

ALCOHOL

Fachpresseschau, zusammengestellt und kommentiert von PD Dr. med. Ulrich W. Preuss (Ltd. Oberarzt, Klinik für Psychiatrie und Psychotherapie, Martin-Luther-Universität Halle-Wittenberg):

Aktuelle Veröffentlichungen zu verschiedenen Rubriken:

Editorial: Mein Standpunkt zu aktuellen Forschungsberichten

1. Grundlagenforschung, Genetik, Molekularbiologie
2. Pharmakologie, Zellstoffwechsel
3. Verhaltensneurobiologie, Umweltfaktoren und Konsum
4. Diagnose und Behandlung
5. Epidemiologie und Prävention
6. Somatische Alkoholeffekte
7. Editorials, Übersichten
8. Links

Editorial comment:

## **Direkte Biomarker für Alkoholkonsum: eine Erfolgsgeschichte.**

In den Journalen „Addiction“ und „Alcoholism Clinical and Experimental Research“ beschäftigen sich in den letzten 2 Monaten gleich 3 Artikel mit direkten Markern des Alkoholkonsums.

Eine Studie aus Norwegen (Høiseith et al, ACER, 33, 812-816) verglich traditionelle Marker des Alkoholkonsums (Carbohydrat-Deficient Transferrin, CDT, Transaminasen wie AST ALT und GGT) mit Ethylglucuronid (EtG) in Haaren bezüglich des geschätzten täglichen Alkoholkonsums innerhalb der letzten 3 Monate. 16 Alkoholabhängigen Patienten zu Beginn ihrer Entzugsbehandlung wurden untersucht. Diese Validierungsstudie ergab, dass die höchste Sensitivität für einen hohen („heavy“) Alkoholkonsum mittels EtG (94%) und GGT (93%) Bestimmung erreicht werden konnte, wobei alle anderen erhobenen Marker darunter lagen. Leider wurden in dem Beitrag keine Angaben zur Spezifität gezeigt. Dennoch wies die konsumierte Alkoholmenge keinen signifikanten Zusammenhang mit allen Markern außer EtG auf.

Die Studie von Morini et al (Addiction 104; 915-920) beschreibt die Analyse von EtG in Haaren. Dabei ist es vordringliches Ziel dieser Studie, einen Grenzwert für den Konsum von Alkohol in den letzten Monaten festzulegen. Die Ergebnisse weisen auf einen spezifischen Wert dieses Markers hin, der hoch sensitiv (0.92) und spezifisch (0.95) einen riskanten Alkoholkonsum nachzuweisen vermag, ohne dass diese Messung durch mögliche Confundierungen (Alter, Geschlecht, BMI, Rauchen, Art des alkoholischen Getränks, Haarfärbungen u.a.m.) signifikant beeinflusst wird. Eine weitere, aus Deutschland stammende Untersuchung von Junghanns et al (Addiction 104: 921-926) untersuchte EtG und einen weiteren direkten Marker des Alkoholkonsums, Ethylsulfat (EtS) im Urin von entzogenen Alkoholabhängigen longitudinal über einen Zeitraum von 12 Wochen. Erklärtes Ziel dieser Untersuchung war es, die Übereinstimmung der Ergebnisse beider Marker zu bestimmen und den Zusammenhang zwischen positiven Screeningwerten beider Indikatoren mit der Abbruchrate der Therapie zu evaluieren. Bereits 13.5% der Patienten wiesen positive Werte für beide Marker bereits bei Beginn der Beobachtung auf, zwischen 12% und 28% hatten im Verlauf positive Screeningergebnisse. Die Rate der Rückfälligkeit war bezüglich der Urinscreenings zu allen Zeitpunkten deutlich höher, als durch klinische Untersuchung oder Atemalkoholtests nachweisbar waren. Patienten mit positiven Werten beider Marker im Urin besuchten in der Folge in nahezu keinem Fall mehr die Therapieangebote und können damit in der großen Mehrzahl als rückfällige Therapieabbrecher gewertet werden.

In jedem Fall weisen diese und vorangegangene Studien innerhalb der letzten Jahre auf die vergleichsweise hohe Sensitivität und Spezifität dieser direkten Alkoholmarker, insbesondere EtG, zur Erfassung eines kürzlich (im Urin) oder sogar länger zurückliegenden Alkoholkonsum (3 Monate, Haare) hin. Auch kristallisiert sich heraus, dass die Erfassung der Marker in verschiedenen Körperbestandteilen (Urin, Haare) durch mögliche Confounder nicht signifikant verfälscht oder beeinträchtigt wird. Für den klinisch Tätigen ist bei der Behandlung von Alkoholabhängigen natürlich

wichtig, einen ausreichend validen, reliablen, sensitiven und spezifischen Marker eines aktuell (oder auch längerfristig) stattgehabten Alkoholkonsums zur Verfügung zu haben, um damit Konsum oder Rückfälligkeit während der Therapie (z.B. bei Ausgängen, Wochenendbeurlaubungen, Belastungstrainings) zur Verfügung zu haben. Da die Angaben aus klinischen Interviews, Atemalkoholmessungen und Konsummengen häufiger von den Ergebnissen abweichen, die durch die Erfassung der direkten Biomarker erhalten werden können, so lassen sich unterschiedlich Angaben vielleicht auch therapeutisch sinnvoll verwenden. Marker aus Alkoholmetaboliten haben natürlich auch Grenzen hinsichtlich ihrer therapeutischen Wertigkeit. Sie stellen einen Alkoholkonsum fest, nicht jedoch alkoholkonsum-assoziierte Störungen, wie einen riskanten, schädlichen oder abhängigen Konsum. Diese Eigenschaften oder Diagnosen werden sinnvollerweise immer noch klinisch gestellt und bewertet, wobei direkte Alkoholmarker bei der Diagnosestellung und Therapiemonitoring eine wichtige Hilfe und Ergänzung darstellen können.

## 1. Grundlagenforschung, Genetik, Molekularbiologie

Gen-Umwelt-Interaktionen wird eine wichtige Rolle bei der Erklärung der Ursachen von Abhängigkeitserkrankungen zugeschrieben. Dieser Artikel fasst die aktuellen Befunde zu diesem Themenbereich zusammen und erarbeitet Vorschläge für zukünftige Studien. So sollten nach Ansicht der Autoren bessere theoretische Annahmen über die biologischen Mechanismen vorgenommen werden und Stichproben longitudinal hinsichtlich der langfristigen Entwicklung von Gen-Umwelt Interaktionen im Verlauf untersucht werden.

## **Gene–environment interactions and alcohol use and dependence: current status and future challenges**

Carmen S. van der Zwaluw & Rutger C. M. E. Engels

*Addiction*, 104, 907–914

### **ABSTRACT**

**Aim** To discuss the current status of gene–environment interaction research with regard to alcohol use and dependence.

Further, we highlight the difficulties concerning gene–environment studies. **Methods** Overview of the current evidence for gene–environment interactions in alcohol outcomes, and of the associated challenges in gene–environment studies. **Results** Attention to the causative roles of gene–environment interactions in alcohol use and dependence is increasing. Studies with twin designs are beginning to examine gene-shared environment effects, and animal studies have investigated gene–environment interaction effects on alcohol intake in primates. Thirteen studies incorporated gene–environment interactions in examining alcohol use or dependence in humans. These studies held a variety of candidate genes and environmental risk factors and their heterogeneity made it impossible to draw firm general conclusions. **Conclusions** Challenges for future gene–environment studies are abundant, and consist of, for example, the development of clear theoretical assumptions about neurobiological mechanisms and the recruitment of large longitudinal samples that already start in childhood. Replication is essential to prevent an overload of false positive

results. Despite the difficulties, it is crucial to include gene–environment interactions in future studies in order to unravel the aetiological factors of human alcohol outcomes.

Ein zentrales Dogma der biologisch orientierten Abhängigkeitsforschung besagt, dass die Wirkung von Alkohol und anderen Substanzen mit Abhängigkeitsrisiko über das endogene, dopaminerge Verstärkersystem vermittelt wird, das zwischen dem ventralen Tegmentum und dem Nucleus Accumbens verläuft. Ziel dieses Beitrages war es, an neuronalen Zellen die Rolle von Dopamin D2 (DRD2) Rezeptoren auf die GABAerge neuronale Aktivität im ventralen Tegmentum unter Alkoholeinfluss zu untersuchen. Die Ergebnisse zeigten, dass Ethanol die GABAerge Neuronen via D2 Rezeptoren in ihrer Aktivität hemmt und es daraufhin möglicherweise zu einer Herunterregulation der DRD2 Rezeptoren bei diesen GABAergen Neuronen unter chronischer Alkoholexposition kommt.

## Acute and Chronic Ethanol Modulate Dopamine D2-Subtype Receptor Responses in Ventral Tegmental Area GABA Neurons

Kimberly H. Ludlow, Katie D. Bradley, David W. Allison, Seth R. Taylor, Jordan T. Yorgason, David M. Hansen, Christine H. Walton, Sterling N. Sudweeks, and Scott C. Steffensen

Alcohol Clin Exp Res, Vol 33, No 5, 2009: pp 804–811

**Background:** Ventral tegmental area (VTA) *c*-aminobutyric acid (GABA) neurons appear to be critical substrates underlying the acute and chronic effects of ethanol on dopamine (DA) neurotransmission in the mesocorticolimbic system implicated in drug reward. VTA GABA neuron firing rate is reduced by acute ethanol and enhanced by DA via D2 receptor activation. The objective of this study was to evaluate the role of D2 receptors in acute ethanol inhibition of VTA GABA neuron activity, as well as the adaptation of D2 receptors by chronic ethanol consumption.

**Methods:** Using electrophysiological methods, we evaluated the effects of intraperitoneal ethanol on DA activation of VTA GABA neurons, the effects of DA antagonists on ethanol inhibition of their firing rate, as well as adaptations in firing rate following chronic ethanol consumption.

Using single cell quantitative RT-polymerase chain reaction (PCR), we evaluated the expression of VTA GABA neuron D2 receptors in rats consuming ethanol versus pair-fed controls. **Results:** In acute ethanol studies, microelectroretic activation of VTA GABA neurons by DA was inhibited by acute intraperitoneal ethanol, and intravenous administration of the D2 antagonist eticlopride blocked ethanol suppression of VTA GABA neuron firing rate. In chronic ethanol studies, while there were no signs of withdrawal at 24 hours, or significant adaptation in firing rate or response to acute ethanol, there was a significant down-regulation in the expression of D2 receptors in ethanol-consuming rats versus pair-fed controls.

**Conclusions:** Inhibition of DA activation of VTA GABA neuron firing rate by ethanol, as well as eticlopride block of ethanol inhibition of VTA GABA neuron firing rate, suggests an interaction between ethanol and DA neurotransmission via D2 receptors, perhaps via enhanced DA release in the VTA subsequent to ethanol inhibition of GABA neurons. Down-regulation of VTA GABA neuron D2 receptors by chronic ethanol might result from persistent DA release onto GABA neurons.

Die ungünstige Wirkung von genetischen Varianten der Mono-Amin-Oxidase auf die eigentlich protektive Wirkung von Varianten des alkoholabbauenden Ferments ALDH2 beschreibt dieser Beitrag. So konnten die Autoren eine signifikante Interaktion der Varianten beider Gene bei antisozialen Alkoholabhängigen aufzeigen und auf einen möglichen ungünstigen Effekt der MAO-A Variante auf den eigentlich vor Alkoholabhängigkeit schützenden Polymorphismus der ALDH2 feststellen.

## MAOA-uVNTR Polymorphism May Modify the Protective Effect of ALDH2 Gene Against Alcohol Dependence in Antisocial Personality Disorder

Sheng-Yu Lee, Cheng-Yi Hahn, Jia-Fu Lee, Shiou-Lan Chen, Shih-Heng Chen, Tzung Lieh Yeh, Po-Hsiu Kuo, I Hui Lee, Yen Kuang Yang, San-Yuan Huang, Huei-Chen Ko, and Ru-Band Lu

Alcohol Clin Exp Res, Vol 33, No 6, 2009: pp 985–990

**Background:** Antisocial alcoholism is related to dopamine and serotonin which are catalyzed by monoamine oxidase A (MAOA) and acetaldehyde dehydrogenase 2 (ALDH2). The objective of this study is to determine whether the interaction between the MAOA and the ALDH2 genes is associated with subjects with antisocial personality disorder (ASPD) having alcoholism.

**Methods:** A total of 294 Han Chinese men in Taiwan including 132 ASPD with alcoholism (Antisocial ALC) and 162 without alcoholism (Antisocial Non-ALC) were recruited in this study. Alcohol dependence and ASPD were diagnosed according to DSM-IV criteria. Genotypes of ALDH2 and MAOA-uVNTR were determined using PCR-RFLP.

**Results:** A significant difference of ALDH2 polymorphisms ( $p = 3.39E-05$ ), but not of MAOA, was found among the 2 study groups. However, only after the stratification of the MAOA-uVNTR (variable number of tandem repeat located upstream) 3-repeat, a significant association between Antisocial Non-ALC and ALDH2\*1/\*2 or \*2/\*2 genotypes was shown ( $p = 1.46E-05$ ; odds ratio = 3.913); whereas stratification of MAOA-uVNTR 4-repeat revealed no association. Multiple logistic regression analysis further revealed significant interaction of MAOA and ALDH2 gene in antisocial ALC (odds ratio = 2.927;  $p = 0.032$ ).

**Conclusion:** The possible interaction of MAOA and ALDH2 gene is associated with Antisocial ALC in Han Chinese males in Taiwan. However, the protective effects of the ALDH2\*2 allele against alcoholism might disappear in subjects with ASPD and carrying MAOA-uVNTR 4-repeat allele in the Han Chinese male population.

## 2. Pharmakologie, Zellstoffwechsel

In diesem Artikel geht es erneut um die über das Dopamin-vermittelte Wirkung des Alkohols auf andere Stoffwechselfunktionen, hier im besondern um DRD1 Rezeptoren und extrazelluläre Signalpfade von Kinasen (Enzyme, die einen Phosphatrest von einem Nucleosidtriphosphat (z. B. ATP) auf andere Substrate, dort insbesondere auf Hydroxygruppen übertragen helfen). Vermittelt über DRD1, aktiviert Alkohol diese Signalpfade, insbesondere im N. Accumbens und in der Amygdala

## Ethanol-Induced Extracellular Signal Regulated Kinase: Role of Dopamine D<sub>1</sub> Receptors

Federico Ibba\*, Stefania Vinci\*, Saturnino Spiga, Alessandra T. Peana, Anna R. Assaretti, Liliana Spina, Rosanna Longoni, and Elio Acquas

Alcohol Clin Exp Res, Vol 33, No 5, 2009: pp 858–867

**Background:** Addictive drugs activate extracellular signal regulated kinase (ERK) in brain regions critically involved in their affective and motivational properties. The aim of this study was to demonstrate the ethanol-induced activation of ERK in the nucleus accumbens (Acb) and in the extended amygdala [bed nucleus of the stria terminalis lateralis (BSTL) and central nucleus of the amygdala (CeA)] and to highlight the role of dopamine (DA) D<sub>1</sub> receptors in these effects. **Methods:** Ethanol (0.5, 1, and 2 g/kg) was administered by gavage and ERK phosphorylation was determined in the nucleus Acb (shell and core), BSTL, and CeA by immunohistochemistry. The DA D<sub>1</sub> receptor antagonist, SCH 39166 (SCH) (50 lg/kg), was administered 10 minutes before ethanol (1 g/kg). **Results:** Quantitative microscopic examination showed that ethanol, dose-dependently increased phospho-ERK immunoreactivity (optical and neuronal densities) in the shell and core of nucleus Acb, BSTL, and CeA. Pretreatment with SCH fully prevented the increases elicited by ethanol (1 g/kg) in all brain regions studied. **Conclusions:** The results of this study indicate that ethanol, similar to other addictive drugs, activates ERK in nucleus Acb and extended amygdala via a DA D<sub>1</sub> receptor-mediated mechanism. Overall, these results suggest that the D<sub>1</sub> receptors /ERK pathway may play a critical role in the motivational properties of ethanol.

Alkohol und Stillen von Neugeborenen verträgt sich nicht, auch nicht bei Ratten, wie in diesem Beitrag untersucht wurde. Ratten wurden dabei während der Schwangerschaft und Stillzeit mit Alkohol exponiert und mit Selen substituiert. Als Untersuchungszielgröße wurde die Aktivität von diversen antioxidativen Enzymen untersucht. Die Selensubstitution bewirkte dabei eine geringere Rate von Peroxidationsprodukten durch eine bessere Aktivität der antioxidierend wirkenden Enzyme und hilft wohl, die durch Alkohol verursachte, oxidative Belastung zu mindern.

### Alcohol, Gestation and Breastfeeding: Selenium as an Antioxidant Therapy

Ma Luisa Ojeda, Fatima Nogales, Beatriz Vázquez, Ma José Delgado, Ma Luisa Murillo and Olimpia Carreras

*Alcohol & Alcoholism* Vol. 44, No. 3, pp. 272–277, 2009

**Abstract — Aim:** The aim of this paper is to study the relationship between alcohol, selenium and oxidative stress in breastfeeding rat pups exposed to ethanol during gestation and lactation. We have also studied how a Se-supplemented diet among mothers could prevent different oxidative liver disorders in the pups. **Method:** Pups of 21 days were randomized into four groups: control group (C), alcohol group (A), alcohol selenium group (AS) and control selenium group (CS). Alcohol was supplied to their mothers for 13 weeks (induction, reproduction, gestation and lactation periods). The selenium-supplemented diet contained 0.5 ppm as selenite. We determined serum and liver selenium by graphite-furnace atomic absorption spectrometry. We measured antioxidant enzyme activities: glutathione peroxidase (GPx), glutathione reductase (GR), catalase (CAT) and superoxide dismutase (SOD); and lipid peroxidation (TBARS) and protein carbonyl (PC) by a spectrophotometric method in the liver. **Results:** In the liver of pups, exposure to ethanol provoked a decrease in selenium and GPx activity and an increase in GR and CAT activity, as well as in carbonyl groups in protein. A pups had higher Se levels and GPx activity in serum than C pups. Administering Se with alcohol balances the activities of scavenging enzymes and reduces peroxidation protein products. **Conclusion:** These results suggest that selenium could be effective in neutralizing the damage of ethanol consumption during gestation and lactation in pups since it repairs selenium levels in liver as well as the activity of scavenging enzymes and peroxidation protein products. In serum, Se also recovers GPx activity and increases the levels of Se that are available to other organs.

### 3. Verhaltensneurobiologie, Umweltfaktoren und Konsum

Entscheidungsfindung bei Alkoholabhängigen mit antisozialen oder psychopathischen Eigenschaften ist gegenüber Kontrollen beeinträchtigt, wie diese Studie anhand des „Iowa Gambling Tasks“ belegt. Besonders die Personengruppe mit komorbiden Persönlichkeitsstörungen wies ein besonders ungünstiges Abschneiden bei dieser Aufgabe auf.

## Influence of Antisocial and Psychopathic Traits on Decision-Making Biases in Alcoholics

Robert Miranda Jr, James MacKillop, Lori A. Meyerson, Alicia Justus, and William R. Lohvallo

Alcohol Clin Exp Res, Vol 33, No 5, 2009: pp 817–825

**Background:** Although decision-making processes have become a principal target of study among addiction researchers, few studies have specifically examined decision-making among individuals with alcohol dependence (AD) and findings to date are mixed. The present study examined the relationship between AD and decision-making, and tested whether different facets of antisocial and psychopathic traits explain this association.

**Methods:** Participants were men with AD ( $n = 22$ ), AD and comorbid antisocial personality disorder (AD + ASPD;  $n = 17$ ), or a history of recreational alcohol use, but no current or lifetime symptoms of a substance use disorder, conduct disorder, or ASPD ( $n = 21$ ). Decisionmaking was tested using the Iowa Gambling Task (IGT).

**Results:** Across groups, participants reported similar levels of awareness of the contingencies of the task, but the AD groups with and without ASPD had poorer IGT performance compared with controls ( $p < 0.05$ ). A block-by-block analysis revealed that while AD had slow but steady improvement across the task, AD + ASPD exhibited initial improvement followed by a significant decrease in advantageous decision-making during the last 20 trials ( $p < 0.05$ ). This was further confirmed via evidence that impulsive/antisocial personality traits but not psychopathic traits mediated poor IGT performance beyond ASPD diagnosis.

**Conclusions:** Alcohol-dependent males favored risky choices regardless of whether they met criteria for ASPD. However, decision-making deficits were more pronounced among those with ASPD, and personality traits characterized by impulsive and antisocial tendencies mediated the relationship between AD and decision-making.

## 4. Diagnose und Behandlung

Nach den bisherigen diagnostischen Kriterien (im DSM IV anders als im ICD10) werden ein Alkoholmissbrauch und eine Alkoholabhängigkeit unterschieden. Für eine Neubewertung dieser Kriterien im geplanten DSM V hat sich dieser Beitrag zum Ziel gesetzt, beide diagnostisch Entitäten hinsichtlich ihrer einheitlichen latenten dimensional Struktur zu untersuchen. Die Ergebnisse belegen allerdings, dass eher die Alkoholabhängigkeit (DSM IV), nicht aber der Alkoholmissbrauch eine einheitliche und kontinuierliche dimensionale Struktur aufweist. Mögliche Konsequenzen für die Kriterien von Abhängigkeitserkrankungen im DSM V werden erläutert.

## **A taxometric study of alcohol abuse and dependence in a general population sample: evidence of dimensional latent structure and implications for DSM-V**

**Tim Slade, Rachel Grove & Maree Teesson**

National Drug and Alcohol Research Centre, University of New SouthWales, Sydney, Australia

*Addiction*, 104, 742–751

### **ABSTRACT**

**Aims** To explore, with the aid of taxometric analysis, whether alcohol abuse and alcohol dependence are each conceptualized most effectively as single latent dimensions or distinct latent categories. **Design** Data were taken from a nationally representative cross-sectional epidemiological survey of psychiatric and substance use disorders. **Setting** General population of Australia. **Participants** A subsample of all respondents who had consumed at least 12 drinks in the year prior to the survey and who had consumed at least three drinks on at least one single day ( $n = 4920$  of a possible 10 641). **Measurements** DSM-IV criteria for alcohol abuse and dependence were assessed with the Composite International Diagnostic Interview, version 2.1. Two independent taxometric procedures, MAXimum EIGenvalue (MAXEIG) and mean aboveminus below a cut (MAMBAC), together with analysis of simulated dimensional and categorical data sets, were carried out. **Findings** Consistent evidence was found for a single latent dimension underlying the symptoms of alcohol dependence. Less consistent evidence of dimensionality was found for the symptoms of alcohol abuse. **Conclusions** These findings support the growing consensus regarding the need for continuous measures of alcohol use disorders to complement the traditional categorical representations in upcoming versions of the major psychiatric classification systems.

Ethyl-Glucuronid (EtG) gilt als spezifischer Alkoholmarker, der bisher vor allem im Urin nachgewiesen werden kann und auf aktuellen Alkoholkonsum hinweist. Allerdings kann dieser Marker auch mit hoher Sensitivität und Spezifität auch einen Alkoholkonsum von täglich 60g oder mehr in Kopfhaaren nachweisen, unabhängig von möglichen Confoundern wie Geschlecht oder Haarfärbemittel (s. a. Editorial).

## Ethyl glucuronide in hair. A sensitive and specific marker of chronic heavy drinking

Luca Morini<sup>1</sup>, Lucia Polit<sup>2</sup> & Aldo Poletti<sup>3</sup>

*Addiction*, 104, 915–920

### ABSTRACT

**Aims** This study aims to define a cut-off concentration for ethyl glucuronide in hair to determine if there was a history of heavy drinking. **Settings** Pavia, Italy. **Participants** We analysed hair samples from 98 volunteers among teetotallers, social drinkers and heavy drinkers, whose ethanol daily intake (EDI) was estimated by means of a written questionnaire. **Measurements** Ethyl glucuronide hair concentration (HEtG) was measured by liquid chromatography-tandem mass spectrometry (lower limit of quantification: 3 pg/mg) using a fully validated method. **Findings** The HEtG level providing the best compromise between sensitivity (0.92) and specificity (0.96) at detecting an EDI of 60 g or higher during the last 3 months was 27 pg/mg. None of the factors examined among those known to affect ethanol metabolism and/or the diagnostic power of other markers of ethanol use or hair analyses, including age, gender, body mass index, tobacco smoke, prevalent beverage, hair colour, cosmetic treatments and hygienic habits was found to influence marker performance significantly. However, the slight differences in HEtG performance observed for some factors (e.g. body mass index, smoke and hair treatments) require further studies on larger groups of individuals in order to assess their influence more precisely. **Conclusions** Our results confirm further that HEtG is a sensitive and specific marker of chronic heavy drinking.

Die nächste Untersuchung zu direkten Alkoholmarkern, dieses mal aus Deutschland, untersuchte den Zusammenhang von positiven Werten von Ethylglucuronid (EtG) und Ethylsulfat (EtS) prospektiv über 12 Wochen bei Alkoholabhängigen nach Entgiftung. Dabei war die Rate von positiven Werten im Urin für beide Marker höher, als durch klinische Untersuchungen oder Atemalkoholmessungen feststellbar gewesen wäre (s.a. Editorial)

## **Urinary ethyl glucuronide (EtG) and ethyl sulphate (EtS) assessment: valuable tools to improve verification of abstinence in alcohol-dependent patients during in-patient treatment and at follow-ups**

**Klaus Junghanns<sup>1</sup>, Iris Graf<sup>1</sup>, Juliane Pflüger<sup>1</sup>, Gunnar Wetterling<sup>1</sup>, Christian Ziems<sup>1</sup>, Dieter Ehrenthal<sup>1</sup>, Maike Zöllner<sup>1</sup>, Leif Dibbelt<sup>4</sup>, Jutta Backhaus<sup>1</sup>, Wolfgang Weinmann<sup>3</sup> & Friedrich M. Wurst<sup>2</sup>**

*Addiction*, 104, 921-926

### **ABSTRACT**

**Aims** The aims of this study were (i) to assess the effect of additional urinary ethyl glucuronide (EtG) and ethyl sulphate (EtS) assessment on diagnosed relapse rates in detoxified alcohol-dependent patients; and (ii) to compare dropout rates between EtG- and EtS-negative and -positive patients. **Design** Two studies on detoxified alcoholdependent

patients. If patients had no indication of relapse they were asked for a urinary sample at discharge from in-patient treatment 3, 6 and 12 weeks after discharge (study 1) and 1, 3 and 6 weeks after discharge (study 2), respectively. **Setting** Department of Psychiatry, University of Luebeck, Germany. **Participants** A total of 107 and 32 detoxified alcohol-dependent patients having participated in a 3-week in-patient motivation enhancement programme.

**Measurement** Personal interviews, breathalyzer tests, assessment of urinary EtG and EtS with liquid chromatography-tandem mass spectrometry (LC-MS/MS analysis). **Finding** Urinary EtG and EtS were always positive at the same time. In the first study 13.5% of the patients were already positive before being discharged from hospital. At the follow-ups 3, 6 and 12 weeks after discharge 12.2, 19.4 and 28.0%, respectively, of the patients coming to the follow-up and denying relapse were positive on urinary EtG and EtS. In the second study, of those patients showing up for follow-up after 1 week and denying relapse, EtG and EtS were positive in four cases (17.4%). Only one EtG and EtS-positive relapser (3.1%) came to the next follow-ups. In both studies the rates of detected relapses were significantly higher for early follow-ups if urinary EtG and EtS results were considered additionally. Dropout rates

until the next follow-up were significantly higher among positive than EtG- and EtS-negative patients. **Conclusion** Urinary EtG and EtS improve verification of abstinence in studies of alcohol-dependent patients.

Die letzte Studie dieser Serie stammt aus Norwegen, wo Ethylglucuronid (im Kopfhaar) mit anderen Markern (CDT, ALT, AST, GGT) für stattgehabten Alkoholkonsum verglichen wird. Hinsichtlich des Alkoholkonsums in den letzten 3 Monaten wiesen EtG und GGT die höchste Sensitivität auf, Angaben zur Spezifität von EtG und den anderen Markern wurden hingegen in der Studie nicht gemacht (s. a. Editorial).

## Ethyl Glucuronide in Hair Compared With Traditional Alcohol Biomarkers—A Pilot Study of Heavy Drinkers Referred to an Alcohol Detoxification Unit

Gudrun Høiseth, Luca Morini, Aldo Poletini, Asbjørg Christophersen, and Jørg Mørland

Alcohol Clin Exp Res, Vol 33, No 5, 2009: pp 812–816

**Background:** Traditional biomarkers for heavy alcohol use include serum carbohydrate-deficient transferrin (CDT), the enzymes aspartate aminotransferase (AST), and alanine aminotransferase (ALT) as well as gamma-glutamyl transferase (GGT). Measurement of the nonoxidative ethanol metabolite, ethyl glucuronide (EtG) in hair, has been proposed as a new marker with superior qualities. The aim of this study was to investigate the sensitivity of EtG in hair to detect heavy alcohol use compared with CDT, AST, ALT, and GGT. We also wanted to study the quantitative relation between alcohol intake and the different biomarkers.

**Methods:** Sixteen patients with a history of heavy alcohol use over the previous 3 months were recruited directly after admission to a withdrawal clinic. They were thoroughly interviewed about their drinking pattern as well as relevant diseases and use of medicines or drugs. Serum was sampled and analyzed for %CDT, AST, ALT, and GGT. Hair samples were collected and analyzed for EtG.

**Results:** The mean estimated daily intake (EDI) over the previous 3 months was  $206 \pm 136$  g pure alcohol. All patients fulfilled the criteria for heavy alcohol use. The sensitivity to detect heavy alcohol use was 64% for %CDT, 67% for AST, 67% for ALT, 93% for GGT, and 94% for EtG. There was no correlation between the quantitative values of EDI and %CDT, AST, ALT, and GGT. There was a positive, statistically significant correlation between EDI and the level of EtG in hair.

**Conclusions:** In this study, EtG in hair and GGT showed the best sensitivity to detect heavy alcohol use and there was a positive correlation between EDI and the concentrations of EtG in hair. Before giving recommendations for clinical practice, further studies should be carried out on larger materials and populations with a wider range of alcohol intake.

Das transtheoretische Model erklärt den Zusammenhang von Motivationalität und Therapieerfolg bei Abhängigkeitserkrankungen. Ziel dieser Untersuchung war es, anhand der Ergebnisse des United Kingdom Alcohol Treatment Trials (UKATT) das Stadium der Veränderungsbereitschaft mit dem Trinkverhalten prospektiv in Zusammenhang zu stellen. Tatsächlich haben Personen mit Veränderungen im Motivationsstadium größere Veränderungen in ihrem Trinkverhalten. Allerdings wiesen auch solche Personen, die keine Veränderungen ihrer Motivation zeigten, eine zumindest leichte Veränderung ihres Konsumverhaltens auf.

## **Progressive stage transition does mean getting better: a further test of the Transtheoretical Model in recovery from alcohol problems**

**Nick Heather, Johannes Hönekopp & David Smailes on behalf of the UKATT Research Team**

*Addiction*, 104, 949–958

### **ABSTRACT**

**Aims** To test two central assumptions of the Transtheoretical Model (TTM) regarding recovery from alcohol problems:

(i) individuals making a forward transition from pre-action to action stages will show greater drinking improvements than those remaining in pre-action stages; and (ii) individuals remaining in pre-action stages will not demonstrate improvements in drinking outcomes. **Design and setting** Large, multi-centre, randomized controlled trial of treatment for alcohol problems [United Kingdom Alcohol Treatment Trial (UKATT)]. **Measurements** Stage of change, drinks per drinking day and percentage days abstinent at baseline, 3- and 12-month follow-ups.

**Findings** In support of TTM assumption 1, improvements in drinking outcomes were consistently greater among clients who showed a forward stage transition (Cohen's  $d = 0.68$ ) than among those who did not ( $d = 0.10$ ). Two tests of assumption 2 showed a significant improvement in drinking outcomes in non-transition groups, inconsistent with the TTM; one test showed a significant deterioration and the other showed equivalent drinking outcomes across time. An explanation is offered as to why, under the relevant assumption of the TTM, clients in non-transition groups showed small changes in drinking outcomes. **Conclusions** In contrast to a previous study by Callaghan and colleagues, our

findings largely support the TTM account of recovery from alcohol problems in treatment. The discrepancy can be explained by the use in our study of a more reliable and valid method for assigning stage of change.

Seit längerem ist in der Diskussion, ob Mengenangaben in die diagnostischen Kriterien für alkohol-konsum-assoziierte Störungen wie etwa die Alkoholabhängigkeit aufgenommen werden sollen. Dies ist die Grundlage für diese Auswertung der NESARC Studie (National epidemiologic Sample on Alcohol and related Conditions), die (auch) wöchentliches Risikotrinken (WAD) erfasste und dahingehend auswertete, ob die Aufnahme eines solchen Kriteriums die Diagnostik von assoziierten Störungsbildern verbessert. Wenn Missbrauch und Abhängigkeit (DSM IV) in ihren Eigenschaften kombiniert werden, erhöht die Aufnahme einer Konsumvariable die diagnostische Schwelle ( $\geq 5$  Kriterien) und erhöht insgesamt die Rate an positiv diagnostizierten Erkrankungen (3.8% auf 5.0%). Die Autoren weisen abschließend darauf hin, dass die Aufnahme eines solchen Kriteriums möglicherweise die Rate an falsch positiven Diagnosen senken hilft.

## Influence of a Drinking Quantity and Frequency Measure on the Prevalence and Demographic Correlates of DSM-IV Alcohol Dependence

Katherine M. Keyes, Timothy Geier, Bridget F. Grant, and Deborah S. Hasin

Alcohol Clin Exp Res, Vol 33, No 5, 2009: pp 761–771

**Background:** Recent research suggests that adding a quantity/frequency alcohol consumption measure to diagnoses of alcohol use disorders may improve construct validity of the diagnoses for Diagnostic and Statistical Manual of Mental and Behavior Disorders (DSM-V). This study explores the epidemiological impact of including weekly at-risk drinking (WAD) in the DSM-IV diagnostic definition of alcohol dependence via 3 hypothetical reformulations of the current criteria.

**Methods:** The sample was the National Epidemiologic Survey on Alcohol and Related Conditions, a nationally representative sample with 43,093 adults aged  $>18$  in the U.S interviewed with the Alcohol Use Disorder and Associated Disabilities Interview Schedule IV. The current (DSM-IV) definition of alcohol dependence was compared with 4 hypothetical alcohol dependence reformulations that included WAD: (1) WAD added as an eighth criteria; (2) WAD required for a diagnosis; (3) adding abuse and dependence criteria together, and including WAD with a 3 of 12 symptom threshold; (4) adding abuse and dependence criteria together, and including WAD with a 5 of 12 symptom threshold.

**Results:** The inclusion of at-risk drinking as an eighth criterion of alcohol dependence has a minimal impact on the sociodemographic correlates of alcohol dependence but substantially increases the prevalence of dependence (from 3.8% to 5.0%). At-risk drinking as a required criterion or as part of a diagnosis that combines abuse with dependence criteria with a higher threshold (5+ criteria) decreases prevalence and has a larger impact on sociodemographic correlates.

Blacks, Hispanics, and women are less likely to be included in diagnostic reformulations that include WAD, whereas individuals with low-income and education are more likely to remain diagnosed.

**Conclusions:** Including WAD as either a requirement of diagnosis or as an additional criterion would have a large impact on the prevalence of alcohol dependence in the general population. The inclusion of a quantity/frequency requirement may eliminate false positives from studies of alcohol disorder etiology and improve phenotype definition for genetic association studies by reducing heterogeneity in the diagnosis, but may also reduce eligibility for treatment services among women and racial/ethnic minorities compared.

Alkohol-assoziierte Erkrankungen bedeuten für Patienten mit akuten Traumata häufig ungünstigere Therapieergebnisse und Prognosen. Um die diagnostische Sicherheit für relevante Diagnosen zu erhöhen, setzt die Arbeitsgruppe der Charité bei dieser Patientengruppe seit Jahren auf eine Diagnostik mittels Fragebogen (Alcohol Use Disorder Identification Test, AUDIT) und Biomarker. Dabei war die diagnostische Sensitivität und Spezifität des AUDIT besser als die der Biomarker.

## Screening Trauma Patients With the Alcohol Use Disorders Identification Test and Biomarkers of Alcohol Use

Tim Neumann, Larry M. Gentilello, Bruno Neuner, Edith Weiß-Gerlach, Hajo Schürmann, Torsten Schröder, Christian Müller, Norbert P. Haas, and Claudia D. Spies

Alcohol Clin Exp Res, Vol 33, No 6, 2009: pp 970–976

**Background:** Alcohol screening and brief interventions have been shown to reduce alcohol-related morbidity in injured patients. Use of self-report questionnaires such as the Alcohol Use Disorder Identification Test (AUDIT) is recommended as the optimum screening method. We hypothesized that the accuracy of screening is enhanced by combined use of the AUDIT and biomarkers of alcohol use in injured patients.

**Methods:** The study was conducted in the emergency department of a large, urban, university hospital. Patients were evaluated with the AUDIT, and blood sampled to determine carbohydrate-deficient transferrin, gamma-glutamyl-transferase, and mean corpuscular volume. Alcohol problems were defined as presence of ICD-10 criteria for dependence or harmful use, or high-risk drinking according to World Health Organization criteria (weekly intake >420 g in males, >280 g in females). Screening accuracy was determined using Receiver Operating Characteristic curves.

**Results:** There were 787 males and 446 females in the study. Median age was 33 years. The accuracy of the AUDIT was good to excellent, whereas all biomarkers performed only fairly to poorly in males, and even worse in females. At a specificity >0.80, sensitivity for all biomarkers was <0.43, whereas sensitivity for the AUDIT was 0.76 for males and 0.81 for females. The addition of biomarkers added little additional discriminatory information compared to use of the AUDIT alone.

**Conclusions:** Screening properties of the AUDIT are superior to %CDT, MCV, and GGT for detection of alcohol problems in injured patients and are not clinically significantly enhanced by the use of biomarkers.

## 5. Epidemiologie und Prävention

Die „German Epidemiological Survey of Substance Abuse“ (ESA) Studie wird in diesem Artikel auf den Zusammenhang zwischen Konsummustern (durchschnittlicher Konsum, Rauschtrinken) mit alkohol-assoziierten Störungen und sozialen Problemen bei mehr als 12.600 Konsumenten untersucht. Der stärkste Zusammenhang von Alkoholkonsummustern mit assoziierten Störungsbildern ergab sich bei Personen mit vier oder mehr Rauschtrinkegelegenheiten im letzten Monat und war ein besserer Prädiktor für relevante Schädigungen als der durchschnittliche Alkoholkonsum.

Association of Average Daily Alcohol Consumption, Binge Drinking and Alcohol-Related Social Problems: Results from the German Epidemiological Surveys of Substance Abuse  
Ludwig Kraus<sup>1,\*</sup>, Sebastian E. Baumeister<sup>2</sup>, Alexander Pabst<sup>1</sup> and Boris Orth<sup>3</sup>

*Alcohol & Alcoholism* Vol. 44, No. 3, pp. 314–320, 2009

**Abstract — Aims:** The present study investigates the combined effect of **average volume and binge drinking** in predicting alcohol-related social problems and estimates the proportion of **alcohol-related harms related to specific drinking patterns** that could be prevented if transferred to a low-risk drinking group. **Methods:** Data came from the 1997 and 2000 German Epidemiological Survey of Substance Abuse (ESA) (age: 18–59 years; response rate: 65% and 51%, respectively). The pooled sample consisted of 12,668 current drinkers. By using nine categories of average daily intake and three groups of binge drinking, individuals were grouped into 22 mutual exclusive groups. Social problems were defined as the occurrence of ‘repeated family quarrels’, ‘concern of family members or friends’, ‘loss of partner or friend’ or ‘physical fight or injury’ in relation to alcohol. **Results:** The effect of average daily intake is modified by binge drinking frequency such that the association was strongest in those with four or more binge drinking occasions during the last 30 days. Within each binge drinking group, adjusted relative risks (aRR) increased with alcohol intake up to a certain threshold and decreased thereafter. Overall, compared to the reference group ( $\leq 7$  g ethanol/day—no binge), the population-attributable fraction (PAF) related to the other drinking groups was 71.4% (95% CI: 64.4–77.1%). **Conclusions:** The frequency of binge drinking occasions seems to be a better predictor of alcohol-related social problems than volume. Alcohol-related social harms especially among drinkers with moderate volume per day may be reduced by targeting prevention strategies towards episodic heavy drinkers.

Während ein deutlicher Pro-Kopf Konsum von Alkohol in Europa, besonders in Osteuropa, hinlänglich nachgewiesen wurde, zeigt diese epidemiologisch-orientierte Studie, dass Alkoholkonsum und starkes Trinken auch in China keine Seltenheit sind. Die Raten einer Alkoholabhängigkeit sind mit 1.7% (12 Monatsprävalenz) und 4.3% (Lebenszeitprävalenz) allerdings etwas niedriger als in der westlichen Welt. Das Risikoprofil von chinesischen Alkoholkonsumenten ist allerdings möglicherweise nur schwer mit dem anderer Kulturen vergleichbar.

## Alcohol-Related Disorders in Beijing, China: Prevalence, Socio-Demographic Correlates, and Unmet Need for Treatment

Yu-Tao Xiang, Xin Ma, Jin-Yan Lu, Zhuo-Ji Cai, Shu-Ran Li, Ying-Qiang Xiang, Hong-Li Guo, Ye-Zhi Hou, Zhen-Bo Li, Zhan-Jiang Li, Yu-Fen Tao, Wei-Min Dang, Xiao-Mei Wu, Jing Deng, Kelly Y. C. Lai, and Gabor S. Ungvari

*Alcohol Clin Exp Res*, Vol 33, No 6, 2009: pp 1111–1118

**Background:** The study aimed to determine the prevalence of alcohol use, episodic heavy drinking, and alcohol dependence and their socio-demographic correlates in Beijing, China. **Methods:** A total of 5,926 subjects were randomly selected in Beijing and interviewed using the Composite International Diagnostic Interview (CIDI 1.0). Data on basic socio-demographic and current major medical conditions were also collected.

**Results:** The 12-month prevalence of alcohol use and episodic heavy drinking were 32.5 and 13.8%, respectively. The 12-month and lifetime prevalence of alcohol dependence were 1.7 and 4.3%, respectively. Age above 24 years, male sex, being married and employed, low education level (junior high school, primary school or illiterate), rural residence, and having comorbid psychiatric disorders were all significantly associated with a higher likelihood of alcohol-related disorders. Only 2.4% of the subjects with alcohol dependence were receiving treatment, and a mere 1.4% had sought treatment from mental health professionals.

**Conclusions:** Nationwide surveys are urgently needed to further explore the prevalence of alcohol-related disorders in China.

Als ob der Alkoholkonsum alleine nicht schon gefährlich genug ist, weist diese populationsbasierte Studie außerdem nach, dass Personen in der Nähe von Alkoholverkaufsstellen (USA) signifikant häufiger beschossen wurden, besonders bei ebenfalls vorhandener Alkoholintoxikation.

## Alcohol Consumption, Alcohol Outlets, and the Risk of Being Assaulted With a Gun

Charles C. Branas, Michael R. Elliott, Therese S. Richmond, Dennis P. Culhane and Douglas J. Wiebe

Alcohol Clin Exp Res, Vol 33, No 5, 2009: pp 906–915

**Background:** We conducted a population-based case–control study to better delineate the relationship between individual alcohol consumption, alcohol outlets in the surrounding environment, and being assaulted with a gun.

**Methods:** An incidence density sampled case–control study was conducted in the entire city of Philadelphia from 2003 to 2006. We enrolled 677 cases that had been shot in an assault and 684 population-based controls. The relationships between 2 independent variables of interest, alcohol consumption and alcohol outlet availability, and the outcome of being assaulted with a gun were analyzed. Conditional logistic regression was used to adjust for numerous confounding variables. **Results:** After adjustment, heavy drinkers were 2.67 times as likely to be shot in an assault when compared with nondrinkers ( $p < 0.10$ ) while light drinkers were not at significantly greater risk of being shot in an assault when compared with nondrinkers. Regression-adjusted analyses also demonstrated that being in an area of high off-premise alcohol outlet availability significantly increased the risk of being shot in an assault by 2.00 times ( $p < 0.05$ ). Being in an area of high on-premise alcohol outlet availability did not significantly change this risk. Heavy drinkers in areas of high off-premise alcohol outlet availability were 9.34 times ( $p < 0.05$ ) as likely to be shot in an assault.

**Conclusions:** This study finds that the gun assault risk to individuals who are near off-premise alcohol outlets is about the same as or statistically greater than the risk they incur from heavy drinking. The combination of heavy drinking and being near off-premise outlets resulted in greater risk than either factor alone. By comparison, light drinking and being near on-premise alcohol outlets were not associated with increased risks for gun assault. Cities should consider addressing alcohol-related factors, especially off-premise outlets, as highly modifiable and politically feasible approaches to reducing gun violence.

## 6. Somatische Alkoholeffekte

Bekanntermaßen sind die Enzyme aus den Gruppen der Alkoholdehydrogenasen (ADH) und Azetaldehyddehydrogenasen (ALDH) die wichtigsten Fermente für den Abbau von Alkohol. Die Rolle dieser Enzyme bei der Entstehung von alkoholbedingten Pankreasschäden, deren Ätiologie bisher nicht ausreichend geklärt ist, wird in diesem Beitrag über Expressionsuntersuchungen behandelt. Unterschiedliche Expressionsmuster verschiedener ADHs und ALDHs in verschiedenen Zelltypen der Bauchspeicheldrüse konnte bei Personen mit Pankreatitis oder Pankreaskarzinomen nachgewiesen werden. Insbesondere zeigte sich eine erhöhte Expression von ADH1C, dem von den Autoren demzufolge eine wichtige pathophysiologische Rolle bei der Entstehung von alkoholbedingten Pankreaserkrankungen zugeschrieben wird.

## Expression Pattern, Ethanol-Metabolizing Activities, and Cellular Localization of Alcohol and Aldehyde Dehydrogenases in Human Pancreas: Implications for Pathogenesis of Alcohol-Induced Pancreatic Injury

Chien-Ping Chiang, Chew-Wun Wu, Shiao-Pieng Lee, Chia-Chi Chung, Chi-Wei Wang, Shou-Lun Lee, Shin Nieh, and Shih-Jiun Yin

Alcohol Clin Exp Res, Vol 33, No 6, 2009: pp 1059–1068

**Background:** Alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) are major enzymes responsible for metabolism of ethanol. Genetic polymorphisms of ADH1B, ADH1C, and ALDH2 occur among racial populations. The metabolic effect and metabolites contribute to pathogenesis of pancreatic injury. The goal of this study was to determine the functional expressions and cellular localization of ADH and ALDH families in human pancreas.

**Methods:** Fifty five surgical specimens of normal pancreas as well as 15 samples each for chronic pancreatitis and pancreatic cancer from archival formalin-fixed paraffin-embedded tissue specimens were investigated. Class-specific antibodies were prepared by affinity chromatographies from rabbit antisera raised against recombinant human ADH1C1, ADH4, ADH5, ADH7, ALDH1A1, ALDH2, and ALDH3A1. The isozyme expression patterns of ADH/ALDH were identified by isoelectric focusing, and the activities were assayed spectrophotometrically. The protein contents of ADH/ALDH isozymes were determined by immunoblotting, and the cellular localizations were detected by immunohistochemistry and histochemistry.

**Results:** At 33 mM ethanol, pH 7.5, the activities were significantly different between allelic phenotypes of ADH1B. The activity of ALDH2-inactive phenotypes was slightly lower than ALDH2-active phenotypes at 200 IM acetaldehyde. The protein contents were in the following decreasing order: ALDH1A1, ALDH2, ADH1, and ADH5. ADH1B was detected in the acinar cells and ADH1C in the ductular, islet, and stellate cells. The expression of ADH1C appeared to be increased in the activated pancreatic stellate cells in chronic pancreatitis and pancreatic cancer.

**Conclusions:** Alcohol dehydrogenase and ALDH family members are differentially expressed in the various cell types of pancreas. ADH1C may play an important role in modulation of activation of pancreatic stellate cells.

Thiaminmangel bei chronischem Alkoholkonsum kann das Entstehen von hirnorganischen Psychosyndromen fördern, spielt aber möglicherweise auch bei der alkoholbedingten Kleinhirnatrophie eine signifikante Rolle. Diese Vorgänge, hier an Zellkulturen von granulären Neuronen untersucht, wird über eine Reihe komplexer Mechanismen vermittelt. Dabei war die höchste Rate des neuronalen Zelltodes bei der gemeinsamen Wirkung von Alkohol und Thiaminmangel nachweisbar.

## Ethanol Promotes Thiamine Deficiency-Induced Neuronal Death: Involvement of Double-Stranded RNA-activated Protein Kinase

Zun-Ji Ke, Xin Wang, Zhiqin Fan, and Jia Luo

Alcohol Clin Exp Res, Vol 33, No 6, 2009: pp 1097–1103

**Background:** Heavy alcohol consumption causes cerebellar degeneration, and the underlying mechanism is unclear. Chronic alcoholism is usually associated with thiamine deficiency (TD) which is known to induce selective neurodegeneration in the brain. However, the role of TD in alcohol-induced cerebellar degeneration remains to be elucidated. The double-stranded RNA-activated protein kinase (PKR) is a potent antiviral protein. Viral infection or binding to dsRNA causes PKR autophosphorylation and subsequent phosphorylation of the  $\alpha$ -subunit of eukaryotic translation factor-2a, leading to inhibition of translation or apoptosis. PKR can also be activated by cellular stresses.

**Methods:** In this study, we used an *in vitro* model, cultured cerebellar granule neurons (CGNs), to investigate the interaction between TD and ethanol and evaluate the contribution of their interaction to neuronal loss. TD was induced by treatment with amprolium in association with ethanol. Cell viability was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide assay. PKR expression/phosphorylation and subcellular distribution was analyzed with immunoblotting and immunocytochemistry.

**Results:** Thiamine deficiency caused death of CGNs but ethanol did not. However, TD plus ethanol induced a much greater cell loss than TD alone. TD-induced PKR phosphorylation and ethanol exposure significantly promoted TD-induced PKR phosphorylation as well as its nuclear translocation. A selective PKR inhibitor not only protected CGNs against TD toxicity, but also abolished ethanol potentiation of TD-induced loss of CGNs.

**Conclusions:** Ethanol promoted TD-induced PKR activation and neuronal death. PKR may be a convergent protein that mediates the interaction between TD and ethanol.

Keine Neuigkeit ist, dass chronischer und hochdosierter Alkoholkonsum Leberschäden hervorrufen kann. Eine Leberverfettung wird weiterhin begünstigt durch hohe Spiegel des Lipoproteins APO-A1 (Bestandteil des HDL), hohen BMI und arteriellen Bluthochdruck, die auch als direkte und indirekte Zeichen eines metabolischen Syndroms gelten können.

## Predictive Factors for Pure Steatosis in Alcoholic Patients

Sylvie Naveau, Juliette Thauray, Nade`ge Barri-Ova, Axel Balian, Barbara Dauvois, Micheline Njike'-Nakseu, Sophie Pre' vot, He' le`ne Agostini, and Gabriel Perlemuter

**Background:** Bearing in mind the mechanisms involved in nonalcoholic fatty liver disease, this study aims to verify whether metabolic syndrome or its various individual components are independent predictive factors for steatosis >10% in alcoholic patients.

**Methods:** This study included 281 consecutive alcoholic patients with abnormal liver tests and either normal liver histology or steatosis <10% (n = 119) or steatosis >10% (n = 162). Logistic regression analysis was used to study the relationship between metabolic syndrome components and various risk factors and the presence of steatosis >10%. We assessed apolipoprotein A1 (ApoA-1) levels, a major protein component of plasma high-density lipoprotein (HDL), rather than HDL-cholesterol levels.

**Results:** Plasma ApoA-1 levels ( $p < 0.01$ ), body mass index (BMI) ( $p < 0.01$ ), and waist circumference ( $p < 0.05$ ) were significantly higher in patients with steatosis >10% than in patients with normal liver histology or steatosis <10%. A higher percentage of patients with steatosis >10% had high blood pressure ( $p = 0.003$ ) than patients with normal liver histology or steatosis <10%. In the logistic regression, ApoA-1 [odds ratio (OR) = 1.57 (1.10–2.22)], BMI [OR = 1.10 (1.01–1.23)], and high blood pressure [OR = 1.84 (1.10–3.06)] were positively and independently correlated with the presence of steatosis >10%. In the multivariate regression high blood pressure was independently and positively correlated with steatosis score ( $r = 0.55$  □ 0.26;  $p < 0.05$ ). On the other hand, when the presence of high blood pressure was the dependent variable, the presence of steatosis >10% positively and independently correlated with it [OR = 1.82 (1.05–3.15)].

**Conclusion:** In alcoholic patients without fibrosis, ApoA-1, BMI, and high blood pressure on the next morning after the admission were predictive of steatosis >10%. High blood pressure was the only metabolic syndrome component associated with the presence of alcoholic steatosis >10% and was not correlated with other metabolic syndrome components. These findings suggest that steatosis mechanisms are different in alcoholic and nonalcoholic fatty liver.

**Key Words:** Alcoholic Steatosis, High Blood Pressure, Plasma Apo-A1, Body Mass Index, Metabolic Syndrome.

## 7. Editorials, Übersichten

In dieser systematischen Übersicht wird über den Einfluss von Werbung und Werbeeexposition auf den Alkoholkonsum bei Jugendlichen berichtet. Hierfür wurde von den Autoren eine umfangreiche Literatursuche durchgeführt. Die verfügbaren Publikationen umfassen 13 prospektive Studien mit mehr als 38.000 Jugendlichen, die Beobachtungszeiten von 8 bis 96 Monaten angaben. In 12 der Studien konnte eine „Dosis-Wirkungsbeziehung“ zwischen Intensität der Medienexposition mit dem Beginn und dem Ausmaß des Alkoholkonsums bei Jugendlichen festgestellt werden.

**Impact of Alcohol Advertising and Media Exposure on Adolescent Alcohol Use:  
A Systematic Review of Longitudinal Studies**

Peter Anderson<sup>1,\*</sup>, Avalon de Bruijn<sup>2</sup>, Kathryn Angus<sup>3</sup>, Ross Gordon<sup>3</sup> and Gerard Hastings<sup>3</sup>  
*Alcohol & Alcoholism* Vol. 44, No. 3, pp. 229–243, 2009

**Abstract — Aims:** To assess the impact of alcohol advertising and media exposure on future adolescent alcohol use.

**Methods:** We searched MEDLINE, the Cochrane Library, Sociological Abstracts, and PsycLIT, from 1990 to September 2008, supplemented with searches of Google scholar, hand searches of key journals and reference lists of identified papers and key publications for more recent publications. We selected longitudinal studies that assessed individuals' exposure to commercial communications and media and alcohol drinking behaviour at baseline, and assessed alcohol drinking behaviour at follow-up. Participants were adolescents aged 18 years or younger or below the legal drinking age of the country of origin of the study, whichever was the higher.

**Results:** Thirteen longitudinal studies that followed up a total of over 38,000 young people met inclusion criteria. The studies measured exposure to advertising and promotion in a variety of ways, including estimates of the volume of media and advertising exposure, ownership of branded merchandise, recall and receptivity, and one study on expenditure on advertisements. Follow-up ranged from 8 to 96 months. One study reported outcomes at multiple time-points, 3, 5, and 8 years. Seven studies provided data on initiation of alcohol use amongst non-drinkers, three studies on maintenance and frequency of drinking amongst baseline drinkers, and seven studies on alcohol use of the total sample of non-drinkers and drinkers at baseline. Twelve of the thirteen studies concluded an impact of exposure on subsequent alcohol use, including initiation of drinking and heavier drinking amongst existing drinkers, with a dose response relationship in all studies that reported such exposure and analysis. There was variation in the strength of association, and the degree to which potential confounders were controlled for. The thirteenth study, which tested the impact of outdoor advertising placed near schools failed to detect an impact on alcohol use, but found an impact on intentions to use.

**Conclusions:** Longitudinal studies consistently suggest that exposure to media and commercial communications on alcohol is associated with the likelihood that adolescents will start to drink alcohol, and with increased drinking amongst baseline drinkers. Based on the strength of this association, the consistency of findings across numerous observational studies, temporality of exposure and drinking behaviours observed, dose-response

relationships, as well as the theoretical plausibility regarding the impact of media exposure and commercial communications, we conclude that alcohol advertising and promotion increases the likelihood that adolescents will start to use alcohol, and to drink more if they are already using alcohol

## Addiction

Volume 104 Issue 5, Pages 685 - 686

EDITORIAL

**What should we be aiming for in the treatment of addiction?**

PETER G. MILLER<sup>1</sup> & WILLIAM R. MILLER<sup>2</sup>

In diesem Editorial wird die Frage behandelt, ob die Konzepte der Behandlung von Abhängigkeitserkrankungen alleine auf den Konsum von Alkohol oder Drogen fokussieren sollte, wie dies nach Ansicht der Autoren bisher meist der Fall ist, oder aber einen umfassenderen Ansatz berücksichtigen muss, der alle damit in Verbindung stehenden Erkrankungen und Probleme beinhaltet (z.B. soziale, ökonomische und gleichzeitig bestehende somatische und komorbide psychische Erkrankungen). Bei dem bisherigen Ansatz, so die Autoren, endet die Therapie Abhängiger gerade da, wo sie eigentlich die meiste Unterstützung benötigen.

Kein Abstract.

# **Unrecorded alcohol: a threat to public health?**

DIRK W. LACHENMEIER & JÜRGEN REHM

*Addiction*, **104**, 875–877

Dieses Editorial wirft die wichtige Frage auf, ob Alkoholkonsum pro Kopf der Bevölkerung häufig nach Verkaufszahlen ermittelt wird, den realen Konsum widerspiegelt. Allerdings bleibt bei dieser Erfassung der von privater Seite hergestellte Alkohol unberücksichtigt. Diese so hergestellten Getränke sollen in einigen Ländern bis zu 30% des konsumierten Alkohols umfassen. Es wird diesen Getränken wegen der darin enthaltenen Begleitstoffe (z.B. Methanol) eine erhebliche Gesundheitsgefährdung zugeschrieben. Allerdings ist dies durch die bisherige Literatur nur unzureichend belegt. Gefahren durch diese Alkoholika treten nach Ansicht der Autoren eher im Zusammenhang mit problematischem Trinkverhalten (z.B. „binge drinking“) von illegal hergestellten Alkoholika auf.

Kein Abstract.

## 8. Links