Subgroups of Alcohol Dependence and their Specific Therapeutic Management: A Review and Introduction to the Lesch- Typology

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Key words: Alcohol dependence, Subgroups, Typologies

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Abstract:

Objective: An estimated 4 percent of the European population are addicted to alcohol. Their chronic alcohol intoxication not only leads to tissue damage in nearly all organs but also changes CNS functions leading to different psychiatric symptoms. As the mere diagnosis "alcohol- dependence" does not comprise much information on etiology, therapy or prognosis, various attempts have been undertaken to reach more precise diagnostic procedures by defining subgroups that hold more therapeutic relevance. **Method:** The typologies most common and most frequently used have been reviewed with special emphasis on the comparison of these typologies to the Lesch-typology. **Results:** Apart from Jellinek´s subgroups, the typologies used most frequently nowadays are those of Cloninger, Barbor and Schuckit. While the other typologies derived empirically by employing multivariate statistical techniques, Lesch´s typology was formulated from theoretical frameworks based on data obtained in a prospective long-term study. These findings have since then been validated in various biological, neurophysiological and treatment studies. The typology differentiates four types, each with different biological correlates, a different syndrome, different needs concerning relapse prevention and a different predicted prognosis. **Conclusion:** Lesch´s typology has implication for both the etiology and the development of

the disease. Thus it provides a new basis for selecting specific pharmacotherapeutic and psychotherapeutic treatment.

Introduction

Wine and beer are daily consumed drinks in most Western countries. While consumption and abuse correlate with a society´s wealth, the number of alcohol addicted remains rather stable. In spite of attempts of more than 150 years to overcome this problem, alcohol still is Europe´s most frequently abused drug. The health authorities in most countries have to face alcohol addiction and alcohol-related problems with costly prevention and treatment programs. About 4 percent of the European population are addicted to alcohol.

Medical Aspects

Alcohol addicted patients suffer in principle from a chronic intoxication leading to tissue damage in nearly all organs. Resorption takes place primarily in the stomach and duodenum, whereby a part of the ingested alcohol is metabolized already by enzymes in the gastric mucosa (“first pass effect”). The remaining alcohol passes the lipoid blood brain barrier as alcohol has lipid-solvable molecules. Liver diseases as well as stomach surgery markedly reduce the first pass effect. About 10 percent of blood alcohol reach the brain, affecting receptors sensibility in nearly all transmitter systems (e.g., GABA, Glutamate, Dopamine,

5HT) as well as the transmission itself. The changed brain functions lead to the typical psychiatric symptoms and alcohol-related disabilities (reduction of intelligence, of self-criticism, enhanced emotional instability, loss of physical and psychic energy and sleep disturbances). Withdrawal symptoms such as tremor, elevated blood pressure and electrolyte changes (natrium, potassium, magnesium) reach a marked degree only in 30 percent of the patients. Those typical alcohol-related disabilities are treated mainly within the frame of the general practitioners work. The physical adaptation to the presence of alcohol modifies the action profiles of most pharmaceutical drugs. As a result of ongoing continuous intoxication, the patients gradually reduce their social contacts, symptomatology homogenizes more and more and social contacts become increasingly characterized by the alcohol-related disabilities.

This etiological model describes the therapeutic consequences. Personality traits are covered by withdrawal, loss of intellectual functioning and social problems, whereby those patients are hard to be "contacted emotionally” and/or to be motivated for changes in drinking style or for any kind of therapy. In up to 50 percent of these patients, we still run aground.

Alcohol Addiction Development

Different studies have revealed that the diagnosis of "alcohol addiction"- implying that it is a homogeneous clinical picture or disease- does not reveal sufficient information on etiology, therapy or prognosis. When people start to drink-craving for alcohol is a quite heterogeneous phenomenon. Only if positive effects (reward or relief) are associated with alcohol consumption they will drink more frequently and may enter a drinking career. At different stages, alcohol is taken for anxiety reduction, as an antidepressant, sleep inducing and tranquilizing agent or for “problem solving.” Only 18 percent of alcohol-addicted patients have started their career due to milieu-dependent, social drinking habits in their specific environment.

Since Magnus Huss introduced the term "chronic alcoholism" more than 100 years ago, the WHO, mainly influenced by Jellinek´s attempts for a better differentiation of alcohol-dependent patients, keeps on ameliorating the diagnostic procedures in the field of alcoholism. The three main criteria "dosage increase, syndrome of abstinence and loss of control" are still valid and are subject to the most prominent investigations in this field.

Diagnostic Guidelines for the Diagnosis of Dependence Syndrome (ICD-10)

Dependence syndrome should only be diagnosed if three or more of the following manifestations have occurred together for at least one month or, if persisting for periods of less than one month should have occurred together repeatedly within a twelve-month period (1):

1. a strong desire or sense of compulsion to take the substance;
2. impaired capacity to control substance-taking behavior in terms of its onset, termination, or levels of use, as evidenced by: the substance being often taken in larger amounts or over a longer period than intended; or by a persistent desire or unsuccessful efforts to reduce or control substance use;
3. a physiological withdrawal state when substance use is reduced or ceased, as evidenced by the characteristic withdrawal syndrome for the substance, or by use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
4. evidence of tolerance to the effects of the substance, such that there is a need for significantly increased amounts of the substance to achieve intoxication or the desired effect, or a markedly diminished effect with continued use of the same amount of the substance;
5. preoccupation with the substance use, as manifested by important alternative pleasures or interests being given up or reduced

because of substance use; or a great deal of time being spent in activities necessary to obtain, take, or recover from the effects of the substance;

6. persistent substance use despite clear evidence of harmful consequences, as evidenced by continuous use when the individual is actually aware, or may be expected to be aware, of the nature and extent of harm.

At hand of this development, it became evident that for providing appropriate therapy not only the diagnosis but also the severity degree of the disease are to be used. For optimal, individualized therapy, the development of therapy-relevant subgroups is necessary. Many attempts have been made to describe subgroups of alcohol dependence, and we will try to reflect some of the concepts that have been established within the last fifty years.

Typologies in the Field of Alcoholism

Jellinek´s Typology (2):

In his typology, Jellinek differentiates between Alpha, Beta, Gamma, Delta and Epsilon drinkers. The Alpha type uses alcohol as a means of coping with social or physical stress. Those patients show no signs of physical but of psychic addiction. They have no loss of control and are able to abstain from drinking without difficulty. The Beta type is the occasional drinker who is not addicted but who is suffering from severe alcohol-related diseases (e.g., polyneuropathy, liver cirrhoses, gastritis). The Gamma type is the episodic drinking, addicted drinker that is able to abstain but is suffering loss of control when consuming alcohol. The Delta type is the regular drinker that can not abstain from drinking and is suffering severe withdrawal symptoms. The Epsilon type drinks regularly or episodically, in the sense of dipsomania (correlates with ICD-10 F10.26)(Jellinek, 1960).

Although about fifty years old, Jellinek´s typology is still well known and used today, with the limitation that it merely reflects the drinking patterns.

Sckuckit`s Typology (3)

Schuckit proposed an approach at subtyping that focuses on the presence or absence of independent major psychiatric disorders.

In this scheme, those labeled as primary (or “relatively straightforward”) alcohol-dependent patients have no evidence of an independent psychiatric disorder (70%). Patients of this group can also present with psychiatric syndromes other than alcohol-dependence; these symptoms disappear within a couple of weeks as having been provoked by alcohol consumption.

Those patients who, in addition to their alcoholism, demonstrate severe psychiatric syndromes that occur independent of heavy drinking are labeled as secondary (or “complicated”) alcohol-dependent individuals. Those patients are using alcohol as a treatment of the underlying disorder.

Cloninger´s Typology (4,5):

Among the more recent typologies, Cloninger proposed a system based on studies on the adopted sons of alcoholics. He identified two types of alcohol abuse that have different genetic and environmental causes.

He identified Type 1 alcoholics as individuals who start abusing alcohol later in life (age of onset >25 years). They can be male or female and require environmental provocation in order to manifest a susceptibility to alcohol. These patients experience withdrawal symptoms and loss of control and often feel guilty about their drinking behavior. Their social behavior is unremarkable.

Type 2 alcoholics are male, exhibit alcohol-seeking behavior early in life (age of onset <25 years), tend to be impulsive and risk-taking, manifest antisocial behavior and have strong inheritable influences independent of the environment.

These patients have often had previous attempts to give up alcohol.

With the application of this typology, it became evident that patients of Type 1 have personality characteristics that include high harm avoidance, low novelty seeking and high reward dependence, whereas personality characteristics of Type 2 patients include low harm avoidance, high novelty seeking and low reward dependence.

Babor´s Typology (6):

Babor developed a system of Type A and Type B alcoholics using an empirical clustering technique. He designated Type A (after the Roman god Apollo) as being of late onset, having fewer childhood risks, less severe dependence, fewer alcohol-related physical and social consequences, less previous treatment for alcohol problems, less psychopathological dysfunction and less distress in the areas of work and family.

Type B (after the Roman god Bacchus) was characterized by more childhood and familial risk factors, earlier onset, greater severity of dependence, polydrug use, more serious consequences, a chronic

treatment history and more life stress and psychopathological dysfunction.

Lesch´s Typology:

The Lesch typology has been developed within a long-term catchment area study involving 444 alcohol-dependent patients (diagnosed according to DSM III). After those patients had been followed for five years, four different courses could be defined and correlated with certain predictors (7).These findings have since been validated in various biological, neurophysiological and treatment studies as well as in a follow-up study performed eighteen years after the initial investigation (8-15). The Lesch typology describes four types of alcoholics who have different reasons for developing addiction, different withdrawal syndromes, a different prognosis and who benefit from different therapeutical approaches. We would like to give a short introduction to the typology by describing the syndrome, biological correlates, relapse prevention and predicted prognosis of each type.

Type I:

Syndrome:

Patients have, when abstaining, no marked craving for alcohol and feel healthy in their psychosocial situation, but develop strong and immediate craving whenever they consume even small amounts of

alcohol. (Patients might describe a feeling as if a "switch" in their brain had been turned on.) They develop severe withdrawal already at early stages of their drinking career and often use alcohol mainly to fight withdrawal symptoms. They frequently have epileptic fits during withdrawal but do not present with seizures when abstaining.

Biological correlates:

Alcohol elimination and metabolism is supposed to be different in this group, when compared to the other types. Patients of this type show rapid methanol elimination with a high elimination constant rate. This implies that, when drinking, these patients have chronically high blood formaldehyde levels. Aldehyde condensation with endogenous amines (e.g., dopamine) leads to the formation of different condensation products like tetraisoquinolines (TIQs) or tetrahydro-beta-carbolines (THBCs), both substances with opiate-like action (16). As fermentation of nutritional sugar leads to a low “basal” production of endogenous alcohols in the body also during abstinence, it can be hypothesized that this endorphin system remains vulnerable as a result of the basal production of these condensation products. This vulnerability may remain even after years of abstinence and - in case of consumption of alcohol - lead to a severe relapse.

Relapse prevention:

These patients do not as a rule present with psychiatric disorders underlying the alcohol consumption. They are believed to develop alcohol addiction due to central nervous vulnerability and thus feel healthy as long as they are abstaining. Although no specific psychotherapy is needed, therapy should focus on dealing with endangering situations and provide information about craving. The regular visit of self-help groups can also be recommended to patients of this type.

Pharmacotherapeutically acamprosate has proven to be the substance best apt to treat craving in this group. Therapy may be started already during the withdrawal phase (2g/day for patients >60 kg; 1.4 g/day for patients < 60 kg) and should also be maintained also if relapse occurs (9,17). The duration of relapse and the amount of consumed alcohol can additionally be reduced by naltrexone and/or gamma-hydroxybutyric acid (GHB). Naltrexone binding to opiate receptors can prevent the alcohol-induced euphoric mood due to the effects of alcohol as well those of condensation products with agonistic function at opiate receptors (18,19,20,21). GHB has been shown to stimulate the firing rate of dopaminergic neurons and dopamine release in specific brain areas, a mechanism which has been believed to prolong the period until relapse (22,23). If a patient is under high drinking pressure, Disulfiram or Cyanamid may also be considered (24).

Neuroleptics can not be recommended in this group as they have been shown to increase relapse rates (25).

Predicted prognosis:

Most patients will manage to abstain for long periods or may be subjected to a life-event-dependent illness course. Considering the triangle of social, biological and psychological factors influencing the course of psychiatric diseases, one could say that these patients have a strong negative influence in the biological but not in the psychological field. Thus the course of the illness will mainly be influenced by their physical and social situation. In this group, no unfortunate illness course is predicted.

Type II:

Syndrome:

In this group, alcohol is used as self-medication and for “conflict solving.” Without alcohol, those patients have a rather passive life style and usually appear over-adapted to society. This behavior is considered to be due to the patient´s low self-esteem. They frequently live with a dominant partner and find it difficult to express their personal needs and opinions. From time to time, they leave their social role with the help of alcohol. Then behavioral changes such as aggressive symptoms may be observed.

Biological correlates:

A lack of tryptophan (and subsequently serotonine) is hypothesized to underlie this type. These patients have high levels of beta-carbolines, which represent condensation products of aldehydes and indolamines. The beta-carbolines influence monoamineoxidase (MAO) and thus the turnover of different transmitters, one of which is serotonine. Smoking also influences beta-carboline levels, but there is not yet any exact data on the influence of nicotine-addiction comorbidity in this group.

Relapse prevention:

While medication can ease psychiatric symptoms underlying the addiction, the most important therapeutic aspect in treatment of this subgroup is continuous psychotherapy, focusing on the enhancement of self-confidence and the development of alternative coping strategies. Thus motivation for psychotherapy should start early in the therapeutic process.

For these patients, reversible monoaminoxidase -A- blockers seem to be effective in treating the underlying disorders as beta-carbolines are hypothesized to have a MAO-blocking capacity. Acamprosate is also useful in this group as it significantly reduces relapse rates (9,17). In patients of this type, craving for alcohol has been observed to root in the search for relief and can be seen as a coping strategy. If patients are agitated and present with sleeping disorders (especially difficulty to

fall asleep) additional sedating antidepressants can be helpful. Sedatives, especially benzodiazepines, should be avoided in this group as they bare a high risk of a shift of the addiction.

Predicted prognosis:

For some patients, the further illness course will comprise slips, but only few relapses. Some patients will change to a life-event-dependent or episodic illness course. As the main therapeutic goal is the modification of personality traits, the course will be very much influenced by the patient´s motivation for psychotherapy. If the patients are successfully being motivated to undergo continuous psychotherapy, no unfortunate course is predicted. Still, 80 percent of these patients develop heterogenous drinking patterns like severe withdrawal symptoms (Type I), chronobiological disorders or depressive episodes (Type III) and seizures independent of alcohol consumption (Type IV).

Type III:

Syndrome:

Affective disorders mark this type, and there is often a positive family history of both alcohol dependence and affective disorders. In those families, alcohol is often used as “self-treatment” by several family members.

As a result of the underlying affective disorder, these patients frequently suffer from sleep disorders as well as from drive and mood changes. Because of alcohol´s sedating effects, these patients usually get the impression that alcohol is the "right" remedy in the early drinking period, while later they may notice that alcohol has deteriorating effects especially on sleep disturbances and mood changes and thus further induces an increase of this symptomatology. After a period of abstinence, the above-mentioned basic symptoms vanish but tend to reoccur episodically (seasonally or independently), even without alcohol consumption. During these episodes, these patients need antidepressant medication or may relapse without proper treatment of the affective disorder. Personality traits are often marked by a tendency to be rigid, depressed and "over-achieving."

Biological correlates:

Biochemical factors that are important for affective disorders are hypothesized to be of importance in this type. Recent research has focused on serotonin and the role of MAO-inhibitors.

Relapse prevention:

In these patients, craving for alcohol can be seen as an urge for self-treatment and will only diminish when the underlying disease is treated effectively. Depending on the kind of the disorder, most

psychopharmaceutical substances can be used. Substances with phase-prophylactic properties (Lithium, Carbamazepin, etc.) have also proven to be effective in certain patients of this subgroup. In case of relapse, naltrexone and/or GHB can reduce severity and duration of relapse for the same reasons as described above (18,19,20,21). Neuroleptics can not be recommended for these patients, as they have been shown to decrease the time to the first relapse (25).

Patients have got to be sensitive towards “warning signs” of commencing depressive periods. The psychotherapeutic approach should focus on the usually rigid and over-achieving personality structure. Furthermore, it is important that patients learn to reduce intellectual control and to deal with their feelings.

Predicted prognosis:

As these patients often suffer from diseases that have an episodic course (e.g., depression, bipolar disorders), an episodic course can also be expected concerning the drinking periods. Few patients may switch to an unfortunate illness course because of an increasing severity of the underlying disease.

Type IV:

Syndrome:

These patients usually suffer from cerebral damage during brain development (i.e., before the age of 14) or negative familial and social circumstances, leading to behavioral problems already during childhood (as, e.g., stuttering, nail biting, and enuresis nocturna). Epileptic seizures occurring independently of alcohol consumption are one of the symptoms that mark these patients, but do not necessarily have to be present to make the diagnosis. Compulsive traits and a loss of criticism concerning their alcohol intake lead to a disability to stand against the drinking pressure of their social surroundings. A tendency to chronification of the disease leads to severe cognitive disturbances and/or somatic disturbances with a loss of impulse control.

Biological correlates:

All mechanisms related to loss of criticism and impulse control, to cognitive disturbances and memory problems are being discussed as biological correlates in this type. Influences with a negative effect on brain development (e.g., trauma, social neglect, meningitis) seem to be of major importance.

Relapse prevention:

Medication is of minor importance in the treatment of these patients, although substances enhancing intellectual performance and impulse-control (e.g., nootropics, thiamine, carbamazepine) can prolong abstaining periods. As patients of this subtype are likely to relapse, adverse treatment can not be recommended. Naltrexone and GHB (alone or in combination) can reduce duration and severity of relapse. In the psychotherapeutic approach, securing and stabilizing measures are helpful. As these patients hardly ever manage to abstain for long periods, it is important to discuss and also practise coping with relapse (e.g., in role plays). For these patients, social stability and a well-structured daily life are important factors. The application of behavioral therapy and the attendance of self-help groups may combine two powerful strategies for patients of this type.

Predicted prognosis:

Even with accompanying medical and psychotherapeutical treatment relapses are very common in this group. Due to intellectual deficits and loss of criticism, a rather unfortunate course is predicted for these patients.

Discussion:

In contrast to relatively static nosologies, syndromes and typologies are developing subject to the new findings in psychiatry (e.g., ICD-development up to the present ICD-10). Some definitions for typologies require all defined symptoms to be present like signs on a coin. If not all symptoms are found, the diagnosis cannot be made. Others require core symptoms, accompanied by a “cloud” of closely related symptoms that are frequently (or may be) part of the clinical picture.

Today most typologies represent guidelines that allow the formation of hypotheses concerning etiology and prognosis of a certain disease. With the development of highly specific medication, we need to be able to detect subgroups of patients in which a certain drug can be expected to help. The same applies to the use of different psychotherapeutic strategies.

The model of covering the whole picture of a nosological entity with all possible kinds of treatment available has become far too expensive for all social security and health care systems around the world. Therefore we need to identify homogenous subgroups within such nosological entities as the “diagnosis” alcohol addiction implies.

Many attempts of subtyping alcohol-dependent patients have been made throughout the last fifty years, apart from the ones discussed in this article (25-29), so given the scope of the subject this review is both incomplete and subjective but tries to focus on the concepts

considered most promising for identifying homogenous subgroups and differentiating which pharmaceutical compounds can be expected to be effective in which patients.

Jellinek's typology is still of historical importance, but, as it only describes the drinking behavior, not taking into account other factors, it is no longer sufficient for developing new therapies. For research and therapy, typologies comprising more details for the description of patients are needed.

There seems to be a growing consensus that the presence or absence of psychiatric disorders independent of alcohol dependency plays an important role in the therapeutical approach towards the patient. Most of the more recent typologies have taken comorbid psychiatric disorders into account but have not focused on the kind of disorder. Thus, this differentiation holds little therapeutic relevance.

In reviewing Cloninger´s typology, for example, many authors questioned the dichotomy and argued that, once patients suffering from comorbid antisocial personality disorder were excluded, the distinction between Type 1 and Type 2 alcoholics no longer offered clinical subtypes with distinct severity (30,31,32). The same line of reasoning can also be applied to the typologies of Babor and Schuckit, who differentiate between the presence or absence of psychiatric disorders independent of the alcohol addiction (Schuckit) as well as the severity of psychopathological dysfunction (Babor).

Another distinction can be made by the fact that most typologies discussed in this article were derived empirically by employing multivariate statistical techniques, while Lesch´s typological classification schemes was formulated from theoretical frameworks based on data obtained in a prospective long-term study.

Lesch´s subtypes, which have implication for both the etiology and the development of alcoholism, have also been linked theoretically to specific neurotransmitter systems. Consequently, the typology provides a hypothetical basis for selecting specific pharmakotherapies and has implications for molecular genetic investigation on alcohol metabolism.

Attempting to provide the best therapy is certainly the primary aim in the work with alcohol-dependent patients. One should also bear in mind that typologies can help identify patients with demands for special therapeutic efforts but should never be used to stigmatize.

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