Alcohol & Alcoholism Vol. 44, No. 1, pp. 46–54, 2009
Advance Access publication 1 October 2008
doi: 10.1093/alcalc/agn080

CLINICAL FEATURES

The Alcoholic Phenotypes among Different Multidimensional Typologies: Similarities and Their Classification Procedures

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This work derived from the presentations of the authors in the 11th Congress of the European Society for Biomedical Research on Alcoholism (ESBRA) in Berlin, 2007.

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(*Received* 20 *June* 2008; *first review notified* 24 *July* 2008; *in revised form* 18 *August* 2008; *accepted* 4 *September* 2008; *advance access publication 1 October 2008*)

Abstract — Aim: This detailed cross-sectional analysis, obtained from a sample of alcohol-dependent patients, attempts to compare multiple methods that have been created to classify or subtype alcoholics. **Methods:** The sample comprised 318 alcohol-dependent patients recruited from the alcoholism unit (NETER) of the Psychiatric Service of Santa Maria University Hospital in Lisbon (Portugal). All subjects were evaluated during the outpatient therapeutical programme for operationalized criteria, reported by each alcoholism typology. **Results:** Regarding concordance agreement (kappa values) for the three type I/II classifications, von Knorring versus Sullivan yielded the higher rate of agreement, followed by von Knorring versus Gilligan and Gilligan versus Sullivan criteria. Chi-square comparisons showed a significant overlap between Babor type A and Cloninger type I of von Knorring and Sullivan. Over-two-type classifications showed the following significant positive relations: Lesch type I versus NETER heredopathic subtype; Lesch type II versus NETER anxiopathic subtype and Babor type A; Lesch type III versus NETER tymopathic subtype; Lesch type IV versus Cloninger type II of von Knorring and Sullivan criteria; and NETER adictopathic subtype versus Cloninger type II of von Knorring, Sullivan and Gilligan criteria. **Conclusions:** There is a significant overlap across many of the multivariate alcoholic subtypes purposed, in which much of the concordance is a function of common characteristics in subtype operationalization. Commonalities among these different subtyping classification systems offers the possibility of identifying important dimensions that better differentiate individuals among problem drinker's populations.

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INTRODUCTION

Different etiopathogenic processes of alcohol addiction yield distinct phenotype manifestations. Efforts have been made to subtype alcoholics in more homogeneous groups in order to predict the future course of the disorder, increase accuracy of neurobiological mechanisms and improve treatments' response effectiveness (Babor and Caetano, 2006; Dvorak *et al*., 2006; Pombo *et al*., 2007). Typology models of alcoholism differ in dimensional procedures (single-domain versus multidimensional) used to congregate subjects; frequency and severity of clinical, behavioural and alcohol related problems; number of extracted subtype solutions and the type of alcoholics samples assessed.

A wide variety of models used to classify alcoholism have been applied in clinical and research settings. Examples include the so-called Cloninger *et al.* (1981), Lesch *et al.* (1988) and Babor *et al.* (1992) multidimensional alcoholic typologies. To apply alcoholism typologies in basic and clinical studies, several subtype classification systems emerged, according to the typologic hypothesis derived from previous research and theory.

There are generally two accepted basic phenotypes of alcohol-dependent drinkers defined as low-severity/vulnerability subgroup and high-severity/vulnerability subgroup. The first one is characterized by a later onset of problem drinking, less severe alcohol dependence and alcohol-related problems. The latter is characterized by an early onset of problem drinking, family history of alcoholism problems, antecedents of psychopathology, and severe alcohol dependence and alcohol-related problems (Babor and Caetano, 2006). In this binary classification, low-severity/vulnerability alcoholics are in some way similar to Cloninger *et al.*'s (1981) type I and Babor *et al.*'s (1992) type A, and high-severity/vulnerability alcoholics are similar to Cloninger *et al.*'s (1981) type II and Babor *et al.*'s (1992) type B. In this direction, Babor *et al.* (1992) and Carpenter and Hasin (2001) hypothesized two mythological broad categories of problem drinkers: Apollonian–Dionysian distinction. Apollonian (types I and A) type is defined by a slower development course, fewer complications and better prognosis and Dionysian (types II and B) type is defined by severe complications and worse prognosis (Carpenter and Hasin, 2001).

Based on familial and environmental features that discriminate Cloninger *et al.*'s (1981) approach, this classification set has been hypothesized to reflect a method of family influences identification involved in alcoholism 'transmission' rather than a method to classify alcoholic subjects (Penick *et al.* 1990). Hence, to improve definitional parameters and transform the etiological basis of types I and II into a clinical procedure, Cloninger *et al.* (1981) introduced two criteria: age of onset of alcoholism and complications associated with drinking.

Efforts to discriminate Cloninger *et al.*'s (1981) type I/type II approach have introduced several classification schemes, however, with important differences among the models. von Knorring *et al.*'s (1985) model differentiated the subtypes by the age of alcohol problem and help seeking onset and the frequency of social-related problems. Sullivan *et al.*'s (1990) set includes the criteria proposed by von Knorring *et al.* (1985) and

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also history of family alcoholism. The last model, preconized by Gilligan *et al.* (1988), used criteria related to emotional problems, drinking binges, liver disease, onset of drinking problems, problems abstaining and social complications.

Penick *et al.* (1999) found that Gilligan's scheme showed a strong association with subtyping methods that use age of onset and a moderate association with subtypes based on psychiatric severity and cognitive function.

Carpenter and Hasin (2001) tested the Apolonian–Dionysian distinction based on five operationalization criteria schemes: three classification procedures of Cloninger's type I and type II, and two sets of Babor type A and type B. In this study, subjects derived from general population and the identification was based on the problem drinker diagnosis (alcohol-related negative consequences) rather than an alcohol dependence disorder. Pairwise classification agreement ranged between 0.35 (Gilligan versus Sullivan model) and 0.95 (Babor versus Schuckit model). Gilligan model demonstrated a poor overall agreement among all classification models.

Epstein *et al.* (2002) examined the overlap of four alcoholic typologies: antisocial versus non-antisocial; early versus late onset; type 1/type 2 and type A/type B. Findings showed a strongest association between early versus late onset and type 1/type 2 and between antisocial versus non-antisocial and type A/type B. This overlap reflects conceptual definitions among models.

In the literature, several multidimensional over-two-type solutions have been released (Zucker, 1987; Lesch *et al*., 1988; Del Boca and Hesselbrock, 1996; Hauser and Rybakowski, 1997; Windle and Scheit, 2004); however, few data are available in what concerns overlap between subtypes. For example, Pombo *et al.* (2007) found a significant overlap between NETER's anxiopathic subtype and Lesch's type II (Anxiety model) and between NETER's thymopathic subtype and Lesch's type III.

Lesch Alcoholic Typology (LAT) from Lesch *et al*. (1988) describes predictors for chronic alcoholism development obtained from a long-term prospective follow-up study (18 years). This model distinguished four evolutionary types depending on family history of alcoholism, previous personal psychopathology and neurobiological substratum. Thus, type I evidences the appearance of early withdrawal symptoms and craving, which can be associated with an endorphinical vulnerability. Type II shows suicidal intentions, anxiety and premorbid conflicts, with changes within the serotoninergic system. Type III typifies an aggressive and impulsive behaviour with the existence of psychiatric comorbidity. In this type a chronobiological change can be previewed. And finally, type IV shows premorbid organic cerebral lesions associated with a deterioration of individual's psychic, organic and social sphere.

The distinction of four subgroups of alcohol-dependent patients has been validated by biological, psychological and physiological measures, and therapeutic studies (Sperling *et al*., 1999; Lesch *et al*., 2001; Dvorak *et al*., 2006; Hillemacher *et al*., 2006; Walter *et al.*, 2006; Pombo *et al*., 2007; Hillemacher and Bleich, 2008).

In Portugal, Cardoso *et al.* (2006) achieved the NETER Alcoholic Typology (NAT), based on alcohol-dependent outpatients recruited from the alcoholism unit of Santa Maria's Universitary Hospital in Lisbon. They concluded a factorial structure organized in five dimensions: anxiopathic type, typifies anxious functioning; heredopathic type, congregates familial and environment influences on alcoholism; thimopathic type, related to affective symptomatology; sociopathic type, characterized by social disruptive behaviours; and adictopathic type, connected to younger individuals who consume alcohol and other types of psychoactive substances. Convergent and discriminant validity of NAT was confirmed by the agreement with Lesch *et al.*'s (1988) subtypes and by the distribution of external measures of gender; tobacco; alcohol syndromes, alcohol-related problems' severity; psychological and behaviour dimensions (Pombo *et al*., 2007).

Indeed, over the last decade, the typology models of Cloninger *et al.* (1981), Lesch *et al.* (1988) and Babor *et al.* (1992) have been employed for patient's distinction in many design methodology procedures, mainly in neurobiological, genetic and psychopharmacological studies (Sullivan *et al*., 1990; Kranzler *et al*., 1996; Lesch *et al*., 2001; Bleich *et al*., 2004; Walter *et al*., 2006; Hillemacher and Bleich, 2008; Pombo *et al*., 2008; Samochowiec *et al*., 2008).

At the present, no single method or taxonomy to operationalize specific subtypes has been universally accepted as definitive and overlap among typologies remains understudied (Penick *et al*., 1990; Epstein *et al*., 2002; Dvorak *et al*., 2006; Pombo *et al*., 2007).

In summary, there are several aspects of typologies' definitions and validity that need to be considered. Firstly, models currently used to classify Cloninger *et al.*'s (1981) approach revealed inconsistency in operational definitions. We believe that different distinction strategies for subgrouping alcoholics could display heterogeneous data and may jeopardize results from clinical and psychopharmacological trials that use subgrouping procedures in research methods. Secondly, previous studies related to validity dimensions and classification overlap among typologies is restricted to unidimensional and binary multidimensional schemes. Thirdly, classification redundancy among type I and type II patients with type A and type B patients in clinical settings has not been studied adequately; and fourthly, patients overlap between dichotomic multidimensional models and available multidimensional over-two-type solutions need to be examined. According to Hesselbrock and Hesselbrock (2006), in spite of diverse theoretical backgrounds and methodologies to subtype alcoholic subjects, there is a remarkable similarity across many of the multivariate alcoholic typologies purposed. This present study was also conducted in order to achieve empirical evidence of this proposal. Indeed, we aim to investigate alcoholic patient's classification concordance among six multidimensional alcoholic typological models: Cloninger's type I/II; von Knorring, Sullivan and Gilligan operationalized criteria; Babor type A/B; NAT and LAT subtypes.

METHODS AND SUBJECTS

The sample comprised 318 alcohol-dependent patients, sequentially admitted (from 2004 to 2007) in the alcoholism unit (NETER) of the Psychiatric Service of Santa Maria University Hospital in Lisbon. During the outpatient therapeutical programme (minimum period of 4 weeks after being admitted in NETER alcoholism unit), clinical and socio-demographic information was collected through the fulfilment of NETER

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Standardized Interview for alcoholic patients. This interview explores patient's socio-demographic information; family history of alcoholism; age of alcohol use, abuse and dependence onset; other substance consumption; previous alcohol treatments; patterns of alcohol consumption and alcohol-related problems. It has been used in other NETER group studies (Pombo *et al*., 2004, 2007, 2008; Cardoso *et al*., 2006). The Michigan Alcoholism Screening Test (MAST) from Selzer (1971) and the Severity Alcohol Dependence Questionnaire (SADQ) from Stockwell *et al.* (1983) were also administered in order to assess alcohol-related problems' severity and alcohol dependence level, and assist patient's allocation process. In addition, all subjects were evaluated in a face-to-face interview and asked directly about the items that comprise the operationalized criteria described by each alcoholism typology.

Here we provide an overview of the clinical criteria and decision process for subtyping the three variations of Cloninger's approach, the Babor typology, NETER alcoholic typology and the Lesch alcoholic typology. Patient's subtype allocation for Cloninger *et al.*'s (1981) models are as follow: the von Knorring *et al.* (1985) criteria for type I were the presence of subjective drinking problems' start after the age of 25 years, first treatment contact after the age of 30 years and few social complications (legal, work problems). Type II included subjective drinking problems start before the age of 25 years, first treatment contact before the age of 30 years and frequent social complications (legal, work problems). In what concerns Gilligan *et al.* (1988) criteria, type I shows guilt about drinking, binges or benders, tried to set limits, liver disease and onset of drinking problems after the age of 25 years. Type II presents fights when drinking, driving under influence of alcohol or having alcohol-related motor vehicle accidents, problems abstaining and treatment other than Alcoholics Anonymous. Sullivan *et al.* (1990) included the same criteria as von Knorring *et al*. (1985) and added negative history of family alcoholism in type I and positive history of family alcoholism in type II.

The decision procedure in the three sets was as follows: when the specified criteria of each subtype (I or II) was present, subjects received a positive score in each item endorsed (+1), and when the specified criteria was not in attendance, subjects received a negative score (−1). Afterwards, for patient's allocation purposes, algebraic sum of the items are performed and the quantitative scores were transformed into categorical data on the basis of higher total positive scores (or less negative) in each subtype. Sums equal to 0 were considered to be undiagnosed classification.

The classification procedure of the four alcoholism subtypes of Lesch *et al.* (1988) was based on a computerized Decision Tree. This PC-guided version of patient's allocation (Decision Tree) is nowadays available in computer software in most European languages and it has already been used in various international trials (Bleich *et al*., 2004; Hillemacher *et al*., 2006; Walter *et al*., 2006; Pombo *et al*., 2007). The descriptors for each type are as follows. Type I: social drinking develops to habitual drinking, medium abstinence syndrome occurs early, craving, positive family history for alcoholism and minimal social effects; type II: alcohol consumption as a coping strategy against anxiety, suicidal intentions (mainly under the influence of alcohol) and no severe somatic alcohol-related disorders or withdrawal; type III: alcohol consumption as a form of self-treatment (depression, sleep disorders), suicidal tendencies, psychiatric comorbidity, aggressive behaviour even without alcohol and mild somatic withdrawal; and type IV: cerebral disturbances or prenatal damage before the termination of brain development, grand mal seizures (not only during withdrawal), enuresis nocturna, deterioration of individual's psychic, organic and social sphere.

For the NAT decision process, the classification process between the five alcoholic subtypes was developed taking into account the scores of each variable that corresponds to a specific alcoholism subtype (internal criteria). This alcoholism subtype delimitation was conventioned in an exclusion way, beginning with adictopathic followed by sociopathic, thymopathic, anxiophatic and heredopathic. Each subtype presents exclusiveness conditions. First—adictopathic (N5; 'polydrug type')—if the patient presents a lifetime history of heroin or cocaine dependence, the adictopathic type should be diagnosed. Second—sociopathic (N4; 'antisocial type')—if the patient presents a severe history of antisocial behaviour and legal problems, the sociopathic type should be diagnosed. Third—thymopathic (N3; 'affective type')—if the patient presents a lifetime history of major depression episodes, the tymopathic type should be diagnosed. Fourth—anxiopathic (N1; 'anxious type')—if the patient presents a lifetime history of anxiety disorders, the anxiopathic type should be diagnosed. Anxiety symptoms have to be differentiated from symptoms related to alcohol withdrawal. Fifth—heredopathic (N2; 'inherited type')—if the patient presents a high prevalence of family history of alcoholism (first or/and second degree), the heredopathic type should be diagnosed. If any of the previous exclusion conditions have been selected, use a quantitative procedure with the conditions that are aggregated to each subtype.

The scoring methods are as follows: for a highly marked condition add three points (+3), if the condition is only present add one point (+1), and if it is not present remove one point (−1). The total score obtained in each alcoholism subtype will be translated to a final categorical type. Scores equal to 0 are indicators of classification absence. [For more details see Cardoso *et al*. (2006) and Pombo *et al*. (2007).]

For Babor *et al.*'s (1992) A/B approach, we considered the following criteria. Type A included low alcoholism family risk (with no first or second degree alcoholism family member), low social alcohol-related problems, mild alcohol dependence level and mild associated psychopathology. Type B criteria were the presence of high alcoholism family risk, high alcohol dependence level, consumption of other drugs and psychiatric comorbidity. The decision procedure was similar to the operationalized models of Cloninger (see above).

The subtyping procedure was performed by a single researcher with clinical skills to assess alcoholic patients and scientific knowledge to manage the principles of each classification system.

All subjects were informed about the study and given the consent for participation, which was approved by the local ethics committee.

The exclusion criteria were: presence of serious physical disease, severe psychiatric disorder (schizophrenia and other psychotic disorders, dementia, delirium), state of alcoholic intoxication (or other toxic substances) during assessment and marked cognitive deficit.

The sample comprised 318 alcohol-dependent patients, with 81.4% males ($N = 259$) and 18.6% females ($N = 59$). Age varied between 22 and 66 years, with a mean value of

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45.1 years (SD = 10.3). The sample was entirely Caucasian (100%), with 11.0% included in high or middle-high social class (I/II), 26.5% middle social class (III), 44.2% middle-low social class (IV) and 18.4% low social class. Regarding marital status, 56.9% were married, 22.3% were single and 20.8% were separated/divorced. In relation to occupational status, 12% integrated high/average corporate employees, 32.1% were qualified as skilled workers (carpenter, mechanic), 35.9% had a nonqualified professional activity (agriculture, services), 11.3% were already retired and 8.7% were unemployed. Concerning education level, 76.6% attended or completed basic school studies, while the others concluded high school (11.9%) or had an academic degree (11.5%).

Concerning clinical characterization of alcohol consumption, data shows that the average age of onset of drinking was 16.0 (SD = 6.1), the age of alcohol abuse onset was 27.8 (SD = 10.2) and the age of alcohol dependence onset was 35.0 (SD = 9.3) years, with a daily average of alcohol consumption of 124.2 g (SD = 88.1). In SADQ (alcohol dependence level), the subjects reported an average score of 25.1 (SD = 13.3) and in MAST (alcohol-related problems) 22.3 (SD = 11.1). History of family alcoholism was positive in 57.1% of the cases. Relative to smoking status, 70.5% of the sample were regular smokers, with an average of 23.7 (SD = 14.9) cigarettes per day. The consumption of others drugs was reported by 25.2% of the cases.

Statistical analysis

Considering normally distributed data (Kolmogorov–Smirnov test), parametric methods were used to calculate numerical relations between data. Statistical analysis was performed with Statistical Package for Social Sciences (SPSS-Version 12.0).

Kappa statistics assessed the concordance rates and agreement of Cloninger's approach between the three sets of von Knorring, Sullivan and Gilligan criteria. The Kappa agreement represents the probability of being classified as a specific subtype, given the same classification by another model. Kappa value reflects the level of agreement between the classification sets, with Kappa ≤ 0.50 suggesting poor agreement, between 0.50 and 0.70 suggesting fair levels of agreement and ≥ 0.70 showing good levels of agreement (Fleiss, 1981). Concordance rates indicate the percentage of subjects that have the same type of alcoholism, in simultaneous, according to the two sets of criteria that have been compared.

Chi-square (2-vs-2) comparisons were used to study the relation between patients classified according to Babor's model and the three sets of Cloninger's model. Percentages showed the overlap between the subjects classified as type I/II and type A/B.

Correlational analysis with additional percentage rates of individuals who fulfilled the criteria for the respective subtype were used to assess the relationship between Lesch and NETER's subtypes and the dicothomic models of Babor, and the three sets of Cloninger and the classification overlap between NETER's and Lesch's typologies. Statistical significance was defined at $P < 0.05$.

RESULTS

Considering the classification systems of over-two-type solutions, the distribution of the alcoholism subtypes in the sample evidenced the predominance of the anxiopathic and tymopathic subtypes in the NAT and the type II and type III in the LAT. Dicothomic typologies of Babor and Cloninger operationalized criteria derived from von Knorring, Gilligan and Sullivan showed higher percentages of individuals classified as type A and type I. Concerning distribution of subtype by gender, NAT and LAT subtypes showed significant differences (< 0.05). Women compared to men were more likely to be Lesch type III and NETER's tymopathic subtype. By the other hand, when compared to men, women were more likely to be Lesch type I and type IV and NETER's anxiopathic and sociopathic subtype.

Regarding undiagnosed alcoholic patients among the classification schemes, Gilligan's model yielded the highest percentage. Table 1 shows the subtype distribution (prevalences) of the alcoholic patients by gender.

The comparison of Cloninger subtype's classification schemes showed higher percentage rates of concordance among the three operationalized criteria in type I patients (92.6%; 88.8%; 80.4%). However, in type II patients the concordance was ≤50% of the cases. Agreement kappa values for the Cloninger's type I/II classification schemes were significant, in which von Knorring versus Sullivan yielded the higher rate of agreement, followed by von Knorring versus Gilligan, and Gilligan versus Sullivan operationalized criteria. Kappa values of all sets of criteria, ranging from 0.11 to 0.37, suggested poor agreement between the subtypes. Table 2 shows the concordance rates and agreement (kappa statistic) of Cloninger typology diagnosed according to von Knorring, Gilligan and Sullivan criteria.

Table 1. Subtypes distribution by gender (prevalences)

	N	Total (%)	Male (%)	Female (%)
Cloninger *et al*. (von Knorring *et al*.'s criteria)				
I	266	84.2	83.3	87.9
II	41	13.0	13.2	12.1
Undiagnosed	9	2.8	3.5	0
Cloninger *et al*. (Gilligan *et al*.'s criteria)				
I	250	78.6	77.6	83.1
II	27	8.5	9.3	5.1
Undiagnosed	41	12.9	13.1	11.9
Cloninger *et al*. (Sullivan *et al*.'s criteria)				
I	246	77.4	76.8	79.7
II	48	15.1	17.0	8.8
Undiagnosed	24	7.5	6.2	13.6
Babor *et al*.				
A	198	62.3	62.2	62.7
B	86	27.0	29.0	18.6
Undiagnosed	34	10.7	8.9	18.6
Lesch *et al*.[a]				
I	61	19.7	22.2	8.8
II	108	35.0	37.3	24.6
III	93	30.1	23.8	57.9
IV	47	15.2	16.7	8.8
Cardoso *et al*. (NAT)[a]				
Anxiopathic	96	31.2	33.9	19.3
Heredopathic	48	15.6	16.3	12.2
Tymopathic	90	29.2	22.7	57.9
Sociopathic	26	8.4	10.0	1.8
Adictopathic	35	11.4	12.4	7.0
Undiagnosed	13	4.2	4.8	1.8

Using Lesch *et al*. PC software to classify alcoholics, all patients were allowed to be diagnosed so there were no undiagnosed patients in this model.
[a]Showed differences between gender ($P < 0.05$).

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Table 2. Concordance rates and agreement (kappa statistic) of Cloninger *et al.*'s typology diagnosed according to von Knorring *et al.*'s, Gilligan *et al.*'s and Sullivan *et al.*'s criteria

		Undiagnosed	Type I	Type II	Kappa
Cloninger *et al.*					
Type I/type II					
von Knorring *et al.*	*N*	1	226	24	0.37**
versus Sullivan *et al.*	%	4.2	92.6	50.0	
von Knorring *et al.*	*N*	3	221	13	0.22**
versus Gilligan *et al.*	%	7.3	88.8	50.0	
Gilligan *et al.* versus	*N*	1	201	12	0.11**
Sullivan *et al.*	%	2.4	80.4	44.4	

**$P < 0.01$.

Table 3. Relation between patients classified according to the Babor *et al.* model and the three sets of Cloninger *et al.*'s model.

Babor *et al.*'s set		Type A	Type B	Chi-square	*P*
von Knorring *et al.*					
Type I	*N*	173	65	4.4	0.05
	%	72.7	27.3		
Type II	*N*	20	16		
	%	55.6	44.4		
Sullivan *et al.*					
Type I	*N*	166	57	18.1	0.01
	%	74.4	35.6		
Type II	*N*	16	24		
	%	40.0	60.0		
Gilligan *et al.*					
Type I	*N*	163	61	3.2	NS (0.07)
	%	72.8	27.2		
Type II	*N*	12	10		
	%	54.5	45.5		

A relation between Babor's classification scheme and the sets of von Knorring, Gilligan and Sullivan was verified. Subgroups showed a higher agreement between Babor's type A and type I of all three sets of Cloninger's operationalized criteria, with von Knorring subjects showing 72.7% of concordance, Sullivan 74.4% of concordance and Gilligan 72.8% of concordance. However, chi-square comparisons only showed a significant overlap between the Babor criteria and the sets of von Knorring and Sullivan. Table 3 shows the relation between patients classified according to Babor's model and the three sets of Cloninger's model.

To assess the link between Lesch and NETER's over-two-type classification schemes and the binary models of Babor, von Knorring, Sullivan and Gilligan correlation analysis were performed. Positive relationship between variables translates an overlap between the patients' subtypes. Table 4 shows the correlations between Lesch's four-type classification scheme and the dicothomic models of Babor and the three sets of Cloninger's.

In what concerns to the relation between NETER subtypes and the three dicothomic sets of Cloninger and Babor classification, Table 5 shows the correlations between NETER's five-type classification scheme and the dicothomic models of Babor and the three sets of Cloninger's and Table 6 shows the classification overlap between NETER's and Lesch's subtypes.

Table 4. Relation between Lesch four-type classification scheme and the dicothomic models of Babor *et al.* and the three sets of Cloninger *et al.*'s

Lesch *et al.*		Type I	Type II	Type III	Type IV
von Knorring *et al.*					
Type I	*N*	53	96	77	32
	%	17.3	31.3	25.1	10.4
	r	0.04	0.10	0.00	−0.17**
Type II	*N*	8	7	12	13
	%	2.6	2.3	3.9	4.2
	r	0.00	−0.14	0.00	0.18**
Sullivan *et al.*					
Type I	*N*	47	90	74	27
	%	16.0	30.6	25.2	11.0
	r	0.00	0.10	0.05	−0.19**
Type II	*N*	10	10	12	15
	%	3.4	3.4	4.1	4.7
	r	0.02	−0.12*	0.04	0.19**
Gilligan *et al.*					
Type I	*N*	47	87	67	39
	%	17.0	31.4	24.2	14.1
	r	0.01	0.03	0.09	0.04
Type II	*N*	5	8	8	6
	%	1.8	2.9	2.9	2.2
	r	0.00	0.02	0.01	0.04
Babor *et al.*					
Type A	*N*	31	86	51	22
	%	10.9	30.3	18.0	7.7
	r	−0.12*	0.25**	−0.09	−0.13*
Type B	*N*	25	12	29	19
	%	8.8	4.2	10.2	6.7
	r	0.15**	−0.26**	0.06	0.13*

% = concordance rate between patients; *r* = correlation between the subtypes (Spearman).
*$P < 0.05$; **$P < 0.01$.

Table 5. Relation between NETER's five-type classification scheme and the dicothomic models of Babor *et al.* and the three sets of Cloninger *et al.*'s

NETER's scheme		N1	N2	N3	N4	N5
von Knorring *et al.*						
Type I	*N*	87	43	77	17	22
	%	29.2	14.4	25.8	5.7	8.5
	r	0.13*	0.06	0.02	−0.12*	−0.21**
Type II	*N*	8	4	11	7	10
	%	2.7	1.3	3.7	2.3	3.4
	r	0.09	−0.05	0.00	0.10	0.17**
Sulivan *et al.*						
Type I	*N*	80	34	74	16	22
	%	28.1	11.9	26.0	5.6	7.7
	r	0.09	−0.06	0.06	−0.08	−0.13*
Type II	*N*	11	2	9	8	11
	%	3.9	2.5	3.2	2.3	3.9
	r	−0.07	0.00	0.08	0.10	0.16**
Gilligan *et al.*						
Type I	*N*	79	44	72	12	23
	%	29.6	16.5	27.0	4.5	8.6
	r	0.06	0.13	0.00	−0.20**	−0.11**
Type II	*N*	8	1	4	7	7
	%	3.0	0.4	1.5	2.6	2.6
	r	0.00	−0.13*	−0.07	−0.18**	0.16**
Babor *et al.*						
Type A	*N*	72	26	53	11	16
	%	26.2	9.5	19.3	4.0	5.8
	r	0.18**	−0.07	0.05	−0.10	−0.13
Type B	*N*	13	14	27	14	16
	%	4.7	5.1	9.8	5.1	5.8
	r	−0.20**	0.02	0.06	0.14*	0.16**

% = concordance rate between patients; *r* = correlation between the subtypes (Spearman).
*$P < 0.05$; **$P < 0.01$.

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Table 6. Classification overlap between NETER's and Lesch's subtypes.

Lesch *et al.*'s versus NETER's scheme		Type I	Type II	Type III	Type IV
N1	*N*	20	60	6	11
	%	6.5	19.4	1.9	3.6
	r	0.02	0.40**	−0.35**	−0.06
N2	*N*	18	10	7	13
	%	5.8	3.2	2.3	4.2
	r	0.20**	−0.12*	−0.13*	0.15**
N3	*N*	3	8	62	7
	%	1.0	2.9	20.2	3.9
	r	−0.24**	−0.30*	0.58**	−0.01
N4	*N*	7	8	8	7
	%	2.3	2.6	2.6	2.3
	r	0.03	0.05	0.01	0.07
N5	*N*	10	10	10	4
	%	3.2	3.2	3.2	1.3
	r	0.09	0.03	0.00	−0.03

% = concordance rate between patients;
r = correlation between the subtypes (Spearman).
*$P < 0.05$; **$P < 0.01$.

DISCUSSION

Considering previous studies that take into account patients' subtype distribution prevalences, typology classification systems have distinguished the predominance of Cloninger type I, Babor type A, Lesch type II and type III, and NETER's anxiopathic and tymopathic subtypes (Lykouras *et al*., 2004; Carpenter and Hasin, 2001; Bleich *et al*., 2004; Hillemacher *et al*., 2006; Pombo *et al*., 2007).

Like in other studies focused on alcohol-dependent and general populations, unclassified alcoholics yielded the highest percentage among patients classified according to Gilligan's model (Anthenelli *et al*., 1994; Carpenter and Hasin, 2001).

Subtype-specific agreement represents the probability of being classified as a specific subtype, given the same classification by another model (Fleiss, 1981). Like in previous studies, current purposed methods for identifying Cloninger's type I and type II alcoholics showed poor agreement rates between the subtypes, confirming important definitions inconsistencies (Lamparski *et al*., 1991; Anthenelli *et al*., 1994). Concerning subtype-specific overlap, Cloninger's subtypes classification schemes showed the higher percentage rates of concordance among the three operationalized criteria in type I patients. In type II patients, the concordance was much lower (≤50% of the cases).

In the study, agreement kappa values of the three sets of criteria ranged from 0.11 to 0.37. Lamparski *et al.* (1991), in a male alcoholic population, compared the criteria purposed by von Knorring *et al.* (1985) with those of Gilligan *et al.* (1988), to operationalize Cloninger's type I/type II approach, having found a low overall concordance between the two systems (rate of 14%, kappa of 0.21). Anthenelli *et al.* (1994) studied alcoholic males' overlap given the three documented sets of type I/type II classification, yielded by von Knorring, Sullivan and Gilligan, founding kappa agreements between 0.18 (Gilligan versus Sullivan) and 0.69 (von Knorring versus Sullivan). Like in these authors research, a higher agreement level between the subjects labelled as von Knorring and Sullivan classification would be expected, given the overlap between the schemes of the following criteria: age of alcohol-related problems and severe social consequences of drinking onset. In conclusion, models that emphasize the number of social consequences and age of onset showed a significantly better classification concordance. Studies considered that 'early versus late onset' (alcohol use, alcohol-related problems) remains an effective feature to operationalize Cloninger's alcoholic classification with a prominent place in the history of alcoholism typologies (Penick *et al*., 1990; Lykouras *et al*., 2004). Nevertheless, it may be unclear if it represents a condition to distinct an alcoholic subtype or, rather, a good marker for a primary or secondary alcohol disorder (Anthenelli *et al*., 1994).

Chi-square comparisons in Anthenelli *et al.*'s (1994) report showed a significant overlap between Sullivan's classification for Cloninger's type I and type II and primary and secondary alcoholism distinction, with type I subjects showing a 73% concordance with primary alcoholism and type II subjects showing a 73% concordance with secondary alcoholism with primary antisocial personality disorder.

Carpenter and Hasin (2001) studied in a general population that subjects overlap between the three models of type I/type II and type A and type B classifications. Overall kappa agreements for the pairwise model comparisons in the general population range from 0.32 (Babor versus Gilligan) to 0.86 (Babor versus von Knorring). The 1-year longitudinal analysis indicated that subtypes based on Sullivan's criteria (0.94) and von Knorring's model (0.83) presented the highest overall classification agreement, followed by Gilligan's model (0.42). Indeed, Penick *et al.* (1990) concluded that Gilligan's method for subtyping problem drinkers is probably of little value to the clinician or researcher working with alcoholics in treatment.

Subgroups' comparison in binary classification models yielded a significant overlap between Babor's type A and type I of the sets of von Knorring (72.7% of concordance) and Sullivan (74.4% of concordance). Carpenter and Hasin (2001) found a fair agreement between Babor's model and von Knorring and a greater concordance among the Apollonian (similar to type I and A) classifications. On the other hand, Epstein *et al.* (2002), in a multi-site study, examined the overlap among alcohol typologies but did not find any strong association between type I/type II model and type A/type B classification.

Regarding the relation between Lesch subtypes and the three dicothomic sets of Cloninger and Babor classifications, we found a moderate overlap between Lesch type I and Babor type B, between Lesch type II and Babor type A, and between Lesch type IV and von Knorring and Sullivan type II and Babor type B. On closer examination of patients' classification concordance, these results may be explained by the overlap of some operationalized criteria used to define each alcoholic subtype.

Babor type B and Lesch type I present high alcoholism family risk; Babor type B patients showed psychiatric comorbidity as internal criteria, which can be related to Lesch type IV descriptors as cerebral disturbances or prenatal damage before the termination of brain development and complications in psychic, organic and social life not only related to alcohol intake, and Babor type A and Lesch type II share the characteristic of the mild somatic alcohol dependence level in the subgroup profile.

Some studies have used Lesch and Cloninger typologies (Walter *et al*., 2006; Reulbach *et al*., 2007) in their methodology procedure; however, only the study of Walter *et al.* (2006)

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investigated the relationship between these two models. The authors did not find any significant association between these classifications.

In what concerns to the relation between NETER's subtypes and the three dicothomic sets of Cloninger and Babor classification, we found a moderate overlap between anxiopathic type with von Knorring type I and Babor type A, sociopathic type with Babor type B and addictopathic type with von Knorring, Sullivan and Gilligan type II and Babor type B. On closer examination of patients' classification concordance, these results may be explained by the overlap of some operationalized criteria used to define each alcoholic subtype. Anxiopathic type, von Knorring type I and Babor type A define three subgroups characterized by the presence of few social complications related to alcohol consumption (legal, work problems); sociopathic and addictopathic types in comparison with type II and type A alcoholics share some common diagnostic definitions such as antisocial behaviour, consumption of other drugs, psychiatric comorbidity, aggressive behaviour and frequent social complications (namely, legal problems).

Like in a previous study of both typologies (Pombo *et al.* 2007), Lesch and NETER's over-two-type classification schemes showed a fair agreement between NETER's anxiopathic subtype ('anxious type') and Lesch's type II (Anxiety model, alcohol as a conflict solver) and between NETER's thymopathic subtype ('affective type') and Lesch's type III (Depression model, alcohol as an anti-depressant), reflected the overlap of both (anxiety and depression) underlying alcoholism models.

Thus, in Lesch's type II patients, alcohol is consumed as a coping strategy against anxiety (sedation). Patients may become aggressive when intoxicated. NETER's anxiopathic subgroup typifies a neurotic functioning marked by anxiety, emotional instability and aggressive behaviour during withdrawal from alcohol and craving. Lesch's type III patients are characterized by an accumulation of family-based affective disturbances causing motivational, existential and occasionally also sleeping disorders. Suicidal tendencies may also occur. NETER's thymopathic subtype expresses a change in affection regulation, being characterized by alexithymic traits, depressive symptoms and work problems.

We also saw a moderate overlap between NETER's heredopathic subtype (type 2) and Lesch type I (allergy model) and type IV (Habit Forming model, pre-alcoholic cerebral damages and infantile development disorders). This result may be explained by the association of some descriptors that characterize these alcoholic subtypes. For example, positive family history of alcoholism is a redundant criterion to Lesch type I and heredopathic subtype. The heredopathic subtype also congregates individuals who grow up in a limited social and education background, who develop a severe alcohol dependence level. This alcoholism phenotype may have been influenced by brain maturity and interfere with subjects' social, psychic and organic complications not only related to alcohol consumption (Lesch's type IV descriptors).

If we see patients allocation overlap from a viewpoint that alcoholic subtypes classification exists on a spectrum of severity, we may conceptualize the association between Lesch patients allocated as severe courses (types I and IV) with generally accepted basic high-severity/vulnerability subgroup (e.g. Babor type B and Cloninger type II). Walter *et al.* (2006) found that 81.5% of Cloninger's type I patients were also in Lesch's mild illness course subtypes (types II and III), and only 33.3% of Cloninger's type II patients were classified as Lesch's severe course subtypes (types I and IV). Thus, looking to NETER's typology classification overlap with typology dichotomic models and Lesch types, we may hypothesize anxiopathic and tymopathic patients as a mild illness course (Lesch types) and low-severity/vulnerability subgroup (Babor type A and Cloninger type I), and sociopathic and addictopathic patients as a severe course and high-severity/vulnerability subgroup.

In this study we should consider some limitations. The study sample comprised patients that were admitted in an alcoholism unit to receive treatment. Therefore, the use of treatment entry alcohol-dependent samples might contribute to the decrease of discriminant validity power by increasing the degree of symptom overlap evidenced in the various alcoholic subtypes in clinical context. In addition, results should be generalized to other alcoholic populations with caution. Subjects included suffering from alcohol dependence with some comorbid conditions like polydrug abuse or dependence, anxiety or depressive disorders, which in addiction with many clinical factors might have heterogenized alcoholic sample and biased subtype classification distinctions. As we have previously mentioned, study exclusion criteria contained marked cognitive deficit, however Lesch's type IV patients are characterized by organic cerebral lesions and neurocognitive disabilities. This fact removes some patients from the sample that normally would be classified as Lesch's type IV. So, it might influence the outcomes of concordance analysis. We have also to consider misclassification. In the classification procedure of Sullivan *et al.* (1990), personality traits were not measured. Patients' subtype distinction was made cross-sectionally what may have increased the probability of erroneous classification. Finally, a point regarding Babor's subtyping procedure. This study used a non-traditional approach to classifying patients as type A and type B, with a scoring decision process based on clinical criteria, rather than a typically *k*-means clustering algorithm that incorporates a range of psychosocial, medical and substance use indices to place patients in a classification faction.

Like in other studies, a low level of agreement between the proposed methods for identifying Cloninger's type I/II alcoholics was verified. We also observed a significant overlap between several phenotypes derived from multivariate typologies available in alcoholism literature.

Therefore, our results go in accordance with Hesselbrock and Hesselbrock's (2006) conclusions, when they put emphasis on the fact that in spite of diverse theoretical backgrounds of the researchers, the samples examined and the methods used to structure the typology, there is a remarkable similarity across many of the multivariate alcoholic typologies purposed. The authors suggested four main phenotypes of alcoholism: chronic/severe type, depressed/anxious type, mildly affected type and an antisocial type.

Currently used pharmaceutical agents have also been studied in different alcohol-dependent phenotypes. Studies have demonstrated the efficacy of selective serotonin reuptake inhibitors (SSRIs) in specific alcoholic subtypes using Babor *et al.*'s (1992) A/B approach (Kranzler *et al.*, 1996; Pettinati *et al.*, 2000) and also observed reductions in drinking in

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selected alcoholic subtypes distinguished by early versus late onset of alcoholism given a serotonin receptor antagonist 5-HT_3—ondansetron (Johnson *et al*., 2000; Kranzler *et al*., 2003). Lesch *et al.*'s (1988) alcoholic typology has also been related to anticraving medications. In one randomized prospective study comparing acamprosate and placebo, with a 1-year treatment phase and 1-year follow-up phase, Lesch *et al.* (2001) found that acamprosate is effective in Lesch type I and type II patients. Naltrexone is only effective during drinking in Lesch type III alcohol-dependent patients (Kiefer *et al.* 2005). Nevertheless, in reality, there is a frequent disconnect between what is found in research and what is used in real-world alcoholism treatment settings (NIAAA, 2006). Based on the fact that nowadays a four-cluster subgrouping phenotypes of alcohol dependence is well established in research and predictors of response to anticraving medications (acamprosate and naltrexone) revealed pertinent conditions like gender, onset, comorbidity, antisocial personality disorder and typologies, Cloninger *et al.* (1981), Lesch *et al.* (1988), Babor *et al.* (1992) and Lesch (2007) mention that the above typological categories should be included in the classification systems of DSM-V and ICD-11. Nevertheless, this proposal has been considered premature without further international research (Babor and Caetano, 2006).

In conclusion, this study analysed the concordance of several different subtyping algorithms among treatment-enrolled alcohol-dependent subjects. Models presently used to classify Cloninger's approach revealed some discrepancy regarding definitional parameters. Alcoholism phenotypes derived from multivariate typologies confirmed a significant overlap, in which much of the concordance is a function of common characteristics in subtype operationalization.

Commonalities among these different subtyping classification systems offer the possibility of identifying important dimensions that better differentiate individuals among clinical and research problem drinker's populations.

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