formulated:

- Age, degree of education, so as craving, perceived depression and anxiety from each of three time points form multifactorial structure; manifest variables are exclusively correlated with one of orthogonal factor.
- Craving, perceived depression and anxiety from each of three time points form multifactorial structure; manifest variables are exclusively correlated with one of orthogonal factor.

2. Method

2.1 Participants

The sample of the study included 133 patients who were consecutively recruited upon entering inpatient treatment at the Centre for Alcohol Dependence Treatment of the University Psychiatric Hospital Ljubljana (second part of the year 2009 and first part of 2010 admissions). All patients were eligible for the study. Patients were informed about study procedures and 110 patients provided written informed consent. 23 patients declined to participate. The 1st time point assessment was conducted 1 week after admission to inpatient treatment ($n = 110$), the 2nd time point 5 weeks after admission to inpatient treatment (= beginning of day hospital) ($n = 88$), and the 3rd time point at the end of 10 weeks outpatient treatment (day hospital; = end of whole intensive treatment programme) ($n = 73$). The average age was 47.87 years ($SD = 9.21$). There were 27.1 % female and 72.9 % male participants. The average number of days of inpatient treatment was 35.1 ($SD = 12.9$) and of outpatient treatment 32.9 ($SD = 20.1$).

2.2 Applied instruments

2.2.1 The 1st time point

(1 week after beginning of treatment); expression "score" everywhere means summative score

- Information about demographic characteristics, medical, psychiatric, and family histories
- Questionnaires upon dependence intensity:
 - Alcohol Use Disorder Identification Test AUDIT - score (Cronbach alpha = 0.88; ten items with answering scale from 0 to 4) (Reinert & Allen, 2002).
 - The Substance Abuse Subtle Screening Inventory SASSI - 10 sub scores (Miller et al., 1994).

- Obsessive Compulsive Drinking Scale – score (Cronbach alpha =0.90; scale with 14 questions with mostly five points answering scale from 0 to 4, only one item from 1 to 5) (Anton et al., 1995).
- The Stages of Change Readiness and Treatment Eagerness Scale SOCRATES score (19 items of Likert type five points answering scale, Cronbach alpha = 0.95; Cronbach alphas of subscores Recognition = 0.87, Ambivalence = 0.78, Taking Steps = 0.92; correlations total score and subscores, all $p < 0.001$: Recognition 0.93, Ambivalence 0.89, Taking Steps 0.93) (Miller & Tonigan, 1996).
- State Anxiety Inventory – score (Cronbach alpha =0.93); twenty items with four points answering scale (Spielberger et al., 1983).
- Zung Self-Rating Depression Scale – score (Cronbach alpha =0.86; all together 20 items with four points answering scale (Zung, 1965).
- Family climate questionnaire – score (Cronbach alpha = 0.90;); originally constructed by Rus-Makovec M. et collaborators as summative scale/semantic differential, 15 bipolar continuums of semantic differential, with 7 – point bipolar answering scale, constructed according to the demands for summative ratings.

2.2.2 The 2nd time point

(5 weeks after beginning of treatment)

- More complex autoanamnesic information
- Questionnaire upon dependence intensity:
 - Obsessive Compulsive Drinking Scale – score (Cronbach alpha =0.94)
- State Anxiety Inventory – score (Cronbach alpha =0.96)
- Trait Anxiety Inventory – score (Cronbach alpha = 0.94)
- Zung Self-Rating Depression Scale – score (Cronbach alpha =0.91)
- Life events in last 12 months
- The Mini-International Neuropsychiatric Interview (M.I.N.I.)(Sheehan et al., 1998).

2.2.3 The 3rd time point

(at the end of whole intensive treatment – about 10 weeks after beginning of treatment)

- Evaluation of different components of the programme, different self evaluations
- Questionnaires upon dependence intensity:
 - The Substance Abuse Subtle Screening Inventory SASSI
 - Obsessive Compulsive Drinking Scale– score (Cronbach alpha =0.89)
- State Anxiety Inventory – score (Cronbach alpha = 0.94)
- Zung Self-Rating Depression Scale – score (Cronbach alpha = 0.89)
- Family climate questionnaire – score (Cronbach alpha = 0.91).

The whole research is designed as one-group quasi-experimental approach, with no simultaneously control such as group neither in therapeutic nor in after care period. Anyway, comparison with certain quasi-control groups, comparing particular chosen variables is possible, but not included into present report. Univariate, bivariate and multivariate statistical analyses were executed, when parametric approaches permitted. There was a problem connecting decisions for within-subjects (repeated measures) and between-subjects approach (independent groups). Only a small segment of the whole project results is shown here.

Ethical approval was provided by the Ethical commission of Health Ministry of Slovenia.

3. Results

3.1 Results of verification of hypothesis H1 - H1a

“Cravings” (Obsessive Compulsive Drinking Scale – score) in each of three time points were compared and tests of within – subject’s effects without any covariate were applied. Zero risk level of differences between the periods of therapy showed highly significant differences between the cravings ($F(2, 114) = 44.29, p = 0.00, \text{part. } \eta^2 = 0.44$). Repeated measure approach embraced all together $n = 58$ patients, because several dozens of the declined to be tested in each of three periods/time points. The results show, approaching to the end of therapy, progressively lower and lower level of craving (Table 1).

	M	SD	N
Craving 1	24.77	10.29	58
Craving 2	15.93	12.14	58
Craving 3	10.31	8.88	58

Note:

Craving i ($i = 1, 2, 3$) = Obsessive Compulsive Drinking Scale – score (three time points, the first one = 1, the second one = 2, the third one = 3).

Table 1. Descriptive statistics for cravings in three time points – repeated measures approach without covariates.

3.2 Results of verification of hypothesis H1b and H1c

In the next step, nine covariates were included into the already existing repeated measures (within – subjects) design. Almost all covariate effects were found as non – significant, except two of them: years of education ($F_{\text{educ}}(2, 68) = 3.01, p = 0.056$) and depression 1 (in the beginning/ the first time point ($F_{\text{depr1}}(2, 68) = 5.8, p = 0.005$). When covariates included, the differences between the “cravings” were not found significant ($F_{\text{factor1}}(2, 68) = 1.22, p = 0.30$). The function of mentioned depression is the complex one. It does not belong to the same factor (factor analysis) as “craving 3”, but it significantly contributes to the understanding of the within – subjects differences between the time points. Other results were as follows: $F_{\text{SOCRATES}}(2, 68) = 0.26, p = 0.77$; $F_{\text{anks1}}(2, 68) = 1.16, p = 0.32$; $F_{\text{depr2}}(2, 68) = 0.45, p = 0.64$; $F_{\text{anks2}}(2, 68) = 0.54, p = 0.59$; $F_{\text{depr3}}(2, 68) = 1.34, p = 0.27$; $F_{\text{anks3}}(2, 68) = 0.62, p = 0.54$; $F_{\text{age}}(2, 68) = 2.00, p = 0.14$.

	M	SD	N
Craving 1	23.93	10.60	44
Craving 2	14.02	11.35	44
Craving 3	10.27	9.15	44

Note:

Craving i ($i = 1, 2, 3$) = Obsessive Compulsive Drinking Scale – score (three time points, the first one = 1, the second one = 2, the third one = 3).

Covariates: depression and anxiety in each of three time points, readiness for change, age and years of education.

Table 2. Descriptive statistics for cravings in three time points – repeated measures approach with nine covariates.

I also wanted to know, what happens, when “only” seven covariates, without “age” and “years of education” are included (covariates: depression and anxiety in each of three time

points and readiness for change - seven covariates). Again, only the depression, as perceived in the beginning of therapy ($F_{depr1} (2, 92) = 7.06, p = 0.00$), had a significant covariate effect on »craving«, and »within - subjects« effect was highly non - significant ($F_{factor1} (2, 92) = 0.23, p = 0.79$). Covariate effects of »depressions« and »anxieties«, as perceived in other time points, were found as follows: $F_{depr1} (2, 92) = 7.06, p = 0.00$; $F_{anxi1} (2, 92) = 0.43, p = 0.65$; $F_{depr2} (2, 19) = 0.19, p = 0.89$; $F_{anxi2} (2, 92) = 0.90, p = 0.41$; $F_{depr3} (2, 92) = 0.82, p = 0.44$; $F_{anxi3} (2, 92) = 0.34, p = 0.71$. Highly non - significant was also the covariate effect of the readiness for the change (SOCRATES): $F_{SOCRATES} (2, 92) = 0.22, p = 0.80$.

	M	SD	n
Craving 1	24.62	10.23	54
Craving 2	15.98	12.07	54
Craving 3	10.25	8.78	54

Note:

Craving i ($i = 1, 2, 3$) = Obsessive Compulsive Drinking Scale - score (three time points, the first one = 1, the second one = 2, the third one = 3).

Covariates: depression and anxiety in each of three time points and readiness for change.

Table 3. Descriptive statistics for cravings in three time points - repeated measures approach with seven covariates.

3.3 Results of verification of hypothesis H2a and H2c

SASSI subscores at the end of treatment	Craving 1	SOCRATES	Depression 1	Anxiety 1
FVA	0.231	0.016	0.165	0.170
FVOD	0.009	0.004	0.218	0.204
SYM	0.236	-0.129	0.239	0.162
OAT	0.128	-0.092	0.185	0.196
SAT	0.236	0.000	0.094	0.230
DEF	-0.294*	-0.086	-0.327**	-0.265*
SAM	-0.186	-0.081	-0.099	0.061
FAM	-0.100	0.167	-0.152	-0.182
COR	0.304*	-0.044	0.315*	0.244

Note:

number of participants $65 = > n = 64$

SASSI subscores: FVA = face valid alcohol; FVOD = face valid other drugs; SYM = symptoms; OAT = obvious attributes; SAT = subtle attributes; DEF = defensiveness; SAM = supplemental addiction measure; FAM = family vs. controls; COR = correctional

Craving 1 = Obsessive Compulsive Drinking Scale - score, the first time point

Depression 1 = Zung Self-Rating Depression Scale - score, the first time point

Anxiety 1 = State Anxiety Inventory - score, the first time point

SOCRATES = readiness for change in the beginning of therapy.

Table 4. Spearman coefficients of rank correlations between subscores of SASSI at the end of therapy and chosen variables from the beginning of therapy.

*, $p < 0.05$; **, $p < 0.01$

3.4 Results of verification of hypothesis H2b and H2c

SASSI subscores at the end of treatment	Craving 3	SOCRATES	Depression 3	Anxiety 3
FVA	0.408**	0.016	0.204	0.211
FVOD	-0.166	0.004	0.108	0.244*
SYM	0.219	-0.129	0.248*	0.175
OAT	0.268*	-0.092	0.405**	0.279*
SAT	-0.014	0.000	-0.039	0.214
DEF	-0.366**	-0.086	-0.550**	-0.560**
SAM	0.276*	-0.081	0.128	-0.005
FAM	-0.084	0.167	-0.261*	-0.404**
COR	0.264*	-0.044	0.410**	0.240

Note:

number of participants 65 = > n > = 64

SASSI subscores: FVA = face valid alcohol; FVOD = face valid other drugs; SYM = symptoms; OAT = obvious attributes; SAT = subtle attributes; DEF = defensiveness; SAM = supplemental addiction measure; FAM = family vs. controls; COR = correctional

Craving 3 = Obsessive Compulsive Drinking Scale – score, the third time point

Depression 3 = Zung Self-Rating Depression Scale – score, the third time point

Anxiety 3 = State Anxiety Inventory – score, the third time point

SOCRATES = readiness for change in the beginning of therapy.

Table 5. Spearman coefficients of rank correlations between subscores of SASSI at the end of therapy and chosen variables from the end of therapy, *, $p < 0.05$; **, $p < 0.01$

I was also interested into the question, how do SASSI subscores at the end of therapy correlate with the craving, depression, readiness for change and anxiety, so from the beginning, as from the end of therapy. When four chosen variables from the beginning of therapy were taken into account, craving 1 correlated significantly ($p < 0.05$) with DEF and COR and almost significantly with SYM and SAT. Craving 3 correlated significantly with FVA, OAT, DEF, SAM and COR. It seems that correlations with DEF and COR are stable: correlations between craving and FVA, OAT and SAM appear as new significant ones at the end of therapy. Lower defensiveness at the end of the intensive treatment is significantly correlated with higher levels of craving and more intense negative affective states in beginning of treatment (and vice versa); the same trend can be seen with craving and negative affect at the end of treatment.

No significant correlations were found between SASSI subscores on one side and readiness for change on another side. They were found neither in the beginning, nor at the end of therapy.

DEF and COR correlated significantly with the depression, as perceived so in the beginning, as at the end of therapy. At the end, significant correlations were found also for SYM, OAT and FAM.

Anxiety, as perceived in the beginning, correlated significantly ($p < 0.05$) with the DEF and almost significantly with the COR. At the end of therapy, significant correlations with FAM and OAT appeared.

3.5 Results of verification of hypothesis H3

There was a variation in testing participation in each time point; that’s why I decided to compare those, who participated and who did not participate testing in the second and in the third time point (= end of therapy). In such a case, the only possible comparison is comparison in variables from previous time points, in which they had participated. Mentioned comparisons are important also for the evaluation of the repeated measures design. If there are not significant differences in particular relevant previous variable between the participants and non - participants in particular time point of testing, also the validity of within - subjects (repeated measures) design is greater, although reduced number of people is taken into account.

The following proportions of (non) participants in the second and in the third time point could be identified:

M2 = proportions of participants, who: 1 = participated in the second time point, 2 = did not participate in the second time point.

M3 = proportions of participants, who: 1 = participated in the third time point, 2 = did not participate in the third time point.

Four groups with regard to participation	variable	M	SD
1 n = 51	SOCRATES	81.19	12.26
	Craving 1	24.97	10.04
	Depression 1	40.59	9.84
	Anxiety 1	38.40	12.99
2 n = 28	SOCRATES	80.81	8.53
	Craving 1	25.25	8.80
	Depression 1	40.23	8.54
	Anxiety 1	40.07	13.06
3 n = 18	SOCRATES	79.77	18.20
	Craving 1	19.77	8.86
	Depression 1	38.28	7.34
	Anxiety 1	36.88	10.94
4 n = 6	SOCRATES	88.16	6.24
	Craving 1	26.83	7.54
	Depression 1	39.33	9.89
	Anxiety 1	35.33	12.09
Total n= 103	SOCRATES	81.25	12.42
	Craving 1	24.21	9.48
	Depression 1	39.99	8.98

Note:

Craving 1 = Obsessive Compulsive Drinking Scale – score, the first time point

Depression 1 = Zung Self-Rating Depression Scale – score, the first time point

Anxiety 1 = State Anxiety Inventory – score, the first time point

SOCRATES = readiness for change in the beginning of therapy.

Table 6. Descriptive statistics for chosen variables from the beginning of therapy for four groups: groups of (non)participants in the second and in the third time point with chose

Four groups could be formed as criterion for discriminant analysis, if M2 and M3 are crossed (1 = participated in the second and in the third (n = 51); 2 = participated in the second, not in the third (n = 28); 3 = did not participate in the second, but participated in the third time point (n = 18); 4 = participated neither in the second, nor in the third time point (n = 6)). Chosen variables from the beginning of therapy were treated as predictors.

Test of Function(s)		Wilks' Lambda	Chi-square	df	Sig.
Dimension	1 through 3	0.922	7.557	12	0.819
	2 through 3	0.974	2.409	6	0.879
	3	0.995	0.462	2	0.794

Table 7. Wilks' Lambda for three discriminant functions
Box's M, F approx = 1.45, p = 0.054

Otherwise, the demand for homogeneity of covariance's was just satisfied (Box's M, F approx = 1.45, p = 0.054). Wilks' test of equality of group means, otherwise included as option of multivariate discriminant test, showed no significant differences in any of chosen variables from the beginning of therapy, when four groups were compared (look Table 11, please). Also no one of three discriminant function was found as significant: no Wilks Lambda was significant (look, please Table 12) and further analysis in the sense of discriminant analysis was not any more relevant (for example, the interpretation of structure matrix, where the degree of correlation between the (significant) discriminant function and particular predictor (chosen variables from the beginning of therapy) explain relative importance of particular predictor for the discrimination between the levels of variation of criterion (in "our" case four groups of (non)participants) and four possible centroids for each of eventually three possible significant discriminant functions.

3.6 Results of verification of hypothesis H4

Variables	M3	n	M	SD	t	df	p
Craving 2	1	53	15.60	11.97	-0.207	80	0.836
	2	29	16.17	11.69			
SOCRATES	1	66	80.69	13.93	0.079	98	0.937
	2	34	80.47	12.94			
Depression 1	1	69	40.33	9.15	0.310	103	0.757
	2	36	39.76	8.71			
Anxiety 1	1	68	38.41	12.31	-0.173	102	0.863
	2	36	38.86	13.03			
Craving 1	1	69	23.18	10.56	-1.251	101	0.214
	2	34	25.79	8.49			
Depression 2	1	53	36.79	8.36	0.224	80	0.823
	2	29	36.37	7.18			
Anxiety 2	1	55	36.58	12.29	-0.482	82	0.631
	2	29	38.00	13.76			

Note:

M3 = 1 = those, who participate testing in the third time point; M3 = 2 = those, who did not participate testing at the end of therapy:

Craving 1 = Obsessive Compulsive Drinking Scale – score in the first time point
Depression 1 = Zung Self-Rating Depression Scale – score in the first time point
Anxiety 1 = State Anxiety Inventory – score in the first time point
Craving 2 = Obsessive Compulsive Drinking Scale – score in the second time point
Depression 2 = Zung Self-Rating Depression Scale – score in the second time point
Anxiety 2 = State Anxiety Inventory – score in the second time point
SOCRATES = readiness for change in the beginning of therapy.

Table 8. T - tests of difference in chosen variables regarding two groups of participants: those, who participated vs. those, who did not participate testing at the end of therapy

When those, who did not participate the testing at the end of therapy, were compared with those, who had passed the testing, no significant difference for any of treated variable (readiness, craving, depression, anxiety - so from the first, as from the second time point) was found. The results contribute to belief that “missing persons” at the end of therapy do not change the mainstream therapeutic effects.

3.7 Results of verification of hypothesis H5

	M	SD	n
Depression 1	40.39	9.58	56
Depression 2	35.55	7.75	56
Depression 3	35.53	8.44	56

Note:

Depression i (i = 1, 2, 3) = Zung Self-Rating Depression Scale – score (three time points, the first one = 1, the second one = 2, the third one = 3).

Table 9. Descriptive statistics for perceived depression in three time points - repeated measures approach

Within subjects approach showed significant differences in perceived depression in the beginning compared to perceived depression in the middle and at the end of therapy ($F(2, 110) = 15.93, p = 0.00$). No significant difference appears between time point 2 and time point 3 (between middle and the end of therapy).

3.8 Results of verification of hypothesis H6

	M	SD	n
Anxiety 1	39.41	13.56	56
Anxiety 2	35.58	12.95	56
Anxiety 3	35.44	12.00	56

Note:

Anxiety i (i = 1, 2, 3) = State Anxiety Inventory – score (three time points, the first one = 1, the second one = 2, the third one = 3).

Table 10. Descriptive statistics for own perceived anxiety in three time points - repeated measures approach

Within subjects approach showed significant differences in perceived anxiety in the beginning compared to perceived anxiety in the middle and at the end of therapy ($F(2, 110)$)

= 5.02, $p = 0.01$). No significant difference appears between time point 2 and time point 3 (between middle and the end of therapy).

3.9 Factor solutions for different set of variables

3.9.1 Factor analysis for 9 variables

Component		Initial Eigenvalues			Extraction Sums of Squared Loadings		
		Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
dimension	1	4.412	49.018	49.018	4.412	49.018	49.018
	2	1.651	18.347	67.365	1.651	18.347	67.365
	3	0.952	10.577	77.942	0.952	10.577	77.942
	4	0.531	5.895	83.838			

Note:

Table is reduced to number of factors which sufficiently show, how many factors have the eigenvalue $> = 1$ (Kaiser's criterion), $df = 36$.

Table 11. Factor analysis for 9 variables: eigenvalues and correspondent percents of explained variance

Taking formalistically into account Kaiser's criterion, two factorial model would be taken into account, with about 67 % of explained variance. Anyway, also three factorial, explaining almost 78 % of the whole variance, could be taken into account (the eigenvalue of the third factor is 0.95 and the first three factors, according to their Kaiser values, distinctively enough separate from other factors).

Variables	Component	
	1	2
Craving 1	-0.050	0.859
Craving 2	0.123	0.836
Craving 3	0.129	0.450
Depression 1	0.576	0.513
Depression 2	0.896	0.132
Depression 3	0.873	0.187
Anxiety 1	0.774	0.036
Anxiety 2	0.872	0.214
Anxiety 3	0.876	0.012

Note:

Craving i ($i = 1, 2, 3$) = Obsessive Compulsive Drinking Scale – score
(three time points, the first one = 1, the second one = 2, the third one = 3)

Depression i ($i = 1, 2, 3$) = Zung Self-Rating Depression Scale – score
(three time points, the first one = 1, the second one = 2, the third one = 3)

Anxiety i ($i = 1, 2, 3$) = State Anxiety Inventory – score
(three time points, the first one = 1, the second one = 2, the third one = 3).

Table 12. Rotated varimax matrix for nine studied variables - two factorial solution

Variables	Component		
	1	2	3
Craving 1	-0.036	0.863	0.117
Craving 2	0.136	0.823	0.162
Craving 3	0.125	0.181	0.943
Depression 1	0.589	0.603	-0.247
Depression 2	0.898	0.098	0.088
Depression 3	0.875	0.158	0.081
Anxiety 1	0.776	0.052	-0.085
Anxiety 2	0.874	0.164	0.153
Anxiety 3	0.874	-0.032	0.103

Note:

Craving i ($i = 1, 2, 3$) = Obsessive Compulsive Drinking Scale – score
(three time points, the first one = 1, the second one = 2, the third one = 3)

Depression i ($i = 1, 2, 3$) = Zung Self-Rating Depression Scale – score
(three time points, the first one = 1, the second one = 2, the third one = 3)

Anxiety i ($i = 1, 2, 3$) = State Anxiety Inventory – score
(three time points, the first one = 1, the second one = 2, the third one = 3).

Table 13. Rotated component matrix for nine studied variables – three factorial solution

Factor saturation shows the same trends so for two-, as for three-factorial models. “Craving 3” is either correlated with no factor (two-factorial), or it exclusively relatively highly correlates with the third factor (three factorial solutions).

3.9.2 Factor analysis for 12 variables

Component		Initial Eigenvalues			Extraction Sums of Squared Loadings		
		Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
dimension	1	4.783	39.86	39.86	4.78	39.86	39.86
	2	1.812	15.10	54.96	1.81	15.10	54.96
	3	1.514	12.61	67.57	1.51	12.61	67.57
	4	0.876	7.30	74.87			

Note:

Table is reduced to number of factors which sufficiently show how many factors have the eigenvalue ≥ 1 (Kaiser's criterion).

Table 14. Factor analysis for 12 variables: eigenvalues and correspondent percents of explained variance

Factor analysis for 12 variables resulted in three factorial solution, all three factors together explaining almost 68 % of total variance. Relatively the greatest percent of explained variance corresponds, of course, with the first factor (almost 40 %).

Varimax orthogonal rotation was applied, resulting in rotated matrix with three recognizable and relatively exclusive factors. According to the correlations between particular factor and each of 12 manifest variables, the factors could be interpreted as follows: the first factor, highly correlating with depression and anxiety, regardless the time

Variables	Component		
	1	2	3
Age	-0.063	-0.057	0.669
Years of education	-0.025	0.211	0.829
Craving 1	0.121	0.822	0.050
SOCRATES	-0.136	0.688	0.216
Craving 2	0.198	0.663	-0.470
Craving 3	0.233	0.432	-0.407
Depression 1	0.800	0.264	0.104
Anxiety 1	0.733	-0.083	-0.169
Depression 2	0.875	0.145	-0.185
Anxiety 2	0.901	0.151	-0.148
Depression 3	0.895	0.044	-0.074
Anxiety 3	0.894	-0.085	0.000

Note:

Craving i ($i = 1, 2, 3$) = Obsessive Compulsive Drinking Scale – score
(three time points, the first one = 1, the second one = 2, the third one = 3)
Depression i ($i = 1, 2, 3$) = Zung Self-Rating Depression Scale – score
(three time points, the first one = 1, the second one = 2, the third one = 3)
Anxiety i ($i = 1, 2, 3$) = State Anxiety Inventory – score
(three time points, the first one = 1, the second one = 2, the third one = 3)
SOCRATES = readiness for change in the beginning of therapy

Table 15. Rotated matrix – varimax rotation for 12 manifest variables

point of their appearance, could be labelled as »affect« factor. – The second factor exclusively highly correlates with “craving” in the beginning and in the middle (the second time point), but also with the readiness for change in the beginning of therapy; this combination could be called as before final craving & initial readiness for improvement. Finally, the third factor is a demographic one, containing age and years of education. Final »craving« quite moderately correlates so with the second (positively), as with the third Factor (negatively) but craving 3 correlate expressively with no one of three orthogonal factors.

4. Discussion

Results show, that significant differences in craving regarding different time points (therapeutic phases, when testing occurred) exist in the case H1a. without covariates included; this hypothesis is completely confirmed, but hypothesis H1b. is refused. When age and degree of education, together with perceived anxiety and depression from each time point are included as covariates, the within subjects differences between the cravings are not any more significant. Refused is also hypothesis H 1c. (no significant covariate effects are expected), because quite significant covariate effect of perceived depression was found and almost significant effect of “years of education”.

We can say, although it sounds a little bit strange, that H2a and H2b are mostly accepted (H2: SASSI subscores, obtained at the end of therapy, H2a. mostly significantly correlate with craving, depression and anxiety from the end, but they H2b. mostly do not correlate with anxiety, depression and craving from the beginning of therapy), but hypothesis H2 c is surprisingly refused, because no one significant correlation between SASSI subscores at the end of therapy and beginning readiness for change was found.

Results show that H3 (chosen variables from the beginning of therapy significantly discriminate between four level criterion, formed by groups of (non)tested participants in time point 2 and time point 3, on the level of at least one significant discriminate function (from three possible significant ones) is refused.

Also the H4 was refused (H4: Patients, who participated and who did not participate in testing in time point 3 differ in readiness for change and in any chosen variable from time point 1 and time point 2).

As expected, the alternative hypotheses H5 & H6 were confirmed. Anyway, it's worth repeating again, that significant difference ($p < 0.05$) was found only between time point 1 on one side and time point 2 on other side. It means that perceived depression and anxiety were significantly diminished already in the time point 2 (in the middle of therapy) and that they did not significantly change up to the end of therapy.

We can say that age, degree of education, so as craving, perceived depression and anxiety from each of three time points form multifactorial structure, "where" manifest variables are exclusively correlated with one of orthogonal factor. Factor analysis resulted in three factorial orthogonal structure with factors representing anxiety and depression (factor1), craving1, craving 2 and beginning readiness for change (factor 2) and age and years of education as factor 3. Craving 3 correlated expressively with no one of three orthogonal factors, but more strongly with factor 2 and factor 3 than with factor 1.

Factor solutions showed some interesting differences when different sets of variables were factorized. Results of factorization of 12 variables were already previously mentioned. When nine variables (perceived depression and anxiety) were factorized, so two-factorial, as three factorial model shows very similar trends; factually, the only difference between them is connected with "craving 3" (phenomenon of craving at the end of therapy). In two factorial models, craving factually "belongs" to no factor, but in three factorial models it's expressively the independent one, representing the third factor. Otherwise, so two-, as three - factorial model confirm the fact, that perceived depression in the beginning of therapy ("depression 1") "belongs" so to factor 1, as to factor 2; it means that it independently belongs so to the first (expressing anxieties and depressions in three therapeutic periods) as to the second factor (correlating with craving1 and craving 2, but not also with the craving 3).

It seems, also after a vast survey of relevant literature that analyses of relations between craving and perceived depression/anxiety are relatively very rare, especially in the framework of longitudinal, time points approach. Yet some of the studies addressed perceived depression/anxiety as a significant predictor of alcohol relapse, as well as the relation between perceived depression/anxiety and drinking, which is strongly mediated by alcohol craving (Conner et al., 2009). The craving module of the combined behavioural intervention (Witkiewitz et al., 2011) and Mindfulness-based relapse prevention were found to weaken the relation between perceived depression/anxiety and heavy drinking by fostering greater decreases in craving during treatment (Witkiewitz & Bowen, 2010). In a study of examination the course of affective symptoms and cravings for alcohol use during the initial 25 days of residential treatment addicted to alcohol, 17 subjects reported elevated cravings during the entire treatment stay, 37 subjects reported initially elevated but a slight improvement in craving, and 41 subjects reported relatively low craving from the time of admission to the end of residential treatment. Alcohol craving class was associated with perceived depression/anxiety but not with affects, being contrary to depression and anxiety; results suggested that non-cue induced alcohol craving may define a subtype of alcohol dependence that is less responsive to treatment and may explain heterogeneity in treatment outcomes (Oslin et al., 2009).

The present study's outcomes reflect neurobiological interrelation between craving and perceived depression/anxiety (described in the introductory part). The findings showed positive outcome of researched indicators of therapy success, which can be generalised to whole sample; it seems that "missing persons" at the end of therapy do not change the mainstream therapeutic effects. However, the main advantage of the study is in providing important evidence-based support to dynamics of patients' multilevel mental vulnerability/health change in treatment process. Craving intensity diminished significantly from the beginning to very end of whole intensive treatment. Comparing to the beginning of therapy, craving in any further time point was found as significantly lower. The second time point is at the beginning of outpatient part of treatment, with exposition to environmental alcoholic and non-alcoholic cues of »real life«. Patients, involved in intensive mixture of spectrum of psychotherapy interventions and pharmacotherapy, together with abstinence, are reliably prepared for better beginner coping with higher levels of depression, anxiety and craving. On the other hand, just mentioned levels of depression and anxiety are significantly diminished (together with craving) in the first part of intensive treatment (inpatient/residential part). In times of economic crisis, inpatient treatments of dependence maybe won't be encouraged, but in-patient treatment of alcohol dependence at the beginning of the treatment process obviously can provide context for efficient sustaining at least several weeks of abstinence, allowing craving and affect issues to be addressed efficiently.

One of the expected goals for the patients in treatment of dependence from the side of the therapists is that patients diminish their denial. Correlations between SASSI subscores, craving, levels of depression and anxiety showed particular similar trend so in the beginning, as at the end of therapy. Significant correlations (higher at the end than in the beginning) between craving, levels of depression and anxiety on one side with SASSI subscore DEF on the other side appeared. Participants, who experienced more intense craving and higher levels of depression/anxiety, showed less defensiveness so in the beginning, as at the end of therapy, when the mentioned trend is much more expressed. It can be interpreted, that more vulnerable patients show less defensiveness significantly, but less expressively in the beginning and significantly, but more expressively at the end of treatment. Or patients, who do not tend to be alexithimic, show less denial with regard to their affect and craving. It is concordant with psychodynamic explanation that only patients, who are progressing in treatment and have developed good working alliance, can experience, identify and tolerate higher levels of depression and anxiety - and develop more self-defensive behaviour (Weegmann, 2002).

Weakness of the research is in the fact of missing values, which specially appear in the second and in the third (the end of therapy) time point. This deficiency has somehow tried to be controlled with comparison, in chosen target variables, between participants and non-participants in particular time point. No significant difference was found in any variable (readiness for change, perceived depression, anxiety, and craving) from the beginning of therapy. It means that those, who in some later phase did not participate testing had been not, in the beginning of therapy, differently oriented connecting some basic relevant variables of the research. Not the systematic, but random factors seem to be more relevant reason of their absence in some periods (time points) of testing.

The next weakness of the design is the absence of the adequate control group; that's why the whole design is the one - group quasi experimental one; however, there is a possibility to establish some other groups as quasi control ones. In the same time, this opportunity is, in the same time, the potential (future) advantage of the research: the same set of instruments could be applied on approximately equalized group, what would make some comparisons possible

and relevant. Finally, an additional instrument, measuring some personality structure characteristics, is also supposed to be added in the future, including also some other feelings and emotions of patients in treatment (not only levels of depression and anxiety).

5. Conclusion

Quite important characteristic of the research is the institutional framework of its realization and application. This framework is the Centre for Alcohol Dependence Treatment of the University Psychiatric Hospital Ljubljana, where it is possible to take results of the study into account in applied work and longitudinally follow up. This situation also gives the opportunities for additional specification of evidence based treatment at the centre.

Projects for the future: the same group of ex-patients will be followed also in the future and the new time points will be added.

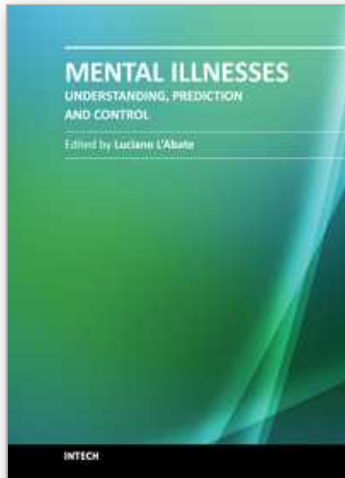
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In the book "Mental Illnesses - Understanding, Prediction and Control" attention is devoted to the many background factors that are present in understanding public attitudes, immigration, stigma, and competencies surrounding mental illness. Various etiological and pathogenic factors, starting with adhesion molecules at one level and ending with abuse and maltreatment in childhood and youth at another level that are related to mental illness, include personality disorders that sit between mental health and illness. If we really understand the nature of mental illness then we should be able to not only predict but perhaps even to control it irrespective of the type of mental illness in question but also the degree of severity of the illness in order to allow us to predict their long-term outcome and begin to reduce its influence and costs to society. How can we integrate theory, research evidence, and specific ways to deal with mental illness? An attempt will be made in the last conclusive chapter of this volume.

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