2003
-2018

ERAB
THE EUROPEAN FOUNDATION FOR ALCOHOL RESEARCH

ERAB RESEARCH

ERAB RESEARCH 2003-2018

CONTENTS

INTRODUCTION

The European Research Advisory Board (ERAB) was set up in 2003 along the lines of a similar organisation in North America – ABMRF/The Foundation for Alcohol Research.

In 2009, the name was changed to "ERAB: The European Foundation for Alcohol Research".

ERAB: The European Foundation for Alcohol Research (ERAB), is an initiative of the European Brewing Sector. Between 2003 and 2018, they have generously funded "arms-length" research into all aspects of alcohol and health. In 2018, they decided to phase out the Brewers' funding of ERAB over two years. This document provides summaries of all the research which ERAB has funded to date, together with all the references in peer reviewed journals, citing ERAB as a source of funding. It will be updated when the final grants (which start in 2019) have ended.

ERAB was established by The Brewers of Europe as a Charity (Fondation d'Utilité Publique) in Brussels in 2003, to fund academic research projects.

The Brewers of Europe is the European confederation of Brewing Trade Associations.

Initially, ERAB was funded through The Brewers of Europe by all of the brewing trade associations, who are their members, and the leading five European Brewers – AB InBev, Carlsberg, Heineken, SABMiller and Scottish and Newcastle. Takeovers and mergers have reduced these five companies to three (AB InBev, Carlsberg and Heineken).

BACKGROUND TO THE ORGANISATION

The purpose of the Foundation, as set out in the By-Laws, is

> *"to promote scientific knowledge of, and education in, the medical, bio-medical, and socio-behavioural effects of alcoholic beverages in general, and beer in particular".*

The Foundation also promotes research on the prevention and the treatment of alcohol-related problems, 'misuse' and the harm caused thereby.

ERAB has invited applications for research funding from researchers from established European research institutions, or universities, at the beginning of each year. The applications are sent for review to experts in the relevant subject from all over the world. The recommendations as to which grants are funded are based on these peer reviews which give great emphasis to the scientific merit of the application. Grants are funded up to the maximum of €100,000 over a two year period.

Over the past 15 years ERAB has funded 99 European research projects from 14 countries.

Funds of just over half a million Euros have been made available each year and, in keeping with the regulations for a Belgian Foundation of Public Utility, more than 90% of funds have been used to fund research.

ERAB was founded with a mandate for an initial three years. This was renewed in 2005. The brewing sector then committed to funding ERAB on an ongoing basis (rolling two years) until 2018.

ERAB encourages applications in any aspect of biomedical and psychosocial research into the health effects of beer and other alcoholic drinks. Grantees are encouraged to publish their findings in peer-reviewed journals, and are given the opportunity to present their research at international conferences. Over 250 papers have been published citing ERAB as a source of funding. More than 25% have an Impact factor above 4, demonstrating the quality of the science funded.

Every 4 years, ERAB has organised a conference, namely the International Meeting on Alcohol and Global Health (IMAG) which is hosted by The Brewers of Europe. The first IMAG organised by ERAB was in 2006 in Copenhagen, Denmark, with the

assistance of Carlsberg and the Danish Brewers Association (Bryggeriforeningen); the second was held in 2010 in Frascati, Italy, with the help of SABMiller and the Italian Brewers Association (Assobirra); the third was held in 2014 in Amsterdam, The Netherlands, with the help of the Dutch Brewers Association (Nederlandse Brouwers). In 2018, it is being held in Leuven, Belgium, with help from ABInBev.

STRUCTURE OF THE BOARDS

ERAB was founded with two Boards.

1 The Board of Directors, which includes: businessmen, personalities of civil society and the academic world, and representatives of brewers and trade associations. However, the by-laws insist on a majority of public members (trustees). The Board has the widest powers to perform all acts of management and disposal, directly or indirectly.

2 The Advisory Board which has advised the Board of Directors on which grant applications should be funded. The Board of Directors acts as guarantor for the independence of the research promoted by the Advisory Board.

The following have served as members of the Board of Directors between 2004 and 2018:

- Mr. Paul **Bergqvist** - Former President of The Brewers of Europe, Denmark. (Industry Member 2004 - 2006).
- Professor Daniel **Bessa** - Accountant, Portugal. (Public Member 2007 - to date).
- Mrs. Sarah **Boselli-Lee** - Heineken, The Netherlands. (Industry Member 2016 - to date).
- Frau Edeltraud **Böhm-Amtmann** - Formerly of the Representation of Bavaria to the EU. (Public Member 2004 - 2007).
- Mr. Demetrio **Carceller** - Former President of The Brewers of Europe, Spain. (Industry Member 2013 - 2016).
- Baron Daniel **Cardon de Lichtbuer** - Formerly with Child Focus Europe, Belgium. (Public Member 2004 - 2007).
- Mr. Alberto **da Ponte** - Former President of The Brewers of Europe, Italy. (Industry Member 2008 - 2012).
- Countess Antoinette **d'Aspremont Lynden** - Political Science Institute in Lille, France. (Public Member 2016 to date).
- Count Rodolphe **de Looz Corswarem** - President of European Historic Houses Association. (Honorary Member 2010 - 2011, Public Member 2011 - to date).
- Emeritus Professor Philippe **De Witte** - Université Catholique de Louvain-la-Neuve, Belgium. (Public Member 2007 - 2016).
- Mr. Markus **Ferber** - MEP, Germany. Public Member (2010 - 2016).
- Mr. Raymond **Georis** - Former Chairman of the Madariaga European Foundation, Belgium. (**Founder Member**) (Public Member and Chairman 2004

- 2010, Honorary Member 2009 - 2010, Public Member and Chairman 2015 - 2016).
- Mr. Rutger **Goethart** - Heineken, The Netherlands. (Industry Member 2008 - 2012).
- Mme. Véronique **Guérin** - Managing Director of the Bureau Européen de l'Agriculture Française, France. (Public Member 2016 - to date).
- Mr. Simon **Jackson** - Formerly CEO of the Institute of Brewing and Distilling, UK. (Industry Member 2009 - to date).
- Emeritus Professor Oliver F. W. **James** - Former pro-vice Chancellor, University of Newcastle, UK. (**Founder Member**) (Public Member 2004 - 2006, Honorary Member 2006 - 2009, Public Member and Chairman 2009 - 2015).
- Mr. Morten Georg **Jensen** - Carlsberg Group, Denmark. (Industry Member 2013 - 2016, Public Member 2017 - to date).
- Emeritus Professor Frans J. **Kok** - Formerly Professor of Human Nutrition, Wageningen University, The Netherlands. (Public Member and Chairman 2016 - to date).
- Dr. Isak **Lindstedt** - General Practitioner, Sweden. (Public Member 2016 - to date).
- Dr. David **Long** MBE - Consultant, Former Director, Brewing, British Beer & Pub Association, UK. (Industry Member 2004 - 2009, Honorary Member 2009 - to date).
- Mr. Jean **Martin** - Former President of the European Confederation of the Food & Drink Industry. (Public Member 2004 - to date).
- Professor Mack **Mitchell** - ABMRF, USA. (Public Member 2004 - 2015).
- Mr. Knud Hedeager **Nielsen** - Carlsberg Group, Denmark. (Industry Member 2006 - 2012).
- Mr. Morten **Nielsen** - Carlsberg Group, Denmark. (Industry Member 2012 - 2013).
- Miss Johanna **Nyman** - President of the European Youth Forum, Finland. (Public Member 2016 - to date).
- Mr. Jacobo **Olalla Marañón** - Cerveceros de España, Spain. (Industry Member 2004 - to date).
- Mr. Pavlos **Photiades** - President of The Brewers of Europe, Cyprus. (Industry Member 2016 - to date).
- Mr. Piero **Perron** - Former President of The Brewers of Europe. (**Founder Member**). (Public Member 2004 - 2006, Honorary Member 2006 - to date).
- Mrs. Heidrun **Piwernetz** - Formerly of the Representation of Bavaria to the EU. (Public Member 2007 - 2010).
- Mr. Artur **Santos Silva** - Formerly with the Portuguese Bank of Investment, Portugal. (Public Member 2004 - 2007).

- Mr. Kieran **Simpson** - Formerly with Heineken, The Netherlands. (Industry Member 2004 - 2008 and 2012 - 2016).
- Dr. Erik **Skovenborg** - Medical Doctor, Denmark. (Public Member 2004 - 2016).
- Emeritus Professor Richard **Smallwood** - Former Commonwealth Chief Medical Officer (1999-2003), Australia. (Honorary Member 2004 - to date).
- Dr. Renate **Sommer** - MEP, Germany. (Public Member 2016 - to date).
- Mr. Ulf **Spendrup** - Former President of The Brewers of Europe, Sweden. (Industry Member 2006 - 2008).
- Mr. Eric **Vaes** - Formerly with InBev, Belgium. (Industry Member 2004 - 2006).
- Mrs. Janet **Witheridge** - ERAB Secretary-General, UK. (Public Member 2009 - to date).
- Ms. Vanessa **Witkowski**. Belgium. (Public Member 2008 - 2011).

The Advisory Board is composed of specialists in the behavioural and bio-medical sciences, with a proven international, independent, scientific stature, and from a variety of countries. Their role is to examine the applications, suggest peer reviewers, and recommend to the Board of Directors which applications should be funded.

The following have served as members of the ERAB Advisory Board:
- Professor Giovanni **Addolorato** - Università Cattolica del Sacro Cuore, Rome, Italy. (2006 - to date).
- Associate Professor Bridgette M. **Bewick** - University of Leeds, UK. (2015 - to date).
- Dr. Marie **Choquet** - INSERM, France. (2003 - 2005).
- Emeritus Professor Philippe **De Witte** - University of Louvain la Neuve, Belgium. (2003 -2016) Chairman (2006 - 2016).
- Professor Christopher P. **Day** - University of Newcastle-upon-Tyne, UK. (2003 - to date), **Chairman** (2016 - to date).
- Professor Juan **Díez Nicolás**, Complutense University of Madrid, Spain. (2003 - 2005).
- Associate Professor Ramon **Estruch** - University of Barcelona, Spain. (2011 - to date).
- Professor Antonio **Gasbarrini** - Catholic University of Rome, Italy. (2003 - 2006).
- Professor Oliver F. W. **James** - University of Newcastle upon Tyne, UK. (Chairman
- 2003 - 2006).
- Professor Wolfgang **Koenig** - University of Munich, Germany. (2003 - to date).
- Associate Professor Marianne **Nissen Lund** - University of Copenhagen, Denmark. (2015 - to date).

- Dr. Kari **Poikolainen** - Finnish Foundation for Alcohol Studies, Helsinki, Finland. (2006 - 2010).
- Professor Pekka **Sulkunen** - University of Helsinki, Finland. (2010 - 2015).
- Professor Piet A **van den Brandt** - Maastricht University, The Netherlands. (2003 - 2006).
- Dr. Dr. Sascha **Venturelli** - Eberhard Karls University Tuebingen, Germany. (2015 - to date).
- Professor Matty P. **Weijenberg** - Maastricht University, The Netherlands. (2007 - to date).

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Role of different types of alcohol on the risk of cancer: analysis of data from case-control studies conducted in Italy, Greece and Switzerland over the last two decades (2003) (EA 03 05)

Gallus S, Laboratory of Epidemiology, Instituto di Ricerche Farmacologiche Mario Negri, Milan, Italy

This research quantified the role of various aspects of alcohol consumption and particularly of type of alcoholic beverages, on the risk of several common cancers and cardiovascular diseases in Southern Europe, based on case-control studies.

Regarding to cancer there was no association between cutaneous malignant melanoma and alcohol consumption. Alcohol consumption showed no consistent association with prostate cancer risk, but a significant inverse trend in risk for benign prostatic hyperplasia. For oral and pharyngeal cancer the risk increased with 3-4 drinks/day or more. For laryngeal cancer the risk increases with 5-7 drinks/day or more.

For upper aero-digestive tract cancers, for similar levels of ethanol consumption, the risk for drinkers of beer and spirits appeared to be comparable or lower to those of wine drinkers.

This study suggests that the most prevalent alcoholic beverage in the country tends to be associated with the highest risk for cancer. The apparent discrepancy between health outcomes of alcohol consumption can be explained in terms of different patterns of drinking, and variable (baseline) characteristics of heavy drinkers in various populations.

Regarding to cardiovascular diseases, alcohol drinking during meals was inversely related with risk of acute myocardial infarction (MI), whereas alcohol outside meals only was unrelated to the risk. Even after stopping drinking, the protection of alcohol drinking against MI may partly persist for several years.

Publications

Garavello W, Bosetti C, Gallus S, Dal Maso L, Negri E, Franceschi S and La Vecchia C (2006) Type of alcoholic beverage and the risk of laryngeal cancer. *European Journal of Cancer Prevention*, 15:69-73

Randi G, Altieri A, Gallus S, Franceschi S, Negri E, Talamini R and La Vecchia C (2005) History of cirrhosis and risk of digestive tract neoplasms. *Annals of Oncology*, 16:1551-1555.

Altieri A, Garavello W, Bosetti C, Gallus S and La Vecchia C (2005) Alcohol consumption and risk of laryngeal cancer. *Oral Oncology*, 41:956-965.

Negri E, La Vecchia C, Pelucchi C and Tavani A (2005) The risk of acute myocardial infarction after stopping drinking. *Preventive Medicine*, 40:725-728. (S. Gallus team).
Altieri A, Bosetti C, Gallus S, Franceschi S, Dal Maso L, Talamini R, Levi F, Negri E, Rodriguez T and La Vecchia C (2004) Wine, beer and spirits and risk of oral and pharyngeal cancer: a case-control study from Italy and Switzerland. *Oral Oncology*, 40:904-909.
Augustin LSA, Gallus S, Tavani A, Bosetti C, Negri E and La Vecchia C (2004) Alcohol consumption and acute myocardial infarction: a benefit of alcohol consumed with meals ? *Epidemiology*, 15(6):767-769
Crispo A, Talamini R, Gallus S, Negri E, Gallo A, Bosetti C, La Vecchia C, Dal Maso L and Montella M (2004) Alcohol and the risk of prostate cancer and benign prostatic hyperplasia. *Urology*, 64:717-722.
Naldi L, Gallus S, Tavani A, Imberti GL and La Vecchia C (2004) Risk of melanoma and vitamin A, coffee and alcohol: a case-control study from Italy. *European Journal of Cancer Prevention*, 13:503-508.

Alcohol, inflammation and atherosclerosis (2003) (EA 03 06)

Imhof A, Department of Internal Medicine, University of Ulm, Ulm, Germany

Moderate alcohol consumption is associated with reduced cardiovascular mortality compared to non-consumption of alcohol and heavy drinking. In a randomized controlled trial the effect of consumption of moderate amounts of alcoholic and non-alcoholic beverages on monocyte migration, a crucial step in atherogenesis, was assessed. This short-term intervention showed that moderate amounts of alcohol inhibit monocyte migration.
In the same study moderate amounts of ethanol-containing beverages increased adiponectin concentrations, but sex-specific effects might depend on type of beverage consumed. Adiponectin might represent an important link between insulin resistance, type 2 diabetes, and atherosclerosis. Adiponectin improves insulin sensitivity and has several anti-inflammatory properties, and high concentrations of adiponectin were associated with lower risk of type 2 diabetes and future cardiovascular events.
These findings might represent mechanisms by which alcoholic beverages lower cardiovascular disease risk.

Publications

Kächele M, Wolff S, Kratzer W, Haenle M, Homann J, Trischler G, Koenig W, Imhof A. (2015) Presence of fatty liver and the relationship between alcohol consumption and markers of inflammation. *Mediators of inflammation*.

Imhof A, Plamper I, Maier S, Trischler G and Koenig W (2009) Effect of drinking on adiponectin in healthy men and women. *Diabetes Care*, 32:1101-1103.

Imhof A, Blagieva R, Marx N and Koenig W (2008) Drinking modulates monocyte migration in healthy subjects: a randomised intervention study of water, ethanol, red wine and beer with or without alcohol. *Diabetes and Vascular Disease Research*, 5:48-53.

Alcohol consumption and risk of genetic alterations in genes involved in colorectal cancer in the Cohort Study on Diet and Cancer (2003) (EA 03 07)

Weijenberg MP, Departments of Epidemiology and Pathology, University of Maastricht, Maastricht, The Netherlands

In this project, the associations between consumption of alcohol and risk of colorectal cancer was investigated in the prospective Netherlands Cohort Study on diet and cancer. This study includes over 120 000 men and women with baseline information of total and beverage-specific alcohol consumption, including retrospective information on alcohol consumption five years prior to baseline. After 7.3 years of follow-up it was concluded that a daily high consumption of alcohol of 30 grams or more, compared to abstaining, is associated with an increased risk of colorectal cancer in both men and women. The data suggest that the association is mainly explained by the alcoholic content of alcoholic beverages, rather than other constituents. The association with alcohol appeared to be slightly stronger for more distal than proximal tumours, but there was no differential association for different molecular endpoints depending on markers for microsatellite instability and/or chromosomal instability. Specifically, beer consumption was also not significantly associated with colorectal tumors harbouring G>A mutations in the KRAS gene, as was hypothesized due to potential past contamination of beer with relatively large amounts of N-nitrosodimethylamine (NDMA). Both alcohol dehydrogenase 1C (ADH1C) genotype and alcohol consumption were independently associated with an increased risk of CRC. However, there was no apparent evidence for modification of the association of alcohol consumption with

colorectal cancer through the ADH1C genotype. Nevertheless, the interaction deserves further investigation in larger genetic epidemiologic studies.

Publications

Bongaerts BW, de Goeij AF, Wouters KA, van Engeland M, Gottschalk RW, Van Schooten FJ, Goldbohm RA, van den Brandt PA, Weijenberg, MP (2011) Alcohol consumption, alcohol dehydrogenase 1C (ADH1C) genotype, and risk of colorectal cancer in the Netherlands Cohort Study on diet and cancer. *Alcohol*, *45*(3), 217-225.

Bongaerts BWC, van den Brandt PA, Goldbohm RA, de Goeij AFPM and Weijenber MP (2008) Alcohol consumption, type of alcoholic beverage and risk of colorectal cancer at specific subsites. *International Journal of Cancer*, 123(10): 2411-2417.

Bongaerts BWC, de Goeij AFPM, de Vogel S, van den Brandt PA, Goldbohm RA and Weijenberg MP (2007) Alcohol consumption and distinct molecular pathways to colorectal cancer. *British Journal of Nutrition*, 97(3): 430-434.

Bongaerts BWC, de Goeij AFPM, van den Brandt PA and Weijenberg MP (2006) Alcohol and the risk of colon and rectal cancer with mutations in the K-ras gene. *Alcohol,* 38(3): 147-154

Bongaerts BW. Alcohol consumption as a risk factor for colorectal cancer. An epidemiological study on genetic susceptibility and molecular endpoints (PhD Thesis). Maastricht, 2008: Datawyse, Universiteit Pers Maastricht.

Neuropsychobiological mechanisms underlying the co-dependence alcohol-nicotine and the respective neurotoxicities occurring during their combined consumptions and their withdrawals (2003) (EA 03 12)

De Witte P, Laboratory of Behavioural Biology, Université Catholique de Louvain, Louvain-la- Neuve, Belgium

In this study the action of nicotine on a specific part of the brain was investigated by microdialysis in rats. In addition, the release of specific amino acids in the withdrawal stage following a 4-week period of nicotine and alcohol administration was studied.

The findings show that small doses of nicotine may have a modulating effect on symptoms during the initial stages of ethanol withdrawal. The imbalance occurring between excitatory and inhibitory amino acids during withdrawal of alcohol after

long term exposure and during acute nicotine administration may be responsible for additional problems.
This research is of relevance to the treatment of alcoholics. It will help scientists to understand alcohol withdrawal symptoms and how they are affected by co-dependency with other drugs such as nicotine.

Publications

Lallemand F, Ward RJ, De Witte P and Verbanck P (2011) Binge drinking +/- chronic nicotine administration alters extracellular glutamate and arginine levels in the nucleus accumbens of adult male and female Wistar rats. *Alcohol and Alcoholism*, 46(4):373-382.

D'Souza El-Guindy NB, Kovacs EJ, De Witte P, Spies C, Littleton JM, de Villiers WJS, Lott AJ, Plackett TP, Lanzke N and Meadows GG (2010) Laboratory models available to study alcohol-induced organ damage and immune variations: choosing the appropriate model. *Alcoholism: Clinical and Experimental Research*, 34(9):1489-1511.

Lallemand F, Ward RJ and De Witte P (2007) Nicotine increases ethanol preference but decreases locomotor activity during the initial stages of chronic ethanol withdrawal. *Alcohol and Alcoholism*, 42(3):207-218

Lallemand F, Ward RJ, Dravolina O and De Witte P (2006) Nicotine-induced changes of glutamate and arginine in naïve and chronically alcoholized rats: an in vivo microdialysis study. *Brain Research*, 1111:48-60.

Kashkin V and De Witte P (2005) Nicotine increases microdialysate brain amino acid concentrations and induces conditioned place preference. *European Neuro-Psychopharmacology*, 15:625-632.

Genetic and environmental influences on risk factors of adolescent alcohol use and problem use (2003) (EA 03 13)

van den Bree MBM, Cardiff University, UK

This study aimed to provide insight into why some children show no signs of alcohol related problem while the lives of others are seriously harmed by the development of alcohol use and abuse. Focus of this twin study using questionnaires was the aetiology of substance use and misuse in adolescence and early adulthood.
The initiation of alcohol use appears more strongly influenced by environmental factors such as parental attitudes, school policy on substance use and the local

neighbourhood. Progression to more frequent use of alcohol is more strongly influenced by genetic factors. Peer substance use is not only an environmental risk factor, as the genes that increase adolescents' risk of heavy and problem alcohol use, are also, to some extent, the same genes that lead them to affiliate with peer groups that regularly use alcohol.

These findings have implications for intervention programmes and policy development by highlighting the role of environmental factors that may account for adolescent alcohol use while also underscoring the need to further understand the interplay between an adolescents' alcohol use and their likelihood of associating with an alcohol-using friendship group.

Publications

Glaser B, Shelton KH, van den Bree MBM (2010) The moderating role of close friends in the relationship between conduct problems and adolescent substance use. *Journal of Adolescent Health*, 47(1):35-42.

Fowler T, Shelton K, Lifford K, Rice F, McBride A, Nikolov I, Neale MC, Harold G, Thapar A and van de Bree MBM (2007) Genetic and environmental influences on the relationship between peer alcohol use and own alcohol use in adolescents. *Addiction*, 102:894-903.

Fowler T, Lifford K, Shelton K, Rice F, Thapar A, Neale MC, McBride A and van den Bree MBM (2007) Exploring the relationship between genetic and environmental influences on initiation and progression of substance use. *Addiction*, 101(3):413-422.

A comprehensive identification and characterisation of genes that are differentially expressed during the development and progression of alcohol induced liver disease (2003) (EA 03 15)

Reeves HL, The Liver Group, Newcastle University, Newcastle upon Tyne, UK

Although nonalcoholic fatty liver disease (NAFLD) is increasingly common, only a minority of affected individuals develop fibrotic liver disease. The reasons for these differences in individual susceptibility to progressive disease are unclear, but family/ethnic studies suggest that genetic factors play a significant role.

This study found a functional polymorphism in the *KLF6* gene associated with advanced NAFLD. Further study of KLF6 may enhance understanding of this disease process.

Publications

Miele L, Beale G, Patman G, Nobili V, Leathart J, Grieco A, Abate M, Friedman SL, Narla G, Bugianesi E, Day CP and Reeves HL (2008) The Kruppel like factor 6 genotype is associated with fibrosis in non-alcoholic fatty liver disease. *Gastroenterology*, 135(1):282-291.

Development of a rodent model of beer consumption: investigation on the differential contribution of gustatory and pharmacological factors to beer drinking behavior (2004) (EA 0401)

Colombo G, Neuroscience Institute, National Research Council of Italy, Cagliari, Italy

The present study evaluated the effect of an environmental manipulation being a prolonged exposure to non-alcoholic beer with increasing concentrations of alcohol on the genetically determined predisposition and avoidance to consume alcohol of Sardinian alcohol-preferring (sP) and Sardinian alcohol-non preferring (sNP) rats, respectively. It was predicted that long-term exposure to a highly palatable beverage, made of non-alcoholic beer plus alcohol, would have permanently (a) increased – to "unusually" high levels – alcohol consumption in sP rats, and (b) overcome the inherent reluctance of sNP rats to consume alcohol. Both results would have been interpreted as the demonstration of the development of "psychological" dependence on alcohol.

However, the results of the study unequivocally demonstrated that, in both rat lines, (a) beer drinking was mostly driven by the gustatory aspects of beer, and (b) this long-term exposure to alcoholic beer did not produce any permanent, "unusually" high intake of alcohol once the beer taste was removed.

Publications

Lobina C, Carai MAM, Froestl W, Mugnaini C, Pasquini S, Corelli F, Gessa GL, Colombo G (2011) Activation of the $GABA_B$ receptor prevents nicotine-induced locomotor stimulation in mice. *Frontiers in Psychiatry*, 2:76.

Maccioni P, Thomas AW, Carai MAM, Gessa GL, Malherbe P and Colombo G (2010) The positive allosteric modulator of the $GABA_B$ receptor, *rac*-BHFF, suppresses alcohol self-administration. *Drug and Alcohol Dependence*, 109:96-103.

Orrù A. Lobina C, Maccioni P, Gessa G.L., Carai MAM and Colombo G. (2007) Repeated exposure to alcoholic beer does not induce long-lasting changes in alcohol self-administration and intake in Sardinian alcohol-preferring and Sardinian non-preferring rats. *Alcohol and Alcoholism*, 42(6):513-524.

Maccioni P, Orrù A, Korkosz A, Gessa GL, Carai MAM, Colombo G and Bienkowski P (2007) Cue-induced reinstatement of ethanol seeking in Sardinian alcohol-preferring rats. *Alcohol*, 41:31-39.

Challenging alcohol-related aggression expectancies (2004) (EA 04 02)

McMurran M, University of Nottingham, UK

Expectancies may be one target in interventions to reduce alcohol-related aggression. In a study with male students, participants were asked to recall both alcohol-related aggressive and alcohol-related non-aggressive events. Both seem to have the potential to increase alcohol-aggression outcome expectancies. This may elevate the risk for alcohol-related aggression, at least temporarily.

In treatment for alcohol-related aggression, asking clients to recount incidents where they were aggressive or violent after drinking may temporarily increase their risk by increasing alcohol-aggression outcome expectancies. This needs to be taken into account by advising those in treatment to avoid risky situations. In this study it was hypothesized that recounting incidents where drinking did not lead to violence would lead to a reduction in alcohol-aggression expectancies, and hence reduce risk. This was not the case, and indeed alcohol-aggression expectancies were elevated in this condition. Therefore, indications are that this is not a useful therapeutic strategy for risk reduction. It is important that therapists are aware of this. Effective ways of challenging alcohol-related aggression expectancies remain to be identified.

Publications

McMurran M and McCulloch, A (2009) Alcohol-aggression outcome expectancies and their responsiveness to event recall. *Addiction Research and Theory*, 17(1):54-63.

McMurran M (2009). The relationships between alcohol use, trait aggression and the alcohol-aggression outcome expectancy in male students. *Journal of Substance Use*, 14(1):1-9.

Mechanisms of the protective effects of alcohol consumption on cardiovascular risk and on myocardial preconditioning (2004) (EA 04 07)

Crea F, Institute of Cardiology, Catholic University of the Sacred Heart, Rome, Italy

The aim of the present research project is to investigate potential biological mechanisms explaining the association between moderate alcohol consumption and lower cardiovascular risk observed in several previous observational studies. These mechanisms were investigated in healthy subjects and in patients with coronary artery disease.

First of all, the problem of confounding that has recently been raised as a radical critique to observational studies on alcohol and health appears to be of minor concern, as abstainers and moderate drinkers from Moli-sani cohort were comparable in the majority of aspects, only socio- economic status appearing as a possible true confounder. Taken together, our results show that moderate alcohol consumption has a remarkably positive effect on risk profile for cardiovascular diseases.

In contrast, heavy alcohol consumption increases the risk of cardiovascular events through a variety of mechanisms including activation of inflammatory cells, hypertension and abolition of ischemic preconditioning. The latter, in particular, is likely to play a key role in explaining the higher mortality following an acute myocardial infarction observed in heavy and binge drinkers.

Publications

Marinaccio L, Lanza GA, Niccoli G, Fabretti A, Lamendola P, Barone L, Di Monaco A, Di Clemente F, Crea F. (2008) Effect of low doses of alcohol on the warm-up phenomenon in patients with stable angina pectoris. *American Journal of Cardiology*. 102(2):146-149.

Niccoli G, Altamura L, Fabretti A, Lanza GA, Biasucci LM, Rebuzzi AG, Maria Leone A, Porto I, Burzotta F, Trani C and Crea F (2008) Ethanol abolishes ischemic preconditioning in humans. *Journal of the American College of Cardiology*, 51(3):271-275.

Di Castelnuovo A, Costanzo S, Donati MB, Lacoviello L and de Gaetano G (2007) Alcohol consumption and cardiovascular risk: an epidemiological perspective. *Nutrition, Metabolism and Cardiovascular diseases*, 17:561-564.

The e-UNICAL project: e feasibility and effectiveness study into delivering an electronic feedback and social norms intervention designed to decrease university students' consumption of alcohol (2005) (EA 05 08)

Bewick BM, Division of Psychological and Social Medicine, School of Medicine, Faculty of Medicine and Health, University of Leeds, Leeds, UK

The e-UNICAL project investigated the feasibility and effectiveness of delivering a web-based social norms and personalised feedback intervention for alcohol use to university students. It also investigated the relationship between alcohol consumption, associated risk behaviours and mental health.

Intervention participants significantly reduced their units of alcohol per occasion from pre-survey levels. This reduction was maintained at follow-up. There was no significant change within control participants. Intervention participants rated the intervention favourably and in general there was no difference in ratings between low, moderate and high level drinkers. The relative risk of experiencing negative consequences/engaging in risky behaviour was higher in students who consumed alcohol at moderate or high levels in comparison to their low level peers.

These results suggest that a personalised feedback and social norms intervention can be effective in reducing alcohol consumption amongst the UK student population. In light of these findings it is suggested that within the student population web-based social norms and personalised feedback interventions should be more widely available. While the findings are positive further research is needed to understand the mechanisms of change and how the impact of the intervention could be improved.

Publications

Marley, S, Bekker HL and Bewick BM. (2016). Responding to personalized social norms feedback from a web-based alcohol reduction intervention for students: Analysis of think-aloud verbal protocols. *Psychology and Health*, 31(9): 1007-1024.

Bewick BM, West RM, Barkham M, Mulher, B., Marlow R., Traviss G and Hill AJ. (2013). The effectiveness of a web-based personalized feedback and social norms alcohol intervention on United Kingdom university students: Randomized controlled trial. Journal of Medical Internet Research, 15(7): e137.

Bewick BM, West RM, Gill J, O'May F, Mulhern B, Barkham M and Hill AJ. (2010). Providing web-based feedback and social norms information to reduce student alcohol intake: A multi-site investigation. *Journal of Medical Internet Research*, 12(5): e59.

Cunningham JA, Khadjesari Z, Bewick BM and Riper H (2010) Internet-based interventions for problem drinkers: from efficacy trials to implementation. *Drug and Alcohol Review*, 29(6): 617-622.

Bewick BM, Mulhern B, Barkham M, Trusler K, Hill AJ and Stiles WB (2008) Changes in undergraduate student alcohol consumption as they progress through university. *BMC Public Health*, 8:163.

Identification of a candidate gene influencing alcohol intake, using a mouse line with alcohol preference induced by ENU mutagenesis (2005) (EA 05 09)

Thomas HC, Department of Medicine Imperial College, St Mary's Hospital, UK

This study provides a new and important link between a specific gene and increased alcohol consumption that could underlie some forms of alcohol abuse.

The first ENU induced model of alcoholism (alco-22) has now been mapped demonstrating that the mutation resulting in the increased alcohol intake is in the gene encoding the GABA-A B1 subunit. This project was funded to allow mapping of the mutation in a second mouse line (alco-2) to determine whether a second gene might be involved.

The results from the study have narrowed down the candidate region for high ethanol preference in the ALCO/2 mouse line to 10 Mb at the telomeric end of chromosome 11. This region includes interesting candidate genes like Sstr2 and Grin2c, and the QTL's for alcohol preference Alcp 18 (male specific) and 20 (female specific).

Further funding would be needed to support the ongoing breeding, genotyping and phenotyping efforts of the offspring of the ALCO/2 line, including three possibly informative recombinants.

Publications

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Investigations on glutamatergic and GABAergic disturbances that may result in fetal alcohol syndrome (2005) (EA 05 12)

Zink M, Departments of Psychiatry Psychopharmacology, Central Institute of Mental Health, Mannheim, Germany

The fetal alcohol syndrome (FAS) is the most common cause of mental retardation. However, the molecular details of the detrimental influences exerted by ethanol are not clear until now. This research established an animal model and was able to reproduce a variety of core-features of FAS- children in rats. The last trimenon of human pregnancy was defined as the most critical period with regard to the learning disabilities. Alterations in gene expression were observed. Because the functions of these genes are well described, the results contribute to an improved understanding of the pathogenesis of FAS and might lead to the development of new procedures in prophylaxis and treatment.

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Rainer Spanagel, Mathias Zink, Wolfgang Sommer. Neurobiology of Alcohol Addiction. In: Donald Pfaff (Editor in Chief): Neuroscience in the 21. Century Springer Verlag 2013, pp 2745-2773.

Alcohol-induced neurogenesis: Functional characterization of increased formation of nerve cells in hippocampus in response to moderate voluntary ethanol intake (2005) (EA 05 18)

Brene S, Department of Neurotec division of Psychiatry, Karolinska University Hospital, Stockholm, Sweden

This study analysed hippocampal neurogenesis in the two-bottle free-choice model alcohol consumption in single housed rats and mice. The results show that depending on circumstances alcohol consumption can increase, decrease or have no effect on hippocampal neurogenesis; the process by which nervous system cells, known as neurons, are produced by neural stem cells. Most likely what determines which effect the voluntary alcohol consumption has on hippocampal neurogenesis is whether there is a stress component involved in the overall consumption behavior. Overall it appears that alcohol consumption has the potential to alter the rate of the formation of new nerve cells. Thus, the long- term effects of alcohol on brain function can in part be mediated via modulation of the rate of formation of new nerve cells.

Publications

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Effect of ethanol drinking on the metabolism of essential fatty acids in 3 very different European populations (2005) (EA 05 20)

De Lorgeril M, Laboratoire Nutrition, Vieillissement et Maladies Cardiovasculaires (NVMCV), Université Joseph Fourier, La Tronche, France

The main aim of the study was to investigate the effects of moderate ethanol drinking on the metabolism of the essential omega-3 fatty acids in humans. A secondary aim was to investigate whether some genetic polymorphisms may play a role in that interaction.

The data, obtained from a quite large sample of middle aged men and women, confirm previous human and animal findings suggesting that moderate alcohol consumption results in increased omega-3 fatty acid levels in both the plasma and cell membranes. It looks like drinkers eat fatty fish.
This means that the effect of moderate alcohol drinking on the metabolism of omega-3 fatty acids could, at least partly, explain the protective effect of alcohol on the risk of cardiovascular diseases. This is a totally new finding regarding the role of moderate ethanol drinking in the context of cardiovascular diseases.

Publications

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Stress reactivity, psychopathology and age at first alcohol use (2006) (EA 06 09)

Huizink A, Department of Child and Adolescent Psychiatry, Erasmus Medical Centre, Rotterdam, The Netherlands

For the prevention of (heavy) alcohol use in youth, it is important to better describe, identify, and predict the complex nature and course of alcohol use and associated psychopathology. This research looked at the age of alcohol initiation among adolescents with either symptoms of antisocial behaviour (so-called externalizing problems) or symptoms of depression (so-called internalizing problems). The researchers used stress response tasks to measure the change in heart rate in these adolescents. This was used as a measure of autonomic functioning to see if it influences the age of alcohol initiation. Results show that there is no association between antisocial behaviour or depression symptoms and the age of alcohol initiation. Greater heart rate reactivity however, might predict earlier initiation

of alcohol use. This could mean that alcohol is used at an early age to lower stress reactivity instead of using it to raise arousal levels (as suggested by other studies). This research contributes to the identification of adolescents at risk for using alcohol at an early age and may provide insights for better health promotion interventions.

Publications

Evans BE, Greaves-Lord K, Euser AS, Franken IHA, Huizink AC (2012) The relation between hypothalamic–pituitary–adrenal (HPA) axis activity and age of onset of alcohol use. *Addiction*, 107(2):312-322.

Greaves-Lord K, Tulen JHM, Dietrich A, Sondeijker FEPL, van Roon A, Oldehinkel AJ, Ormel J, Verhulst FC and Huizink AC (2010) Reduced autonomic flexibility as a predictor for future anxiety in girls from the general population: the TRAILS study. *Psychiatry Research*, 179(2):187-193.

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A double-blind randomized controlled study on alcohol intake and craving reduction in alcohol-dependent patients comparing baclofen 10 mg, baclofen 20 mg and placebo (2006) (EA 06 19)

Leggio L, Institute of Internal Medicine and Department of Neuroscience, Catholic University of Rome, Rome, Italy

Baclofen is used as a medication in alcohol dependent individuals to reduce alcohol intake and craving. Chronic alcohol abuse alters hormone levels and body composition.

The researchers have investigated, in several longitudinal studies, the role of other hormones in alcohol dependent patients treated with Baclofen. Data suggest that specific hormones related to the hypothalamic-pituitary-thyroid axis (e.g. TSH and

free T3) could be involved in the neurobiology of alcohol craving. An additional study, on the role of volume-regulating hormones, suggests that alcohol craving could be influenced by fluid volume intake. Another study shows that hormones of the hypothalamic-pituitary-adrenal axis can play a role in nutritional and metabolic parameters in alcoholics, for example changes in fat mass. Conversely, these hormones might also play a role in the nutritional recovery after a period of total abstinence. Finally, the researchers evaluated the association between affective and psychiatric disorders (e.g. anxiety) among alcoholics with craving and the effect of a period of abstinence.

The results suggest that Baclofen, which has anti-craving properties, could be helpful in ameliorating psychiatric features in alcohol dependent patients.

Publications

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Delineating the role of TGF-β signal transduction in alcohol dependent steatosis and steatohepatitis (2006) (EA 06 24)

Dooley S, Department of Medicine II, University Hospital, Mannheim, Germany

Alcohol intake can induce liver damage. This research investigated how ethanol interacts with other molecules within liver cells. Experiments in isolated liver cells found that the transforming growth factor (TGF)-β, a cell signalling protein, regulates the expression of enzymes involved in alcohol metabolism. TGF-β contributes to alcohol induced liver damage by stimulating fatty liver and liver fibrosis processes. Both, ethanol and TGF-β are toxic to liver cells. A combination of the two further enhances the effect and can lead to cell death.

In studies with mice having a pre-existing liver damage, presence and signalling of TGF-β enhance the deleterious effect of alcohol intoxication compared to mice with undamaged livers.

The results need to be further delineated and then have potential to develop better treatment strategies for patients with liver damage due to alcohol intoxication.

Publications

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A follow-up study on determinants for early alcohol debut and consequences of early debut for later psychosocial well-being, lifestyle and health (2006) (EA 06 27)

Grønbæk M, The Danish National Institute of Public Health, Copenhagen, Denmark

This research aimed at identifying risk factors for adolescents' health and health behaviour. First, the characteristics of participants of the Danish Youth Cohort was assessed and compared with non-participants to identify any differences in these groups. A follow-up study focused on social inequality in drinking onset. Results show that especially boys from the wealthiest families are most at risk of early drinking onset. No differences in early drinking onset were found among socio-economic groups among girls. Next to that, the effect of early drinking onset on binge drinking across socioeconomic groups was investigated. The researchers conclude that the causal effect of early drinking onset on binge drinking do vary across socioeconomic groups among boys. This means that there is social differentiation in the consequences of early drinking onset and indicates that already in adolescence socially differential vulnerability to alcohol does exist.

Publications

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Marie Eliasen, Susanne K. Kjær, Christian Munk, Mari Nygård, Pär Sparén, Laufey Tryggvadottir, Kai-Li Liaw, Morten Grønbæk; (2009) The relationship between age at drinking onset and subsequent binge drinking among women. *European Journal of Public Health*, 19 (4): 378–382 (ERAB not cited).

The Effect Of Ethanol On Histone Acetylation At Pro-Inflammatory Cytokine Genes And Its Contribution To The Clinical Syndrome Of Alcoholic Hepatitis (2006) (EA 06 39)

Jones D.E.J., School of Clinical Medical Sciences, University of Newcastle upon Tyne, UK

Acute alcoholic hepatitis is characterized by a disproportionate inflammation response in the liver. Using cell studies, this research investigated the role of ethanol in cell signalling and gene regulation related to alcoholic hepatitis. Results shows that the association between ethanol, acetate (a breakdown product of ethanol), histone acetylation (essential in gene regulation) and the expression of cell signalling molecule (i.e. cytokines) reveals a possible therapeutic target for acute alcoholic hepatitis. Additionally, the importance of acetyl-coA (a key molecule in cellular processes) reinforces the intimate relationship between metabolism and immunity and the role of the liver as intersection of these vital processes. Moreover, the development of inhibitors of certain enzymes may allow modulation of inflammation in acute alcoholic hepatitis without affecting normal energy generation and storage pathways.

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Generation and characterization of human monoclonal single chain antibodies specific to phosphatidylethanol. (2006) (EA 06 40)

Savolainen M, Department of Internal Medicine, University of Oulu, Oulu, Finland

Phosphatidylethanol (PEth) is a group of alcohol-modified phospholipids present in cell membranes after heavy drinking. This research shows for the first time that antibodies against phosphatidylethanol can be produced with recombinant DNA techniques. Recombinant techniques will provide means to effectively select new monoclonal antibodies that are smaller in size and with higher binding affinity to be used for phosphatidylethanol specific immunoassays.
These antibodies contain protein sequence tags that will help use these antibodies in various ways for PEth analysis and detection. The recombinant antibodies can also be produced in large scale production facilities for commercial purposes.

Publications

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Identification of inflammatory and angiogenic signaling mechanisms modulated by beer and red wine polyphenols (2006) (EA 06 41)

Soares R, Department of Biochemistry, University of Porto, Porto, Portugal

Angiogenesis (the formation of new blood vessels) and inflammation occur in disease such as cancer and atherosclerosis. This research aimed to identify whether polyphenols present in beer and red wine affect the molecular mechanisms of these processes. Results of cell and rat studies demonstrate that specific polyphenols (xanthohumol and isoxanthohumol) can be used as anti-inflammatory and anti-angiogenic agents. Another polyphenol (8- prenylnaringenin), manifested pro-

angiogenic action which might be relevant for pathological conditions exhibiting angiogenic impairment.

Publications

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The impact of methionine metabolism for the incidence and the clinical course of alcohol-dependency (2007) (EA 07 04)

Linnebank M, Dept. Neurology, Hagen-Ambrock and University of Witten/Herdecke, Germany

Various studies have shown that plasma homocysteine (HCY) serum levels are elevated in actively drinking alcohol-dependent patients during alcohol withdrawal, while rapidly declining during abstinence. Hyperhomocysteinemia has been associated not only with blood alcohol concentration (BAC), but also with deficiency of different B-vitamins, particularly folate, pyridoxine and cobalamin. The study included 168 inpatients (110 men, 58 women) after admission for detoxification treatment. BAC, folate, cobalamin, pyridoxine, thiamine and riboflavin were obtained on admission (Day 1). HCY was assessed on Days 1, 7

and 11. HCY levels significantly declined during withdrawal. General linear models and linear regression analysis showed an influence of BAC, folate and riboflavin on the HCY levels on admission as well as on HCY changes occurring during alcohol withdrawal. No significant influence was found for thiamine, cobalamin and pyridoxine. These findings show that not only BAC and plasma folate levels, but also plasma levels of riboflavin influence HCY plasma levels in alcohol-dependent patients.

Publications

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Is brief personalized feedback effective in reducing alcohol-related problems amongst University students in different European countries? (2007) (EA 07 08)

Moreira T, School of Health and Social Care, Oxford Brookes University, Oxford, UK

Students' drinking behaviour is influenced by youth (mis)perceptions of how their peers drink. Young people tend to over-estimate peer group drinking levels. If misperceptions can be corrected, young people may drink less. This research investigated personalised normative feedback to correct misperception of peer drinking levels by providing information about personal drinking levels and patterns compared with norms in similar aged peer groups. Personalised normative feedback is intended to raise motivation for behaviour change. However, results of this trial show that personalised normative feedback was not effective in a UK student population.

This research also involved a systematic review based on 22 controlled trials involving 7275 college or university students. The students were randomly assigned to the social norms intervention or a control group. Interventions delivered using the web or computer, or in individual face-to-face sessions, appeared to reduce alcohol misuse. The evidence was less convincing for group face-to-face sessions. Mailed and group feedback were on the whole no different than with the control intervention. Also interventions using social norms marketing campaigns appeared not to be effective.

Publications

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A psychosocial intervention to reduce high-risk single-session alcohol (binge) drinking among company employees in a workplace setting in four European nations (2007) (EA 07 10)

Hagger M S, School of Psychology, University Nottingham, Nottingham, UK; now with Curtin University, Australia

This research aimed to evaluate the effectiveness of theory-based interventions using motivational and implemental strategies to reduce binge drinking behaviour among students and young employees in the workplace. Two different psychological strategies were tested; a motivational strategy using mental imagery to increase the participants' intentions to reduce binge drinking behaviour, and an implemental strategy using planning to help participants carry out their intentions in situations where they are likely to binge drink. The strategies were tested in students and employees in four European countries; Estonia, Finland, Sweden and the UK. Both printed and online communication of the intervention was effective. More research is needed to further investigate factors that are effective in reducing alcohol consumption among students and young employees.

Publications

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Hagger MS, Lonsdale A, HeinV, Koka A, Lintunen T, Pasi H, Lindwall M, Rudolfsson L and Chatzisarantis NLD (2011) Predicting alcohol consumption and binge drinking in company employees: An application of planned behaviour and self-determination theories. *British Journal of Health Psychology*, 17(2):379-407.

Hagger M S, Lonsdale A and Chatzisarantis NLD (2011). Effectiveness of a brief intervention using mental simulations in reducing alcohol consumption in corporate employees. *Psychology, Health and Medicine*, 16(4):375-392.

Extending growth mixture modelling for the longitudinal study of adolescent alcohol use (2007) (EA 07 12)

Percy A, Institute of Child Care Research, Queens University, Belfast, UK

The general aim of this study was to test, replicate and extend longitudinal growth models in the study of adolescent alcohol use.
Specific empirical analysis has been undertaken. Extending growth mixture models include various predictors of the various latent trajectory classes. Evaluating the direct or mediating influences of various contextual factors on the development of teenage alcohol use. Examining the association of putative risk factors, time independent covariates from multiple domain and trajectory group membership in ZIP within a theoretical model. Use a genetic relationship matrix generated from a multigenerational pattern of substance to obtain more robust parameter estimates and to examine the proportionate contributions of genes and environment to substance use development and subsequent abuse.
The results show that the shared environmental influences of family non-shared environmental effects accounted about 0.97 percent of total variance of alcohol use.
Also, the growth curve modeling that explicitly considers both intra-individual change and inter- individual differences in alcohol use and delinquency disorder. However the assumption of homogeneity in the growth parameters for these two traits is unrealistic and statistical analyses and their effects can be seriously biased if heterogeneity is ignored.

Publications

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The bidirectional relationship between the biological clock and alcohol addiction (2007) (EA 07 14)

Jacobs EH, Department of Cell Biology and Genetics, Erasmus University Medical Center, Rotterdam, The Netherlands

The biological clock regulates diverse processes such as behaviour, physiology and metabolism. The clockwork consists of genes that switch each other on and off with a periodicity of about 24 hours and is hence called a circadian (*circa*: about; *dies*: day) oscillator. Organisms keep up with the daily light-dark rhythm of 24 hours by light-mediated adjustment of their internal clock to this rhythm. The biological clock is an important factor in proper mammalian functioning. There are many examples of disturbances of the clock, such as shift work, trans-meridian flights resulting in jet lag, ageing and genetic disturbances of the clockwork. Malfunctioning of this system may well play a role in a wide array of diseases, such as cancer, psychiatric and neurological disorders. In this project we have investigated in mouse models with a circadian defect how a disturbed biological clock may affect alcohol consumption. It seems that for alcohol consumption and preference an intact circadian oscillator is not required, but it may be important for the *motivation* to receive alcohol. We also investigated how alcohol consumption might change the performance of the biological clock. It appeared that alcohol consumption does not change the clock itself, but it diminishes the clock resetting effect of light. This work may give insight into a novel aspect of alcohol addiction, possibly leading to pharmacological tools to intervene.

Publications

Papachristos, E. B., Jacobs, E. H., & Elgersma, Y. (2011). Interval timing is intact in arrhythmic Cry1/Cry2-deficient mice. *Journal of biological rhythms*, *26*(4), 305-313.

‘Blind Drunk?’ Differentiating the Psychopharmacological and Expectancy Effects of Alcohol Consumption on Attentional Bias (2007) (EA 07 15)

Albery I, Department of Psychology, London South Bank University, London, UK

Attentional biases, the phenomenon whereby individuals find they are distracted by objects or information that is relevant to them, have been consistently demonstrated among alcohol consumption and drug use in laboratory studies. This research investigates attentional bias among social drinkers in an alcohol-related environment (i.e. a pub).

Results show that both actual and expected alcohol consumption do not affect attentional biases for alcohol-related stimuli. The extent to which individuals demonstrate these biases may vary depending on whether they are drinking, and whether they are in a drinking-related setting or not.

Findings suggest that attentional bias is a more complex phenomenon than earlier suggested by laboratory research. Interventions for dependent users that are aimed at manipulating these biases should proceed cautiously until the mechanisms are more clearly elucidated.

Publications

Albery, Ian P., et al. “Testing a frequency of exposure hypothesis in attentional bias for alcohol-related stimuli amongst social drinkers.” Addictive Behaviors Reports 1 (2015): 68-72. (ERAB not mentioned as funding)

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Moss, A.C., Albery, I.P., Rycroft, N.R., & Fenn, R. Attentional bias for alcohol-related stimuli in a dot-probe field study. To be submitted to Psychology of Addictive Behaviors.

Rycroft, N.R., Albery, I.P., Moss, A.C., & Fenn, R. Acute effects of alcohol on attentional biases for alcohol-related words in a dot probe detection task. To be submitted to Journal of Psychopharmacology.

Molecular and cellular damage induced by "Binge drinking" in adolescents. Can this be diminished by targeted protaurine drugs? (2007) (EA 07 23)

Della Corte L, Department of Preclinical and Clinical Pharmacology, University Firenze, Firenze, Italy

Binge drinking can induce adverse effects in specific brain regions, especially in female susceptible individuals. This research investigated these effects of binge drinking by using an adolescent female rat model. The results show that binge drinking induces inflammation leading to changes in specific cells to release damaging compounds. This causes brain damage in a specific brain region, the hippocampus. This may be responsible for the memory deficits, which occur in susceptible individuals after taking alcohol in such a fashion. The use of specific compounds which prevent such inflammation will stop such damaging changes in the brain.

Publications

Stefanini C, Colivicchi MA, **Della Corte L**, Ward RJ, De Witte P, Lallemand F, Hemmings K, Pitard A, Page MI, Nayak K and Dexter DT (2014) Ethane-b-sultam modifies the activation of the innate immune system induced by intermittent ethanol administration in female adolescent rats. Journal of *Alcoholism & Drug Dependence*, 2(2).

Ward RJ, Lallemand F, De Witte P, Crichton RR, Piette J, Tipton K, Hemmings K, Pitard A, Page M, **Della Corte L**, Taylor D and Dexter D (2011) Anti-inflammatory actions of a taurine analogue, ethane b-sultam, in phagocytic cells, *in vivo* and *in vitro*. *Biochemical Pharmacology*, 81(6):743-751.

Lallemand F, Ward RJ and De Witte P (2009) The influence of chronic nicotine administration on behavioural and Neurochemical parameters in male and female rats after repeated binge drinking exposure. *Alcohol and Alcoholism*, 44(6):535-546.

Ward RJ, Lallemand F and De Witte P (2009) Biochemical and neurotransmitter changes implicated in alcohol induced brain damage in chronic or 'binge drinking' alcohol abuse. *Alcohol and Alcoholism*, 44(2):128-135

Ward RJ, Colivicchi MA, Allen R, Schol F, Lallemand F, De Witte P, Ballini C, **Della Corte L** and Dexter D (2009) Neuro-inflammation induced in the hippocampus of "binge drinking" rats may be mediated by elevated extracellular glutamate content. *Journal of Neurochemistry*, 111(5):1119-1128.

Freinbichler, W., Tipton, K. F., Della Corte, L., & Linert, W. (2009). Mechanistic aspects of the Fenton reaction under conditions approximated to the extracellular fluid. *Journal of inorganic biochemistry,* 103(1), 28-34.

Petkova-Kirova, P., Rakovska, A., Zaekova, G., Ballini, C., Della Corte, L., Radomirov, R., & Vágvölgyi, A. (2008). Stimulation by neurotensin of dopamine and 5-hydroxytryptamine (5-HT) release from rat prefrontal cortex: possible role of NTR1 receptors in neuropsychiatric disorders. Neurochemistry international, 53(6-8), 355-361.

Characterization of the role of immune mechanisms in the progression of alcoholic liver disease (2008) (EA 08 05)

Albano, E. University "A. Avogadro" of East Piedmont, Novara, Italy

It is increasingly recognized that inflammation has an important role in the pathogenesis of alcoholic liver disease (ALD). Nonetheless, the mechanisms by which alcohol maintains hepatic inflammatory processes are still incompletely characterized. In this context, the possible role of adaptive immunity has emerged form evidence of lymphocytes recruitment and activation in the inflammatory infiltrates of ALD. This project aimed to evaluate the actual contribution of oxidative stress-mediated immunity in the development of alcohol liver injury. Animal studies were performed where alcohol-fed mice were pre-immunized with protein-adducts with different lipid peroxidation products. Among the different immunization protocols the use of MDA-adducts was the most effective. As compared to non-immunized mice, upon alcohol exposure MDA-sensitized animals developed more severe liver injury characterized by diffuse lymphocyte infiltration. The hepatic production of pro-inflammatory cytokines/chemokines TNF-α, IL-12, CCL2 was also significantly increased in immunized alcohol-fed animals. Altogether these results indicated that the stimulation of humoral immunity by antigens that are generated by oxidative stress, can contribute in promoting inflammatory reactions during the development of alcoholic liver injury. However, they do not rule out the possibility that cellular immunity might as well contribute to chronic inflammation in ALD.

Publications

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Risk factors for alcohol binge drinking in native adolescents and immigrants in Germany (2008) (EA 08 06)

Hillemacher T, Klinik fûr Psychiatrie, Sozialpsychiatrie und Psychotherapie, Hannover, Germany

This research aimed to determine the prevalence of risky alcohol consumption patterns (binge drinking) in German adolescents. Differences in drinking behaviour between adolescents from different background were also investigated. Additionally, protective and risk factors for binge drinking among German adolescents were explored. The results indicate that binge drinking is a common problem behaviour in German adolescents. Binge drinking is more common among adolescents in rural areas. Adolescents with Turkish roots showed less binge drinking than adolescents of German or Russian descent. Next to that, the two most influential factors found to protect against binge drinking were low economic status and importance of religion. The four most relevant risk factors for binge drinking were life-time prevalence of school absenteeism/truancy, academic failure, suicidal thoughts, and violence at school in the form of aggressive behaviour of teachers.

Publications

Donath C, Graessel E, Baier D, Bleich S, Hillemacher T (2014) Is parenting style a predictor of suicide attempts in a representative sample of adolescents? *BMC Pediatrics*, 14:113.

Donath C, Grässel E, Baier D, Pfeiffer C, Bleich S and Hillemacher T (2012) Predictors of binge drinking in adolescents: ultimate and distal factors – a representative study. *BMC Public Health*, 12:263.

Donath C, Grässe E, Baier D, Pfeiffer C, Karagülle D, Bleich S and Hillemacher T (2011) Alcohol consumption and binge drinking in adolescents: comparison of different migration backgrounds and rural vs. urban residence – a representative study. *BMC Public Health*, 11:84.

Karagülle D, Donath C, Bleich S and Hillemacher T (2010) Rauschtrinken bei Jugendlichen und jungen Erwachsenen. *Fortschritte der Neurologie – PsychiatrieI*, 78(4):196-202.

Alcohol-induced changes in learning bias: a possible 'gateway' to drug addiction (2008) (EA 08 12)

Ripley, T.L. University of Sussex, Falmer, Brighton – UK

This series of experiments used a mouse model to look at the long-term effect of binge intoxication on attentional processes, which may impact upon future behaviours including drug taking. Three important findings have been made. Firstly, binge intoxication leads to a shift in attentional processes, such that animals now favour local cues over global cues in a spatial learning task. If this shift or narrowing of focus is also true in other tasks, it may mean that animals are more prone to conditioning processes where local cues indicate the availability of a natural or drug reward. Indeed, the second finding suggested that this is true. Animals that had been exposed to binge intoxication were more likely to approach a discrete cue that had been associated with ethanol when compared with a control group. Finally, a more sophisticated task was used to look at this type of behaviour. Animals naturally have a greater or lesser tendency to approach environmental stimuli associated with rewards. Those animals that had a natural tendency to approach discrete cues associated with a reward (Pavlovain approach – sign trackers) did so to a far greater extent if they had previously been exposed to ethanol in a binge pattern.

Together these results suggest that binge ethanol exposure leads to long-term changes in attentional focus, with some cues taking on greater salience than normal. As it is known that these types of cues are particularly important in drug addiction, both during consumption and relapse phases, it is possible that a pattern of binge intoxication may increase vulnerability to future drug taking behaviour.

Publications

Ripley TL and Stephens DN (2011) Critical thoughts on current rodent models for evaluation potential treatments of alcohol addiction and withdrawal. *British Journal of Pharmacology*, 164:1335-1356.

The reduction of adolescent alcohol misuse: examining the potential universal effects of a targeted prevention programme (2008) (EA 08 22)

Mackie C, King's College London, UK

Alcohol misuse by young people is a significant and escalating problem in Europe. Delaying the onset of adolescent drinking would have a major impact on reducing both the social and health costs associated with adolescent alcohol misuse. Universal prevention programmes that target the general adolescent population have been met with limited success.

Findings of this study suggest that focused interventions that target individuals who show a heightened risk for alcohol misuse also results in in reduced alcohol use among low risk students attending the same schools. This is due to fewer drinking opportunities and a reduction in alcohol use by their high risk friends. Further analysis will examine whether peer influence can explain the reduction in low risk students alcohol use.

The implication of this study is that by reducing opportunities for alcohol use and attitudes surrounding drinking behaviours, the targeted intervention might transfer its effects to the general adolescent population.

Publications

Conrod PJ, O'Leary-Barrett M, Newton N, Topper L, Castellanos-Ryan N, Mackie C and Girard A (2013) Effectiveness of a Selective, Personality-Targeted Prevention Program for Adolescent Alcohol Use and Misuse A Cluster Randomized Controlled Trial. *JAMA Psychiatry,* 70(3):334-342.

Effects of Alcohol on Rating of Attractiveness: Examining the role of alcohol in social interaction (2008) (EA 08 20)

Munafo M R, School of Psychological Science, University of Bristol, Bristol, UK

This research conducted a series of human laboratory experiment to explore the effect of alcohol on emotion processing. The research also investigated the effect

of alcohol on ratings of attractiveness, both *by* the consumer *of* other individuals, (i.e., intoxicated people viewing sober people), and by other individuals of the consumer (i.e., sober people viewing intoxicated people). Additionally, the possible moderating influence of social and contextual cues to sexual behaviour on the effects of alcohol was investigated. The results indicate that the effects of alcohol on ratings of attractiveness may not be isolated to the consumer. It is possible that low levels of alcohol consumption may influence the attractiveness of the consumer, either through changes in face shape (e.g., resulting from muscle relaxation) or facial colouration (consistent with evidence that faces with a modest degree of red colouration are rated as more attractive than more pallid faces).

Publications

Van Den Abbeele, J., Penton-Voak, I. S., Attwood, A. S., Stephen, I. D., & Munafò, M. R. (2015). Increased facial attractiveness following moderate, but not high, alcohol consumption. *Alcohol and Alcoholism*, 50(3): 296-301.

Penton-Voak IS, Cooper RM, Roberts RE, Attwood AS and Munafo MR (2012) Effects of acute alcohol consumption on the perception of eye gaze direction. *Journal of Psychopharmacology*, 26(2):254-261.

Effects of moderate alcohol consumption on gene expression in subcutaneous adipose tissue in lean and overweight postmenopausal women (2008) (EA 08 21)

Hendriks H, Business Unit Biosciences, TNO Quality of Life, AJ Zeist, The Netherlands

Moderate alcohol consumption has various acute and longer-term effects on low-grade inflammation which may accumulatively affect chronic disease risk. This research provides insights of how moderate alcohol consumption might exert its effect to reduce inflammatory processes in the body by combining and integrating several sophisticated techniques. An integrated approach of large-scale profiling of proteins and genes in blood showed that longer-term moderate alcohol consumption altered several important processes related to signalling, immune response and lipid metabolism. Additionally, results show that both total and high-molecular weight adiponectin concentrations are higher after moderate alcohol consumption compared with abstention in premenopausal women. These effects

were evident after at least three weeks of consumption and occurred concomitantly. Adiponectin is a hormone solely secreted by adipose tissue. It predicts insulin sensitivity. Low levels of this hormone are also predictive for type 2 diabetes. This study showed that moderate alcohol consumption can increase both the total and the high-molecular form adiponectin in younger, normal-weight women. At least three weeks of moderate drinking are necessary to have these effects.

References

Joosten MM, van Erk MJ, Pellis L, Witkamp RF, **Hendriks HFJ** (2011) Moderate alcohol consumption alter both leucocyte gene expression profiles and circulating proteins related to immune response and lipid metabolism in men. *British Journal of Nutrition*, 108(4):620-627.

Joosten MM, Witkamp RF and **Hendriks HFJ** (2011) Alterations in total and high-molecular-weight adinopectin after 3 weeks of moderate alcohol consumption in premenopausal women. *Metabolism Clinical and Experimental*, 60(8):1058-1063.

The reduction of adolescent alcohol misuse: examining the potential universal effects of a targeted prevention programme (2008) (EA 08 22)

Mackie C, King's College London, UK

Alcohol misuse by young people is a significant and escalating problem in Europe. Delaying the onset of adolescent drinking would have a major impact on reducing both the social and health costs associated with adolescent alcohol misuse. Universal prevention programmes that target the general adolescent population have been met with limited success.

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The implication of this study is that by reducing opportunities for alcohol use and attitudes surrounding drinking behaviours, the targeted intervention might transfer its effects to the general adolescent population.

Publications

Conrod PJ, O'Leary-Barrett M, Newton N, Topper L, Castellanos-Ryan N, Mackie C and Girard A (2013) Effectiveness of a Selective, Personality-Targeted Prevention Program for Adolescent Alcohol Use and Misuse A Cluster Randomized Controlled Trial. *JAMA Psychiatry,* 70(3):334-342.

Alcohol Consumption and Mortality Risk among Patients with Cardiovascular Disease: a Meta-Analysis and a Longitudinal Study on Patients with Coronary Artery Disease Undergoing Surgical Revascularization (2008) (EA 08 27)

de Gaetano G, Università Cattolica del Sacro Cuore, Centro di Ricerche e Formazione ad Alta Tecnologia nelle Scienze Biomediche, Campobasso, Italy*

*** Present address: Department of Epidemiology and Prevention, IRCCS Neuromed, Pozzilli, Italy**

This research project aimed to investigate the association between alcohol consumption and mortality risk in subjects with previous CVD. Results of a large meta-analysis and a review show that light to moderate alcohol consumption in significantly associated with a lower incidence of cardiovascular and all-cause mortality in patients with cardiovascular disease. Additionally, the project investigated in a pilot study the association between alcohol consumption and short and long-term prognosis after surgical revascularization (CABG). Results show no significant differences in the major outcomes in relation to alcohol intake, possibly due to the small patient sample examined. The feasibility of a larger study was checked, to improve the power of the study and to investigate the relationship between alcohol consumption and short term outcomes (especially atrial fibrillation) among coronary artery disease patients undergoing a coronary artery bypass graft. This research shows that the beneficial effect of moderate alcohol consumption on cardiovascular risk does apply not only to healthy people but also to patients with a history of ischaemic heart disease. Thus alcohol in moderation may contribute to both primary and secondary prevention of cardiovascular disease.

Publications

Costanzo S, De Curtis A, di Niro V, Olivieri M, Morena M, De Filippo CM, Caradonna E, Krogh V, Serafini M, Pellegrini N, Donati MB, de Gaetano G, Iacoviello L; Polyphemus Observational Study Investigators. (2015) Postoperative atrial fibrillation and total dietary antioxidant capacity in patients undergoing cardiac surgery: The Polyphemus Observational Study. *Journal of Thoracic and Cardiovascular Surgery*. 149(4):1175-82.e1.

Costanzo S, Di Castelnuovo A, Benedetta Donati M, Iacoviello L and **de Gaetano G** (2011) Alcohol consumption in relation to vascular and total mortality in patients with diabetes, hypertension or history of cardiovascular disease: a meta-analysis. *Journal of Wine Research*, 22(2):119-122.

Costanzo S, Di Castelnuovo A, Benedetta Donati M, Iacoviello L and **de Gaetano G** (2010) Alcohol consumption and mortality in patients with cardiovascular disease: a meta-analysis. *Journal of American College of Cardiology*, 55(13):1339-1347.

Costanzo S, Di Castelnuovo A, Benedetta Donati M, Iacoviello L and **de Gaetano G** (2010) Cardiovascular and overall mortality risk in relation to alcohol consumption in patients with cardiovascular disease. *Circulation*, 121(17):1951-1959.

Longitudinal study of social and cognitive risks for alcohol misuse in first year university students (2009) (EA 09 04)

Moore S, Violence and Society Research Group, Cardiff University, Cardiff, UK

This research assessed the barriers, acceptability and validity of text messaging to collect daily alcohol consumption data among young people transitioning from school to university. University life is perceived as strongly associated with alcohol use. However, alcohol perceptions are far from stable. As drinkers move across contexts, the perceived acceptability of alcohol can change. The research also explored the feasibility of a text-delivered intervention. Results show that greater alcohol use was observed on Fridays, Saturdays and Wednesdays as well as notable celebratory events. Interview data indicated that text messaging was acceptable to participants and preferred over email and web-based methods. Additionally, results suggested that a simple text delivered intervention might be effective in eliciting a reduction in alcohol consumption in a future trial.

Publications

Moore SC, Crompton K, van Goozen S, van den Bree M, Bunney J and Lydall E (2013) A feasibility study of short message service text messaging as a surveillance tool for alcohol consumption and vehicle for interventions in university students. *BMC Public Health*, 13:1011.

Moore SC (2010) Substitution and complementary in the face of alcohol-specific policy interventions. *Alcohol and Alcoholism*, 45(5):403-408.

The role of alcohol consumption in the etiology of lymphatic malignancies (2009) (EA 09 10)

Verhage BAJ, Department of Epidemiology, University of Maastricht, Maastricht, The Netherlands

This research examines the association between alcohol consumption and hematologic malignancies; a group of neoplasms arising in lymphoid and myeloid cells throughout the body. Data from a large prospective cohort on diet and cancer in men and women in the Netherlands was used. The results do not show a clear association between alcohol consumption and lymphoid and myeloid neoplasms. For specific alcohol beverages no associations were found as well. The study did not find an association between other dietary factors and the risk of lymphoid and myeloid neoplasms. Additionally, alcohol did not seem to modify the association between folate and these neoplasms.

Publications

Heinen MM, van den Brandt PA, Schouten LJ, Goldbohm RA, Schouten HC and Verhage BAJ (2014) Dietary one-carbon nutrient intake and risk of lymphoid and myeloid neoplasms: results of the Netherlands cohort study. *Cancer Epidemiology, Biomarkers and Prevention*, 23(10): 2153-2164.

Heinen MM, Verhage BAJ, Schouten LJ, Goldbohm RA, Schouten HC and van den Brandt PA (2013) Alcohol consumption and risk of lymphoid and myeloid neoplasms: results of the Netherlands cohort study. *International Journal of Cancer*, 133(7):1701-1713.

Training executive functions to reduce alcohol abuse: restoring control over automatic impulses to drink alcohol (2009) (EA 09 13)

Houben K, Faculty of Psychology and Neuroscience, University of Maastricht, Maastricht, The Netherlands

The hypothesis of this research project was that training working memory and response inhibition increase executive control over automatic impulses to drink alcohol and that training these executive functions may decrease alcohol use. The results from different studies show that training working memory (the ability to maintain goal-relevant information) and response inhibition may be effective strategies to reduce alcohol use by increasing control over automatic impulses to drink alcohol. Integrating such training programs with online cognitive and motivational interventions could improve helping self-selected problem drinkers to reduce their drinking.

Publications

Wiers RW, Houben K, Fadardi JS, van Beek P, Rhemtulla M and Cox WM (2015) Alcohol cognitive bias modification training for problem drinkers over the web. *Addictive Behaviors*, 40:21-26.

Houben K, Havermand RC, Nederkoorn C and Jansen A (2012) Beer à no-go: learning to stop responding to alcohol cues reduces alcohol intake via reduced affective associations rather than increase response inhibition. *Addiction*, 107(7):1280-1287.

Houben K, Wiers RW and Jansen A (2011) Getting a grip on drinking behavior: training working memory to reduce alcohol abuse. *Psychological Science*, 22(7):968-975.

Houben K, Nederkoorn C, Wiers RW and Jansen A (2011) Resisting temptation: decreasing alcohol-related affect and drinking behavior by training response inhibition. *Drug and Alcohol Dependence*, 116(1-3):132-136.

Houben K (2010) Stoppen met drinken kan je leren: 'Een impulsieve en een reflectieve route naar gedragsverandering'. *Psychologie and Gezondheid*, 38(4):153-162.

Analysis of the molecular mechanisms of the synergistic effect of chronic alcohol consumption and obesity on the development and progression of hepatic steatosis, steatohepatitis and fibrosis (2009) (EA 09 20)

Stickel F, Institute if Clinical Pharmacology and Visceral Research, University of Bern, Bern, Switzerland

The aim of this research was to establish and analyze an experimental animal model to investigate the combined effect of chronic alcohol administration and a high-fat diet of liver injury. The first series of animal experiments establishes a novel animal model of chronic alcohol administration and diet-induced fatty liver, and finds an additive effect of either condition on liver fat content, hepatitis activity and liver tissue scarring in mice. The next steps of this research are to focus on therapeutic inventions with the potential to offset these effects.

Publications

Mahli A, Thasler WE, Patsenker E, Müller S, Stickel F, Müller M, Seitz HK, Cederbaum AI, Hellerbrand C. (2015) Identification of cytochrome CYP2E1 as critical mediator of synergistic effects of alcohol and cellular lipid accumulation in hepatocytes in vitro. *Oncotarget*, 6:41464-78.

Patsenker E, Stoll M, Millonig G, Agaimy A, Wissniowski T, Schneider V, Mueller S, Brenneisen R, Seitz HK, Ocker M, **Stickel F** (2011) Cannabinoid receptor type I modulates alcohol-induced liver fibrosis. *Molecular Medicine*, 17(11-12):1285-1294.

Gäbele E, Dostert K, Dorn C, Patsenker E, **Stickel F** and Hellerbrand C (2011) A new model of interactive effects of alcohol and high-fat diet on hepatic fibrosis. *Alcohol: Clinical and Experimental Research*, 35(7):1361-1367.

Stickel F and Seitz HK (2010) Alcoholic steatohepatitis. *Best Practice & Research Clinical Gastroenterology*, 24(5):683-693.

Peer group influences on the relationship between depressive symptoms and substance misuse in adolescence (2010) (EA 10 08)

Van den Bree M B M, Department of Psychological Medicine, University of Wales, Cardiff, Wales, UK

The study found that adolescents who suffered from depressed mood in mid adolescence were at higher risk of having alcohol problems in late adolescence as well as in early adulthood. This link was indirect as adolescents who experienced depressed mood in mid-adolescence were more likely to become friends with peers who engaged in substance use and delinquent activities (i.e., shoplifting, setting things on fire). Engaging with this peer group, subsequently, increased the risk of problem alcohol use in late adolescence and early adulthood. Adolescents with low mood who do not form such relationships may not develop alcohol problems. Similarly, the study found that adolescents who engage in problem alcohol use in mid adolescence were more likely to experience depressed mood in late adolescence if they affiliated with deviant friends who engaged in delinquent activities or substance use. The study found that high levels of parental monitoring (e.g., having to ask for permission before going out) could reduce the impact of a deviant peer group on the development of problem alcohol use in adolescents suffering from depressed mood.

The results also show that sexual minority adolescents are more likely to drink heavily in early adulthood (at age 18) than adolescents who identified as heterosexuals. The risk of problem alcohol use in this group was partly due to high levels of depressed mood experienced by these youths in late adolescence.

Publications

Pesola F, Shelton KH, Heron J, Munafo M, Hickman M, van den Bree M (2015) The developmental relationship between depressive symptoms in adolescence and harmful drinking in emerging adulthood: the role of peers and parents. *Journal of Youth and Adolescence*, 44(9): 1752-66.

Pesola F, Shelton KH, Heron J, Munafo M, Maughan B, Hickman M and van den Bree M (2015) The mediating role of deviant peers on the link between depressed mood and harmful drinking. *Journal of Adolescent Health*, 56(2):153-159.

Pesola F, Shelton KH and van den Bree M (2014) Sexual orientation and alcohol problem use among UK adolescents: an indirect link through depressed mood. *Addiction*, 109(7):1072-1080

Changing the vulnerable brain: a neuromodulation study in alcohol dependence (2010) (EA1027)

Goudriaan A E, University of Amsterdam, Amsterdam UMC, Department of Psychiatry, location Meibergdreef, and Arkin Amsterdam, The Netherlands

Abstinence is one of the main goals of addiction treatment, but over 50% of alcohol dependent patients relapses within the first year. Relapse has been related to craving and impaired processing of emotional information. The results of this project indicate that alcohol dependent patients have reduced activation in the brain during an emotion regulation task, and that the higher craving can be reduced by applying rTMS. Non-invasive brain stimulation techniques like rTMS can reduce craving levels as reported in our meta-analysis. In addition, rTMS can increase the ability to regulate negative emotions. This indicates that rTMS may be clinically relevant and that the study of rTMS as an intervention for alcohol dependence should be focused on in future intervention studies.

Publications

Schluter RS, Jansen JM, van Holst RJ, van den Brink W, Goudriaan AE (2018). Differential effects of left and right prefrontal high-frequency repetitive transcranial magnetic stimulation on resting-state functional magnetic resonance imaging in healthy individuals. *Brain Connectivity,* 8(2): 60-67.

van Timmeren T, Jansen JM, Caan MW, Goudriaan AE, van Holst RJ (2016). White matter integrity between left basal ganglia and left prefrontal cortex is compromised in gambling disorder. *Addiction Biology,* 22(6): 1590-1600.

Jansen JM, van Wingen G, van den Brink W, Goudriaan AE (2015) Resting state connectivity in alcohol dependent patients and the effect of repetitive transcranial magnetic stimulation. *European Neuropsychopharmacology*, 25(12): 2230-2239.

Jansen JM, van Holst RJ, van den Brink W, Veltman DJ, Caan MWA, Goudriaan AE (2015) Brain function during cognitive flexibility and white matter integrity in alcohol-dependent patients, problematic drinkers and healthy controls. *Addiction Biology,* 20(5): 979-989.

Goudriaan A (2014) Stepping up the game. *Addiction*, 109(9): 1409-1413.

Jansen JM, Daams JG, Koeter MWJ, Veltman DJ, van den Brink W and Goudriaan AE (2013) Effects of non-invasive neurostimulation on craving: a meta-analysis. *Neuroscience and Biobehavioral Reviews*, 37(10): 2472-2480.

Binge drinking: Cognitive and brain impairment and their association with immune response (2010) (EA 10 30)

Campanella S, Medical Psychology Laboratory, Brugmann Hospital ULB, Brussels, Belgium

This study investigated the effect of binge drinking in University students on the brain in relation to the immune response. Binge drinking, especially in adolescents, can induce progressive activation of the immune system. Related to that, an increase in pro-inflammatory mediators may lead to modifications of specific brain functions. Binge drinking also alters cognitive performance, because of changes in the brain that facilitate normal behavioural performance. More insight in the association between neuro-cognitive impairments and neuro-inflammation would help to identify adolescents at risk from cognitive impairment and educate and advise such individuals as there is substantial evidence that long term chronic alcoholism may ensue. Binge alcohol consumption leads to changes in cerebral responses that may be considered as vulnerability factors for developing adult substance use disorders.

Publications

Stefanini, C., Colivicchi, M. A., Della Corte, L., Ward, R. J., & de Witte, P. (2014). Ethane–β-Sultam Modifies the Activation of the Innate Immune System Induced by Intermittent Ethanol Administration in Female Adolescent Rats. *Journal of Alcoholism and Drug Dependence*, 2(2):150.

Ward RJ, Lallemand F and De Witte P (2014) Influence of adolescent heavy session drinking on the systemic and brain innate immune system. *Alcohol and Alcoholism*, 49(2):193-197.

Lallemand F, Ward RJ, Witte PD, Petit G, Saeremans M, et al. (2013) Changes in the Innate Immune Responses by Intermittent Ethanol Consumption May Influence Cognition in Susceptible Adolescent Binge Drinkers. *Journal of Alcoholism and Drug Dependence*. 1:114-119.

Campanella S, Peigneux P, Petit G, Lallemand F, Saeremans P, Noël X, Metens T, Nouali M, De Tiège X, De Witte P, Ward RJ and Verbanck P (2013) Increased cortical activity in binge drinkers during working memory task: a preliminary assessment through a functional magnetic resonance imaging study. *PLOS ONE*, 8(4), e6220.

Ward R, De Witte P, Lallemand F, Noël X, Campanella S, & Verbank P. (2011). S14. 3 Can Peripheral Markers Indicate Neuroinflammation? *Alcohol and Alcoholism*, 46(suppl_1), i13-i14.

Book chapters

Crichton RR and Ward RJ. Alcoholic Brain Damage, in *Metal-based neurodegeneration. From molecular mechanisms to therapeutic strategies*. 2nd edition. Wiley & Sons (2013) (ISBN:978-1-119-97714-8) 438 pages.

Roberta J Ward, Robert R Crichton and David T Dexter. Alcoholic Brain Damage, in *Mechanisms and Metal Involvement in Neurodegenerative*. Royal Society of Chemistry – Metallobiology (2013) (ISBN:978-1-84973-588-9) 230 pages.

Role of BDNF signalling in alcohol abuse: new insights from a yoked paradigm (2010) (EA 10 34)

Orru A, Laboratory of Experimental Psychopharmacology, Institute for Pharmacological Research Mario Negri, Milan, Italy

Pre-clinical data suggest that prolonged alcohol use may induce long-lasting structural and physiological change in the brain. These changes may regulate the transition from social drug use to abuse and addiction. This project investigated these changes in rats in specific situations; acute and chronic alcohol exposure, abstinence and relapse. The researchers evaluated the ability of ethanol to modify gene and protein expression of specific effectors, such as brain-derived neurotrophic factor (BDNF), known to be involved in the development and manifestations of alcohol abuse. Results show that ethanol can impact the expression of specific effectors, but it depends on certain aspects such as the brain region, the dose of ethanol, and the way of drug exposure.

Publications

Orrù A, Caffino L, Moro F, Cassina C, Giannotti G, Di Clemente A, Fumagalli F, Cervo L (2016) Contingent and non-contingent recreational-like exposure to ethanol alters BDNF expression and signaling in the cortico-accumbal network differently. *Psychopharmacology*, 233(17):3149-60.

Young people's beliefs about the benefits and risks associated with different alcoholic beverages: A comparison of the UK and France (2011) (EA 11 10)

Terry P, Department of Psychology, Kingston University, London, UK

Young adults in the UK and France have quite a limited understanding of the health consequences associated with drinking different kinds of alcoholic drink. They confuse "healthiness" (and its opposite) with issues of drink production and "naturalness"; artificial additives are widely considered to be at least as important as alcohol content when making judgments about potential adverse health effects. Next to that, the chronic effects of alcohol on health are not a serious consideration for young people in France or the UK. Alcohol's acute effects on health and well-being are recognised, but the possible long-term effects are largely overlooked because – in both countries – young people do not expect to become long-term consumers of alcohol in excess. The research demonstrates a need to make young people aware that binge-drinking, which is increasingly common in France as well as the UK, is not without long-term health risks (such as liver damage) and that these risks are not reduced by drinking beverages perceived to be healthier, e.g. wine rather than spirits.

Publications

Submitted:

Barber, V., Prior, J, and Terry, P. Young people's beliefs about, and perceptions of, different kinds of alcoholic beverage: comparing the UK and France, *British Journal of Health Psychology*, under review.

Conference presentations

Barber, V. and Terry, P. (2017) Young people's perceptions of the health effects of alcohol in two different drinking cultures. *British Psychological Society, Division of Health Psychology, Annual Meeting*, Cardiff, September 2017.

Barber, V., Prior, J. and Terry, P. (2017) Are young people in the UK and France concerned about the health effects of alcohol? *31st Conference of the European Health Psychology Society*, Padua, Italy, August 2017.

Barber, V., Prior, J. and Terry, P. (2015) Young people's beliefs about the benefits and risks associated with different alcoholic beverages: a comparison of the UK and France. *12th Annual Psychology, Health and Medicine Conference* (sponsored by the British Psychological Society), Belfast, N. Ireland, April 2015.

Understanding and promoting young people's strategies for moderate alcohol consumption (2011) (EA 11 11)

de Visser R, University of Sussex, Falmer, UK

In this study skills and strategies were identified that could be taught to young people to enhance their capacity to drink in moderation.

Based on questionnaire data it is suggested there is support among young people for teaching alcohol refusal skills and strategies. Based on interviews a range effective strategies and techniques used by young people to resist expectations to drink and direct pressure to drink have been identified. These strategies and tactics were used to develop video resources. Finally, how these videos were received by young people and professionals working with young people was evaluated.

This study has shown that there is value in using video materials to teach young people skills and strategies to better respond to expectations to drink and direct pressure to drink. The results so far indicate support for the general approach of teaching alcohol refusal skills.

Publications

Graber R, de Visser R, Abraham C, Memon A, Hart A & Hunt K (2016) Staying in the 'sweet spot': A resilience-based analysis of the lived experience of low-risk drinking and abstention among British youth. *Psychology & Health*, 31(1): 79-99.

De Visser RO, Hart A, Abraham C, Graber R, Scanlon T and Memon A (2014) How alike are young non-drinkers, former-drinkers, low-risk drinkers, and hazardous drinkers? *Addictive Behaviors*, 39(8): 1258-1264.

De Visser RO, Hart A, Abraham C, Memon A, Graber R and Scanlon T (2014) Which alcohol control strategies do young people think are effective? *Drug and Alcohol Review*, 33(2) :144-151.

Evaluation of the risk and benefits of moderate beer consumption in 1,000 subjects at high cardiovascular risk using a new beer biomarker (2011) (EA 11 17)

Lamuela-Raventos RM, Department of Nutrition and Food Science, School of Pharmacy, University of Barcelona, Barcelona, Spain

This project first developed and validated a method for the determination of beer prenyflanavoids in human urine. Beer prenylflavanoids constitute a potential new potent biomarker of beer consumption. This method was then applied to analyse human urine from two different clinical trials to evaluate the usefulness, specificity and selectivity of the proposed new biomarker. The results show that isoxanthohumol is an effective new biomarker of beer consumption, with great sensitivity and specificity. Urinary excretion of isoxanthohumol showed dose-response behaviour.

In nutrition and food studies, nutritional biomarkers have several advantages over self-reported data, since they are more precise and provide more objective assessments than data obtained from food questionnaires. Using this new biomarker of beer intake, we can evaluate the possible risks and benefits of moderate beer consumption in human health more objectively, avoiding the bias from Food Frequency Questionnaires (FFQ).

Publications

Quifer-Rada P, Vallverdu-Queralt A, Martinez-Huélamo M, Chiva-Blanch G, Jauregui O, Estruch R and Lamuela-Raventos RM (2015) A comprehensive characterisation of beer polyphenols by high resolution mass spectrometry (LC-ESI-LTQ-Orbitrap-MS). *Food Chemistry*, 169:336-343, 2014-DOI: 10.1016/j.foodchem.2014.07.154, 2015-169 :336-343.

Chiva-Blanch G, Magraner E, Condines X, Valderas-Martinez P, Roth I, Arranz S, Casas R, Navarro M, Hervas A, Siso A, Martinez-Huélamo M, Vallverdu-Queralt A, Quifer-Rada P, Lamuela-Raventos RM and Estruch R (2014) Effects of alcohol and polyphenols from beer on atherosclerotic biomarkers in high cardiovascular risk men: a randomized feeding trial. *Nutrition, Metabolism & Cardiovascular Diseases*, 25(1):36-45.

Quifer-Rada P, Martinez-Huelamo M, Chiva-Blanch G, Jauregui O, Estruch R and Lamuela-Raventos RM (2014) Urinary isoxanthohumol is a specific and accurate

biomarker of beer consumption. *The Journal of Nutrition – Nutrional Epidemiology (ASN)*, 144(4):484-488.

Quifer-Rada P, Martinez-Huelamo M, Jauregui O, Chiva-Blanch G, Estruch R, **Lamuela-Raventos RM** (2013) Analytical condition setting is a crucial step in the quantification of unstable polyphenols in acidic conditions: analysing prenylflavanoids in biological samples by LC-ESI-MS/MS. *Analytical* Chemistry, 85(11):5547-5554.

Psycho-physiological paradigms as predictors of relapse in the treatment of alcohol dependent subjects (2011) (EA 11 23)

Rubio G, Faculty of Medicine, Complutense University, Madrid, Spain

This research investigated how three psychophysiological processes in alcohol dependent patients are related to alcohol relapse. The three investigated processes include: attentional biases, the phenomenon whereby individuals find they are distracted by objects or information that is relevant to them (in this case: alcohol related stimuli); startle magnitude, involves the motivational response to alcohol; and inhibitory control where an individual inhibits their impulses or response to stimuli. The results show that alcohol dependent patients show more attentional bias compared to controls. Patients also had a lower startle magnitude than controls, meaning that they considered alcohol pictures more appetitive. Patients exhibited higher reaction times than controls for inhibiting GO-NoGO actions (as a measure of inhibitory control). All three processes were associated with alcohol relapse. Overall, the best psychophysiological predictors for relapse were attentional bias and difficulty with inhibitory control. Moreover, inhibitory mechanisms appear to be more relevant than the motivational ones in order to explain relapses of alcohol dependent patients. Inhibitory mechanisms are involved in alcohol dependence and in the severity of alcohol dependence, but motivational response to alcohol cues is related to alcohol dependence.

Publications

Sion A, Jurado-Barba R, Alonso MJ, Rubio-Valladolid G. (2017) Inhibitory capacity assessment in alcohol dependent patients: translation from a modified stop signal task. *Actas Espanolas de Psiquiatria*. 45(1):21-31.

M. Marin, G. Rubio, R. Jurado, G. Ponce, I. Martinez, M.J. Alvarez, S. Moratti. (2014) EPA-0843 – Relationship between psychophysiological processes involved in alcohol dependence. *European Psychiatry*. 29(Supplement 2): S674.

Congress participation

Ana Sion, Marta Marín, Rosa Jurado, Isabel Martínez, Gabriel Rubio Valladolid. **"Papel de los procesos inhibitorios en la recaída de pacientes dependientes del alcohol"**. At the XLIV Jornadas Nacionales Socidrogalcohol. 11-13 Mayo 2017, Oviedo.

R. Jurado. **Regulación de procesos inhibitorios y su papel en las recaídas de dependientes del alcohol.** At the XVIII Jornadas Nacionales de Patología Dual. 14-16 Abril 2016. Madrid.

Rosa Jurado-Barba, Maria Jose Alvarez-Alonso, Isabel Martinez-Gras, Gabriel Rubio **Psychophysiological cognitive processes implied in alcohol dependence.** At the XVI World Congress of the World Psychiatry Association which took place in Madrid - Spain, from September 14th to September 18th, 2014.

Jurado Barba R; Álvarez MJ; Martínez Gras I; Rubio G. **Influencia de la modulación afectiva del sobresalto en el riesgo de recaídas en el consumo de alcohol.** At the VIII Simposio de la Asociación de Motivación y Emoción. Granada. 15-17 Mayo 2014.

Neurobiological and behavioural consequences of adolescent alcohol consumption; studies of causal links between early-life conditions and vulnerability for alcohol use disorders (2011) (EA 11 30)

Nylander I, Department of Pharmaceutical Biosciences, Neuropharmacology, Addiction and Behaviour, University of Uppsala, Sweden

Adolescent drug exposure will affect the development of the brain and thereby cause changes in behaviour and in propensity for alcohol use disorders (AUD). This study investigated the impact of adolescent alcohol exposure on brain opioids, dopamine and brain function and also its interaction with early-life psychosocial stress versus no stress (maternal separation in an animal model).

The results show that exposure to rearing conditions related to early-life stress or adolescent alcohol drinking change the behavioural development with regard to, for example, risk assessment behaviour and alter the response to alcohol later in

life. In addition, adolescent voluntary drinking affects endogenous morphine-like substances in the brain and these effects were seen regardless of rearing in early-life protective/beneficial conditions or conditions related to early-life psychosocial stress. Results from our studies shows that the environmental influence in adolescence have a longstanding impact on the brain, on responses to alcohol and on the susceptibility for excessive alcohol consumption and AUD. Both the behavioural effects and the neurobiological effects are of interest since altered risk assessment behaviour and deranged opioid function in the brain has been associated with vulnerability for alcohol use disorders.

Publications

Todkar A, Granholm L, Aljumah M, Nilsson KW, Comasco E, Nylander I (2016) HPA axis gene expression and DNA methylation profiles in rats exposed to early life stress, adult voluntary ethanol drinking and single housing. *Frontiers in Molecular Neuroscience*, 8:90.

Granholm L, Rowley S, Ellgren M, Segerström L, Nylander I (2015) Impact of adolescent ethanol exposure and adult amphetamine self-administration on evoked striatal dopamine release in male rats. *Psychopharmacology*, 232:4421-4431

Bendre M, Comasco E, Nylander I, Nilsson KW (2015) Effect of voluntary alcohol consumption on *Maoa* expression in the mesocorticolimbic brain of adult male rats previously exposed to prolonged maternal separation. *Translational Psychiatry,* 5(12): e690.

Vrettou M, Granholm L, Todkar A, Nilsson KW, Wallén-Mackenzie Å, Nylander I, Comasco E (2015) Ethanol affects limbic and striatal presynaptic glutamatergic and DNA methylation gene expression in outbred rats exposed to early-life stress. *Addiction Biology*, 22(2): 369-380.

Palm S and Nylander I (2014) Dopamine release dynamics change during adolescence and after voluntary alcohol intake. *PLOS ONE*, 9(5): e96337.

Palm S, Momeni S, Lundberg S, Nylander I, Roman E (2014) Risk-assessment and risk-taking behavior predict potassium- and amphetamine-induced dopamine release in the dorsal striatum of rats. *Frontiers in Behavioral Neuroscience*, 8: 236.

Palm S and Nylander I (2014) Alcohol-induced changes in opioid peptide levels in adolescent rats are dependent on housing conditions. *Alcoholism: Clinical and Experimental Research*, 38(12):2978-2987.

Daoura L, Nylander I and Roman E (2013) Qualitative differences in pup-retrieval strategies in a maternal separation paradigm. *Journal of Behavioral and Brain Science*, 3:603-616.

Palm S, Daoura L, Roman E and Nylander I (2013) Effects of rearing conditions on behaviour and endogenous opioids in rats with alcohol access during adolescence. *PLOS ONE*, 8(10):e76591.

Nylander I and Roman E (2013) Is the rodent maternal separation model a valid and effective model for studies on the early-life impact on ethanol consumption? *Psychopharmacology*, 229:555-569.
Nylander I and Roman E (2012) Neuropeptides as mediators of the early-life impact on the brain; implications for alcohol disorders. *Frontiers in Molecular Neuroscience*, 5(77).

Identification of a genetic risk-factor for alcohol seeking and relapse (2011) (EA 11 35)

de Vries T, VU University, Amsterdam, The Netherlands

The main aim of the project was to prove that a genetically engineered level of impulsivity is a vulnerability factor for alcohol addiction.
The results show that in mice enhanced impulsivity coincides with increased motivation to take alcohol, as well as relapse vulnerability. Further studies are needed to determine whether impulsivity/inattention and alcohol seeking depend on common or separate molecular mechanisms.
The identification of the gene (Nrg3) that modulates the level of impulsivity and alcohol addiction related behaviour in mice provides a molecular entry into a better understanding of alcohol addiction.

Publications

Loos M, Staal J, Smit AB, de Vries TJ, Spijker S (2013) Enhanced alcohol self-administration and reinstatement in a highly impulsive, inattentive recombinant inbred mouse strain. Frontiers in *Behavioral Neuroscience*, 7(article 151).

Images of adolescent alcohol use and health in Italy. A study of teenagers' drinking and societal reactions to it (2011) (EA 11 37)

Prina F, Department of Social Science, University of Turin, Italy

This study investigated the images of Italian adolescents and adults of adolescent alcohol use. Results show how young people's images about drinking are quite traditional (as they have a negative attitude towards drunkenness give lot

importance to conviviality of drinking) but also new elements have to be considered especially the rise of so-called pharmaceutical drinking.
Adults' images of youth drinking diverge from young people's ones. Particularly adults overestimate young people's appreciation for drunkenness and at the same time they underestimate the pharmaceutical use of alcohol, aimed to face life's troubles or to enhance social performance. Moreover, adults understate young peoples' risk awareness and seem to be uncertain about what alcohol-specific parenting practices are the best, as they perceive an ongoing change in young people's lifestyles.
This research provides new crucial insights to improve alcohol policies and set effective prevention strategies. Particularly:

- it is outlined how caring adults need more information about what kind of parenting practices related to alcohol are effective;
- gaps of understanding youth drinking between adults and young people have to be filled;
- the growing of youth drinking in order to cope with troubles requires more attention;
- effects of the non-compliance of the formal norms (first of all by adults) have to be valued;
- a general reflection is needed about the dominance of moral panic spread by media about youth drinking and its effects.

Publications

Rolando S and Katainen A (2014) Images of alcoholism among adolescents in individualistic and collectivistic geographies. *Nordic Studies on Alcohol and Drugs*, 31:189-205.

Rolando S, Beccaria F, Petrilli E and Prina F (2014) Adults' views of young people's drinking in Italy: an explorative qualitative research. *Drugs: education, prevention and policy*, 21(5): 388-397.

Petrilli E, Beccaria F, Prina F and Rolando S (2014) Images of alcohol among Italian adolescents – Understanding their point of view. *Drugs: education, prevention and policy*, 21(3): 211-220.

Dietary patterns and nutrient intakes of beer consumers compared to consumers of other (non-) alcoholic drinks (2011) (EA 11 45)

Kees de Graaf, Wageningen University, The Netherlands

A light to moderate intake of alcohol has been shown to have beneficial effects on coronary heart disease. Some studies show that this beneficial effect is stronger for specific alcoholic beverages, such as wine. Yet, it is not known whether wine itself is more beneficial compared to other alcoholic beverages, or that dietary patterns and nutrient intakes might play a role.

This research, based on observational studies, has shown that consumption of beer, wine, and spirits is associated with specific dietary habits, e.g. a healthier diet for wine consumers and less healthy dietary habits for those with a beer preference. However, these differences in dietary habits were largely – if not completely – explained by socio-demographic and lifestyle factors. Hence, the different health effects of beer, wine, and spirits are probably caused by the underlying differences in socio-demographics and lifestyle of the study population.

Therefore, it seems that alcoholic beverage preference may not be independently related to diet and health status but is merely a proxy for socio-demographic and lifestyle factors. It is important to keep all these factors in mind when studying the effects of beer, wine, and spirits on health.

Publications

Sluik D, Jankovic N, Hughes M, O'Doherty MG, Schöttker B, Drygas W, Rolandsson O, Männistö S, Ordóñez-Mena JM, Ferriere J, Bamia C, de Gaetano G, Kiefte-De Jong JC, Franco OH, Sluijs I, Spijkerman AMW, Sans S, Eriksson S, Kromhout D, Trichopoulou A, Wilsgaard T, Brenner H, Kuulasmaa K, Laatikainen T, Söderberg S, Iacoviello L, Boffetta P, Kee F and Feskens EJM (2017) Alcoholic beverage preference and diabetes incidence across Europe: the Consortium on Health and Ageing Network of Cohorts in Europe and the United States (CHANCES) project. *European Journal of Clinical Nutrition*, 71:659–668.

Sluik D, Jankovic N, O'Doherty MG, Geelen A, Schöttker B, Rolandsson O, Kiefte - de Jong JC, Ferrieres J, Bamia C, Fransen HP, Boer JMA, Eriksson S, Martinez B, Huerta JM, Kromhout D, de Groot LCPGM, Franco OH, Trichopoulou A, Boffetta P, Kee F and Feskens E (Dr de Graaf's team) (2016) Alcoholic beverage preference and dietary habits in elderly across Europe: analyses within the consortium on health and ageing: network of cohorts in Europe and the United States (CHANCES) project. *PLoS ONE*, 11(8): e0161603.

Sluik D, Brouwer-Brolsma EM, de Vries JHM, Geelen A, Feskens E (Dr de Graaf's team) (2016) Associations of alcoholic beverage preference with cardiometabolic and lifestyle factors: the NQplus study. *BMJ open*, 6(6):e010437.
Sluik D, Bezemer R, Sierksma A and Feskens E (Dr de Graaf's team) (2016) Alcoholic beverage preference and dietary habits: a systematic literature review. *Critical Reviews in Food Science and Nutrition*, 56(14):2370-2382.

The pathway of early life social economic status to midlife alcohol use to later life ill health (2012) (EA 12 06)

Min Yang, University of Nottingham, UK

This research focused on the complex and indirect relationships between socio-economic status (SES), alcohol use and health problems using a life-course approach. It attempted to throw light on the pathway of early life SES to midlife alcohol use and then to later life health outcomes, with particular reference to health inequalities. To investigate this, 50 years of data from the 1958 British National Birth Cohort study were used.

The main findings are that those with parents in a low socioeconomic status (PSES) are more likely to report worse health outcomes at age 50 compared to the higher PSES trajectory groups and this association is moderated by different levels of midlife alcohol consumption for both men and women. The bottom PSES trajectory group are more likely to consume less alcohol throughout the 27-year period compared to the higher PSES trajectory groups.

At age 23, the bottom PSES group drank more beer on a weekly basis, whereas the top 25% PSES group drank more wine.

Significant risk factors for alcohol use include getting into trouble with the police at age 16, being more aggressive, the teacher's views of the parents being overly interested in the child's education, drinking more alcohol and spending more money on alcohol at age 16. Significant protective factors include white ethnicity and weekly outings with parents at age 11.

Female cohort members' midlife drinking was shown to have a more direct impact on the later life health outcomes at age 50 compared to the men.

This research provides information that will help target health promotion messages that are appropriate to different groups of people (men and women; different socioeconomic groups), at different times across the lifespan, and for different

beverages (beer versus wine). Furthermore, early risk and protective factors have been identified, and these can be addressed in schools and family health initiatives.

Publications

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The effects of psychosocial factors upon risk of developing alcohol use disorders. A longitudinal study (2012) (EA 12 10)

Flensborg T, Institute of Public Health, University of Copenhagen, Denmark

People's overall evaluation of their quality of life/vital exhaustion is a strong predictor of alcohol use disorder (AUD) risk. Social network is a predictor of later development of AUD. It is hypothesized that especially the content i.e. the qualitative experience of one's network is of importance to prevent excess alcohol drinking and thereby a possible development of AUD.
The results of this study show that living alone and not being married or cohabiting with a partner were predictors of developing AUD use disorder among men. Further, frequent contact with friends was associated with higher risk of AUD among both sexes.
A second study found that vital exhaustion was significantly associated with higher risk of AUD in both men as women. Hence, for both genders, the risk of AUD increased dose-dependently with increasing vital exhaustion. Individuals who reported a high vital exhaustion score had a 2- to 3-fold risk of AUD in both men and women.
A third study showed that the accumulation of life events in childhood, adulthood and work life was not associated with increased risk of AUD. A higher risk of AUD was, however, indicated in men and women suffering serious economic problems, and in women being placed in care outside of the home during childhood.

Publications

Just-Østergaard E, Mortensen EL, Flensborg-Madsen T. (2018) Major life events and risk of alcohol use disorders: a prospective cohort study. *Addiction*, 113(1):25-33.

Mikkelsen SS, Tolstrup JS, Becker U, Mortensen EL, Flensborg-Madsen T. (2015) Social network as predictor of onset of alcohol use disorders: A prospective cohort study. *Comprehensive Psychiatry*, 61: 57-63.

Just-Østergaard E, Mortensen EL, Tolstrup J, Flensborg-Madsen T. Vital exhaustion and risk of alcohol use disorders: a prospective cohort study. *Journal of Psychosomatic Research*. In review, 2018.

Neutrophil function in acute alcoholic hepatitis and alcohol-induced liver toxicity utilising a novel in vitro model of acute liver injury (2012) (EA 12 13)

Shawcross D L, Institute of Liver Study, King's College, London, UK

Sepsis and resultant organ failure are frequently the cause of death in patients with acute alcoholic hepatitis. This research investigated the defective pathways of the immune system's response to infection in alcohol-induced liver injury. Neutrophils (a type of white blood cells) play a key role in hepatocellular damage and susceptibility to infection. The underlying mechanism is however poorly understood. Data show that in patients with acute alcoholic hepatitis, neutrophils demonstrate reduced expression of receptors that play a role in the immune system. Additionally, neutrophils fail to appropriately up-regulate these receptors in response to bacteria. Overall, results show impaired neutrophil response to bacterial stimulus in alcohol-related liver injury which could lead to increased susceptibility to infection.

Publications

Tranah TH, Vijay GKM, Ryan JM, Abeles RD, Middleton PK, Shawcross DL (2017) Dysfunctional neutrophil effector organelle mobilization and microbicidal protein release in alcohol-related cirrhosis. *American Jouranl of Physiology. Gastrointestinal and Liver Physiology,* 313(3):G203-G211.

Markwick LJ, Riva A, Ryan JM, Cooksley H, Palma E, Tranah TH, Manakkat Vijay GK, Vergis N, Thursz M, Evans A, Wright G, Tarff S, O'Grady J, Williams R, Shawcross DL, Chokshi S (2015) Blockade of PD1 and TIM3 restores innate and adaptive immunity in patients with acute alcoholic hepatitis. *Gastroenterology*, 148(3):590-602.

Taylor NJ, Manakkat GK, Abeles RD, Auzinger G, Bernal W, Ma Y, Wendon A and Shawcross DL (2014) The severity of circulating neutrophil dysfunction in

patients with cirrhosis is associated with 90-day and 1-year mortality. *Alimentary Pharmacology & Therapeutics*, 40:705-715.

Brain and plasma epigenetic markers for alcohol addiction and its cognitive deficits (2012) (EA 12 21)

Lopez-Moreno J A, Department of Psychobiology, Faculty of Psychology, Complutense University, Madrid, Spain

The aim of this study was to investigate the association between epigenetic gene expression in brain and plasma under several operant alcohol self-administration procedures.

These findings should allow: the unravelling of the role of the expression of epigenetic genes in alcohol addiction and its cognitive deficits and to discover novel central and peripheral epigenetic markers for alcohol addiction

The results have demonstrated that histone deacetylases, a type of genes encoding for proteins that control gene expression, are dysregulated after the consumption of alcohol. During the first exposure to alcohol, the expression of histone deacetylases is reduced; however, when the individual repeatedly uses alcohol the expression of histone deacetylases is normalized or in most cases, increased. This has been shown in blood samples and using humans and rats.

In addition, one study focused on the effects of a pharmacological treatment (topiramate) in the context of the dual dependence of alcohol and cocaine in pre-clinical research (using animal models). Unlike naltrexone, another pharmacological treatment approved for the treatment of alcoholism, topiramate was able to prevent the increase of alcohol intake induced by the administration of cocaine. In this study we showed that these effects were associated with changes in gene expression (e.g., histone deacetylases) in the prefrontal cortex, a brain region that is key in the control and regulation of behaviour.

The results of another study proved that a specific mutation in the gene encoding for one enzyme that metabolizes the endocannabinoids (C385A CC *FAAH)*, such as anadamide, was associated with risky alcohol consumption. We replicated this finding in two independent samples of individuals suggesting that this specific gene mutation would be useful in developing early markers for individuals who are at higher risk for alcohol problems.

More recently, another two studies on this topic have been completed. The first one investigated the effects of one of the most commonly consumed energy drink worldwide, i.e. Red Bull, on alcohol consumption. One key finding was that the

effects of Red Bull on alcohol self-administration depended on the concentration: the higher the concentration of alcohol in the mix, the higher the amount of alcohol consumption. Therefore, Red Bull might be a vulnerability factor to develop alcoholism given that it intensifies the consumption of higher concentrations of alcohol. The second study examined the interaction between hypothyroidism and alcohol consumption. Hypothyroidism increased voluntary alcohol consumption and this was enhanced by thyroid hormone supplementation. Those last results suggested that hypothyroid patients would need more personalized attention in terms of ethanol consumption and the usefulness of embracing the thyroid axis in the study of alcohol addiction, including as a possible therapeutic target for the treatment of alcoholism and its comorbid disorders.

Publications

V. Echeverry-Alzate, K. M. Bühler, J. Calleja-Conde, E. Huertas, R. Maldonado, F. Rodríguez de Fonseca, C. Santiago, F. Gómez-Gallego, A. Santos, E. Giné, J. A. López-Moreno (2018).

Adult-onset hypothyroidism increases ethanol consumption. Psychopharmacology. Under review.

Roldán M, Echeverry-Alzate V, Bühhler KM, Sánchez-Diez IJ, Calleja-Conde J, Olmos P, Boehm SL, Maldonado R, Rodríguez de Fonseca F, Santiago C, Gómez-Gallego F, Giné E, Lopez-Moreno JA (2018). Red Bull® energy drink increases consumption of higher concentrations of alcohol. *Addiction Biology,* 23(5): 1094-1105.

Lopez-Moreno JA, Marcos M, Calleja-Conde J, Echeverry-Alzate V, Bühler KM, Costa-Alba P, Bernardo E, Laso F-J, de Fonseca FR, Nadal R, Paz Viveros M, Maldonado R and Giné E (2015) Histone deacetylase gene expression following binge alcohol consumption in rats and humans. *Alcoholism: Clinical and Experimental Research*, 39(10):1939-1950.

Penasco S, Mela V, Lopez-Moreno JA, Viveros MP and Marco EM (2015) Early maternal deprivation enhances voluntary alcohol intake induced by exposure to stressful events later in life. *Neural Plasticity*, Volume 2015.

Bühler KM, Giné E, Echeverry-Alzate V, Calleja-Conde J, Rodriguez de Fonseca F and Lopez-Moreno J (2015) Common single nucleotide variants underlying drug addiction: more than a decade of research. *Addiction Biology*, 20(5): 845-871.

Echeverry-Alzate V, Giné E, Bühler K-M, Calleja-Conde J, Olmos P, Gorriti MA, Nadal R, Rodriguez de Fonseca F and Lopez-Moreno JA (2014) Effects of topiramate on ethanol-cocaine interactions and DNA methyltransferase gene expression in the rat prefrontal cortex. *British Journal of Pharmacology*, 171(12):3023-3036.

Bühler K-M, Huertas E, Echeverry-Alzate V, Giné E, Molto E, Montoliu L and Lopez-Moreno JA (2014) Risky alcohol consumption in young people is associates with the fatty acid amide hydrolase gene polymorphism C385A and affective rating of drug pictures. *Molecular Genetics and Genomics*, 289(3): 279-89.

The consequences of binge-drinking on learning and memory. How does it work in the brain? (2012) (EA 12 28)

Pierrefiche O, Faculty of Pharmacy, University of Picardie Jules Verne, Amiens, France

This project investigated in adolescent rats the effects of a few binges of ethanol on synaptic plasticity, the cellular mechanisms of learning and memory and on rat's memory performance. The results show that two binges only, can induce cognitive deficits that remain for up to two days after elimination of ethanol. This demonstrates that even a relatively low amount of alcohol is detrimental to cognitive function and that the negative effects on memory performance last for a long period after ethanol elimination from the body.

Publications

Silvestre de Ferron B, Bennouar K-E, Kervern M, Alaux-Cantin S, Robert A, Rabiant K, Antol J, Naassila M and **Pierrefiche O** (2015) Two binges of ethanol a day keep the memory away in adolescent rats: key role for GLUN2B subunit. *International Journal of Neuropsychopharmacology*, 19(1).

More effective change of alcohol-related cognitive biases via enhancement of mediating processes (2012) (EA 12 39)

Gladwin T, University of Amsterdam, The Netherlands

New treatments have been developed for alcohol addiction, but it still needs to be determined what the most effective ways are to help patients. This research focused on improving the ability to treat patients with alcohol dependence using novel techniques involving the stimulation of the brain to enhance learning. The results suggested that transcranial Direct Current Stimulation (tDCS) can reduce craving and relapse rates, in particular in combination with approach-avoidance training, but confirmatory replications are needed. Next steps in the combination of tDCS and Cognitive Bias Modification appear well worth taking as a direction for future

research and clinical interventions, in particular to confirm currently exploratory effects and to further explore novel intervention methods.

Publications

Den Uyl TE, Gladwin TE, Lindenmeyer J, Wiers RW (2018). A clinical trial with combined transcranial Direct Current Stimulation and attentional bias modification in alcohol dependent patients. *Alcoholism: Clinical and Experimental Research*, 22(6): 1632-1640.

Gladwin TE, Salemink E, Garritsen H, Noom S, Kraaij G, Wiers RW (2018). Is alcohol-related aggression related to automatic alcohol-power or alcohol-aggression associations? *Psychology of Violence*, 8(2): 229-237.

Gladwin TE (2017). Negative effects of an alternating-bias training aimed at attentional flexibility: A single session study. *Health Psychology and Behavioral Medicine*, 5(1): 41-56.

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Korucuoglu O, Gladwin TE, Baas F, Mocking RJT, Ruhe HG, Groot PFC, Wiers RW (2016). Neural response to alcohol taste cues in youth: effects of the OPRM1 gene. *Addiction Biology*, 22(6): 1562-1575.

Wiers CE, Gladwin TE, Ludwig VU, Gropper S, Stuke H, Wiers RW, Walter H, Bermpohl F (2016). Comparing three cognitive biases for alcohol cues in alcohol dependence. *Alcohol and Alcoholism*, 52(2): 242–248.

Den Uyl TE, Gladwin TE, Wiers RW (2016). Electrophysiological and Behavioural Effects of Combined Transcranial Direct Current Stimulation and Alcohol Approach Bias Retraining in Hazardous Drinkers. *Alcoholism: Clinical and Experimental Research*, 40(10): 2124-2133.

Korucuoglu O, Gladwin TE, Wiers RW (2016). The effect of acute alcohol on motor-related EEG asymmetries during preparation of approach or avoid alcohol responses. *Biological Psychology,* 114:81-92.

Wiers RW, Boelema S, Nikolaou K, Gladwin TE (2015). On the Development of Implicit and Control Processes in Relation to Substance Use in Adolescence. *Current Addiction Reports* 2(2) :141-155.

Wiers CE, Stelzel C, Gladwin TE, Park SQ, Pawelczack S, Gawron CK, Stuke H, Heinz A, Wiers RW, Rinck M, Lindenmeyer J, Walter H and Bermpohl F (2015) Effects of Cognitive Bias Modification-Training on Neural Alcohol Cue Reactivity in Alcohol-Dependence. *American Journal of Psychiatry*, 172(4):335-343.

Korucuoglu O, Gladwin TE and Wiers RW (2015) Alcohol-induced changes in conflict monitoring and error detection as predictors of alcohol use in late adolescence. *Neuropsychopharmacology*, 40(3):614-21.

Den Uyl TE, Gladwin TE and Wiers RW (2015) Transcranial Direct Current Stimulation, Implicit Alcohol Associations and Craving. *Biological Psychology*, 105:37-42.

Gladwin TE, Rinck M, Eberl C, Becker ES, Lindenmeyer J and Wiers RW (2014) Mediation of Cognitive Bias Modification for Alcohol Addiction via Stimulus-specific Alcohol Avoidance Association. *Alcoholism: Clinical and Experimental Research*, 39(1): 101-107.

Gladwin TE, Mohr SE and Wiers RW (2014) The Potential Role of Temporal Dynamics in Approach Biases: Delay-dependence of a General Approach Bias in an Alcohol Approach-Avoidance Task. *Frontiers in Psychology,* 5: 1398.

Life Course Study of Alcohol Harm in Three Generations: the Importance of Individual and Contextual Factors (2013) (EA 13 05)

Sidorchuk A, Department of Public Health Science, Karolinska Institute, Stockholm, Sweden

The main aim of this study was to establish and study an intergenerational patterning of alcohol use and its medical, psychological and social consequences in a life course perspective of three generations of Swedish people by modelling the trajectories for individuals following a distinct outline of change of alcohol use over age (within generations) and time (between generations).

The results highlight that granddaughters and grandsons from socially disadvantaged families have different risks in developing alcohol-related problems. Also, association between familial history of social hardship and grandchildren's alcohol-related disorders seem to become weaker with time. In contrast, parental social adversity impacts the development of alcohol-related disorders in males, but not in females regardless of time period.

The role of grandparental social class in developing alcohol-related disorders in grandchildren appears to decline over time; however, if social adversity persists in families and both grandparents and parents belong to disadvantage social class it increases the risk of developing alcohol- attributable problems among males.

Publications

A Sidorchuk, A Goodman, I Koupil; Social class, social mobility and alcohol-related disorders in four generations of Swedish families: Anna Sidorchuk, European Journal of Public Health, Volume 26, Issue suppl_1, 1 November 2016, ckw167.022,

Sidorchuk A, Goodman A, Koupil I (2018) Social class, social mobility and alcohol-related disorders in Swedish men and women: A study of four generations. PLoS ONE 13(2): e0191855

Is the neuroimmune response involved in the neurotoxic and behavioural consequences of binge alcohol drinking during adolescence? (2013) (EA 13 08)

Guerri C, Cell Pathology Laboratory, Research Center Prince Felipe, Valencia, Spain

Studies have demonstrated the vulnerability of the adolescent brain to actions of ethanol and the long-term consequences of binge drinking, including the behavioral and cognitive deficits that result from alcohol neurotoxicity, and increased risk to alcohol abuse and dependence. The aim of this research was to assess whether ethanol treatment in adolescence promotes the long-term synaptic and molecular events associated with alcohol abuse and addiction. Using adolescent mice the results demonstrate that the neuroimmune response is involved in the neurotoxic and behavioural consequences of binge alcohol drinking during adolescence.

The project also showed some gender differences in the inflammatory cytokine and chemokine profiles induced by binge ethanol drinking in adolescence. Thus, using plasma of male and female adolescents and young adults during acute alcohol intoxication, we showed that alcohol intoxication increased the plasma levels of several cytokine and chemokine [interferon-γ, interleukin (IL)-10, IL-17A, IL-1β, IL-2, IL-4, IL-6, IL-8, fractalkine, monocyte chemoattractant protein 1 (MCP-1) and macrophage inflammatory protein 1α (MIP-1α)] and upregulated TLR4 mRNA levels in females, while elevation of colony-stimulating factor was only observed in the plasma of males. In wild-type female adolescent mice, intermittent ethanol treatment increased the levels of several cytokines (IL-17A and IL-1β) and chemokines (MCP-1, MIP-1α and fractalkine) in PFC and in serum (IL-17A, MCP-1 and MIP-1α), but significant differences in the fractalkine levels in PFC were observed only in male mice. No changes in serum or prefrontal cortex

cytokine and chemokine levels were noted in ethanol-treated male or female TLR4-knockout mice. The findings revealed that females are more vulnerable than males to inflammatory effects of binge ethanol drinking and suggested that TLR4 is an important target of ethanol-induced inflammation and neuroinflammation in adolescence.

The results highlight a new role of the neuroimmune function in alcohol consumption and addiction and open up new avenues to develop pharmacological treatments that can normalize the immune signaling responsible for long-term effects in adolescence.

Publications

Pascual M, Montesinos J, & Guerri C. (2018) Role of the innate immune system in the neuropathological consequences induced by adolescent binge drinking. *Journal of neuroscience research*, 96(5):765-780.

Pascual M, Montesinos J, Marcos M, Torres JL, Costa-Alba P, García-García F, Laso FJ, Guerri C. (2017) Gender differences in the inflammatory cytokine and chemokine profiles induced by binge ethanol drinking in adolescence. *Addiction biology*, 22(6):1829-1841.

Montesinos J, Gil A, Guerri C. (2017) Nalmefene Prevents Alcohol-Induced Neuroinflammation and Alcohol Drinking Preference in Adolescent Female Mice: Role of TLR4. *Alcoholism: Clinical and Experimental Research*, 41(7), 1257-1270.

Montesinos J, Pascual M, Rodriguez-Arias M, Minarro J and **Guerri C** (2015) Involvement of TLR4 in the long-term epigenetic change, rewarding and anxiety effects induced by intermittent ethanol treatment in adolescence. *Brain, Behavior and Immunity*, 53:159-171.

Alfonso-Loeches S, Urena-Peralta J, Morillo-Bargues J, Gomez-Pinedo U and **Guerri C** (2015) Ethanol-induced TLR4/NLRP3 neuroinflammatory response in microglial cells promotes leukocyte infiltration across the BBB. *Neurochemical Research* 41(1-2):193-209.

Montesinos J, Pascual M, Pla A, Maldonado C, Rodriguez-Arias M, Minarro J and Gueri C (2015) TLR4 elimination prevents synaptic and myelin alterations and long-term cognitive dysfunctions in adolescent mice with intermittent ethanol treatment. *Brain, Behavior, and Immunity*, 45:233-244.

Alfonso-Loeches S, Urena-Peralta JR, Morillo-Bargues MJ, Oliver-De la Cruz J and Guerri C (2014) Role of mitochondria ROS generation in ethanol-induced NLRP3 inflammasome activation and cell death in astroglial cells. *Frontiers in Cellular Neuroscience*, 8(216).

Pascual M, Balino P, Aragon CMG and Guerri C (2014) Cytokines and chemokines as biomarkers of ethanol-induced neuroinflammation and aniety-related behaviour: role of TLR4 and TLR2. Neuropharmacology, 89:352-359.

Impact of alcohol consumption on the atheroprotective process of the reverse cholesterol transport (2013) (EA 13 09)

Zanotti I, Università degli Studi di Parma, Parma, Italy

Reverse cholesterol transport (RCT) may be one of the mechanisms accounting for positive effects of alcohol consumption on cardiovascular health. This study investigated the effects of moderate and excess alcohol consumption on RCT.
Moderate alcohol consumption slightly promoted the first steps of RCT in vivo, at least in part by up-regulating the expression of scavenger receptor class B type I (SR-BI) in the liver. Conversely, moderate/binge alcohol consumption seems not to significantly impair the process. In addition, moderate/binge alcohol ingestion caused a deleterious modification of lipoprotein plasma profile, leading to a significant increase of total and LDL- cholesterol. Interestingly, although a concurrent raise of HDL was observed, these lipoproteins demonstrated to have impaired antiatherogenic functions, as revealed by their reduced capacity to promote cholesterol efflux. It is important to notice that no toxic effects related to these levels of alcohol consumption were evident, as measured by hepatic function.
Moderate alcohol consumption is likely to slightly promote the first steps of RCT, thus exerting potential athero-protective activity. Moderate/binge alcohol consumption, despite devoid of hepatic toxic effects, seems to negatively affect lipoprotein profile and function.
These findings are useful to define nutritional guidelines and perform interventions for subjects with risky drinking behaviour.

Publications

Paper submitted to Nutrition, Metabolism and Cardiovascular disease. Currently under revision.

Synthesis and pharmacological characterization of novel positive allosteric modulators of the $GABA_B$ receptor: focus on their "anti- alcohol" potential (2013) (EA 13 20)

Maccioni P, Neuroscience Institute, National Research Council of Italy, Cagliari, Italy

$GABA_B$ receptors are classified as inhibitory receptors as they reduce the release of neurotransmitter. They are located in the central nervous system and are involved in several behavioural actions of ethanol. This research was designed to synthesize and pharmacologically characterize new positive allosteric modulators (PAMs) of the $GABA_B$ receptor with "anti-alcohol" potential. PAMs are molecules that can increase the activity of $GABA_B$ receptors. Results demonstrate that a newly synthesized $GABA_B$ PAM, named COR659, was potent and effective in reducing oral alcohol self-administration and reinstatement of alcohol seeking in alcohol-preferring rats. Insights in the "anti-alcohol" profile of COR659 as well as known $GABA_B$ PAMs strengthened the hypothesis that they may also represent a new, potentially effective therapeutic option of alcohol use disorder.

Publications

Maccioni, P., Colombo, G., Lorrai, I., Fara, F., Carai, M.A.M., Gessa, G.L., Brizzi, A., Mugnaini, C., Corelli, F. (2018). Anti-addictive properties of COR659 – Additional pharmacological evidence and comparison with a series of novel analogues. *Alcohol*, in press.

Maccioni, P., Fara, F., Lorrai, I., Acciaro, A., Mugnaini, C., Corelli, F., Colombo, G. (2018). Suppressing effect of CMPPE, a new positive allosteric modulator of the $GABA_B$ receptor, on alcohol self-administration and reinstatement of alcohol seeking in rats. *Alcohol*, in press.

Maccioni, P., Lorrai, I., Contini, A., Leite-Morris, K., & Colombo, G. (2017). Microinjection of baclofen and CGP7930 into the ventral tegmental area suppresses alcohol self-administration in alcohol-preferring rats. *Neuropharmacology.*136(A); 146-158.

Maccioni P, Colombo G, Lorrai I, Zaru A, Contini A, Carai MA, Gessa GL, Brizzi A, Mugnaini C and Corelli F (2017) Suppressing effect of COR659on alcohol, sucrose, and chocolate self-administration in rats: involvement of the $GABA_B$ and cannabinoid CB_1 receptors. *Psychopharmacology*, 234:2525–2543.

Porcu A, Lobina C, Giunta D, Solinas M, Mugnaini C, Castelli MP (2016) In vitro and in vivo pharmacological characterization of SSD114, a novel $GABA_B$ positive allosteric modulator. *European Journal of Pharmacology*. 27(791): 115-123.

Colombo G, Lobina C, Maccioni P, Carai MAM, Lorrai I, Zaru A, Contini A, Mugnaini C, Corelli F and Gessa GL (2015) Anxiety-like behaviors at the end of the nocturnal period in sP rats with a "history" of unpredictable, limited access to alcohol. *Alcohol*, 49:707-712.

Maccioni P, Vargiolu D, Thomas AW, Malherbe P, Mugnaini C, Corelli F, Leite-Morris KA, Gessa GL and Colombo G (2015) Inhibition of alcohol self-administration by positive allosteric modulators of the $GABA_B$ receptor in rats: lack of tolerance and potentiation of baclofen. *Psychopharmachology*, 232(10):1831-1841.

Risk and benefits of the ethanol and polyphenol content in beer: effects of moderate consumption on cardiovascular system (2013) (EA 13 24)

Rosa M. Lamuela-Raventós, University of Barcelona, Spain

Moderate alcohol consumption is associated with a decrease in cardiovascular risk, but fermented beverages seem to confer greater cardiovascular protection due to their polyphenolic content. Circulating endothelial progenitor cells (EPC) are bone-marrow-derived stem cells with the ability to repair and maintain endothelial integrity and function and are considered as a surrogate marker of vascular function and cumulative cardiovascular risk. This is the first study to investigate the effects of moderate beer consumption on the number of circulating EPC in high cardiovascular risk patients.

The non-alcoholic fraction of beer increased the number of circulating EPC and the phenolic content of beer reduced leukocyte adhesion molecules and inflammatory biomarkers. The alcohol mainly improves the lipid profile and reduces some plasma inflammatory biomarkers related to atherosclerosis. Moderate beer consumption did not affect body weight and other anthropometric parameters.

In addition to this intervention study the possible risks and benefits of moderate beer consumption on hard endpoints related to cardiovascular disease (stroke, myocardial infarction or cardiovascular death) and any-cause mortality were also evaluated using data of the PREDIMED study. Low and low-to-moderate consumption of beer was statistically and inversely associated with any-cause mortality. In addition, low and low-to-moderate beer consumption was statically significant associated with lower incidence of cardiovascular events.

These findings suggest that moderate beer consumption may decrease the risk of developing cardiovascular diseases by reducing adhesion molecules and inflammatory responses related to atherosclerosis, which may reduce the incidence of cardiovascular events risk and any-cause mortality.

Publications

Vilahur G, Casani L, Mendieta G, Lamuela-raventos RM, Estruch R and Badimon L (2014) Beer elicits vasculoprotective effects through Akt/eNOS activation. *European Journal of Clinical Investigation*, 44:1177-1188.

Chiva-Blanch G, Condines X, Magraner E, Roth I, Valderas-Martinez P, Arranz S, Casas R, Martinez-Huélamo M, Vallverdu-Queralt A, Quifer-Rada P, Lamuela-Raventos RM, and Estruch R (2014) The non-alcoholic fraction of beer increases stromal cell derived factor 1 and the number of circulating endothelial progenitor cells in high cardiovascular risk subjects: a randomized clinical trial. *Atherosclerosis*, 233(2):518-524.

European Survey of University Student Alcohol Use (2013) (EA 13 48)

Cooke R, Aston University, UK

There is a need to understand the variability of patterns and predictors of drinking alcohol across Europe on this population, and this project provided an important contribution by mapping the patterns of alcohol use in European university students. University students in six European countries – Denmark, England, Germany, Italy, Portugal, and Switzerland – participated in the present study.

University students tend to favour heavy alcohol consumption, and as a result, increase their chances of suffering health and social problems. The single most important finding to emerge from this study was the considerable cross-group variability which occurred, not only in the patterns of drinking behaviour on university students which were displayed, but also in the social and psychological variables, such as sex-role egalitarianism or drinking motives.

A practical output from the project was the development of a standardized questionnaire validated for use in at least six European countries. It is worth noticing that collecting information on alcohol use in several European countries, using the same set of measures, allows for a clearer understanding of which factors are important in different countries.

As alcohol use among university students is a Europe-wide concern, policies and interventions on university students' alcohol consumption need to take cultural variability into account.

Publications

Fernandes-Jesus M, Beccaria F, Demant J, Fleig L, Menezes I, Scholz U, de Visser R and **Cooke R** (2016) Validation of the drinking motives questionnaire - revised in six European countries. *Addictive Behaviors*, 62:91-98.

The effect of alcohol on the absorption and toxicity of food chemicals via the gut (2014) (EA 14 02)

Wright M, Institute Cellular Medicine, Newcastle University, UK

This study of mice investigated whether alcohol consumption results in an increased uptake of food chemicals and if so, whether that increased uptake of food chemicals on a background of increased liver inflammation (due to gut leakiness to endotoxin) results in increased liver injury and fibrosis.
The data so far suggest that high level chronic exposure to alcohol does not result in an increased oral uptake of the food chemical tartrazine in a mouse model or to increased liver inflammation, liver injury or fibrosis.

Publications

Meyer SK, Probert PME, Lakey AF, Axon AR, Leitch AC, Williams FM, Jowsey PA, Blain PG, Kass GEN, Wright MC (2017. Hepatic effects of tartrazine (E 102) after systemic exposure are independent of oestrogen receptor interactions in the mouse. *Toxicology Letters*, 273: 55–68.

Study abroad students' drinking behaviour: a mixed methods longitudinal study on social norms and sojourner adjustment (2014) (EA 14 11)

Aresi G, Università Cattolica del Sacro Cuore, Italy

Young adults' alcohol consumption, substance use and unprotected sexual behaviour represent relevant public health concerns. Theories related to other travelling populations (i.e., tourists, spring breakers, sojourners and immigrants) and research on non-European study abroad students suggest that abroad students may be at greater risk for excessive alcohol, drug use and unprotected casual sex. This first European study examined alcohol use and related negative outcomes, drug use and unprotected sexual behaviour in study abroad students (i.e., Erasmus). Students' behaviour was longitudinally assessed before departure, while abroad and once returned to their home countries. Participants (N = 906) increased the amount of alcohol consumed and experienced more alcohol-related consequences during the study abroad experience, though levels fell to below pre-departure levels when students returned home. Pre-departure expectations about alcohol use during the study abroad experience, psychological adjustment to the host country, lower academic involvement, and host country living costs were related to greater alcohol use while abroad. No statistically meaningful change in illicit drug use and unprotected sexual behaviour was observed, suggesting that the study abroad experience is dominated by alcohol. Studying abroad exposes European students to additional time-limited alcohol-related health risks, though riskier habits do not continue upon return.

Findings from this study have important public health implications and different entities (e.g., policy makers, international offices, health professionals in counselling service, student associations) operating in host and home institutions that may consider intervening with reference to relevant risk factors.

Publications

Aresi, G., Moore, S., Berridge, D., & Marta, E. (submitted for publication, review received, re-submitted). A longitudinal study of European students' alcohol use and related behaviours as they travel abroad to study.

Aresi, G., Alfieri, S., Lanz., M., Marta, E., Moore, S. (2018). Development and validation in five languages of a Multidimensional Motivations to Study Abroad Scale (MMSAS) among European Credit Mobility Students. *International Journal of Intercultural Relations*, 63: 128-134.

Aresi, G., Moore, S., & Marta, E. (2016). Drinking, drug use and related consequences among university students completing study abroad experiences: A systematic review. *Substance use & Misuse*. 51(14):1888-1904.
Aresi, G., Fattori, F., Pozzi, M. & Moore, S. (2016). I am going to make the most out of it! Italian university Credit Mobility Students' Social Representations of alcohol use during study abroad experiences. *Journal of Health Psychology*, available online.
Aresi, G., Moore, S., & Marta, E. (2016). Italian credit mobility students significantly increase their alcohol intake, risky drinking and related consequences during the study abroad experience. *Alcohol and Alcoholism*. 51(6): 723–726.

Intervention to measure impact of using unit-marked glasses for alcohol consumption in adults (2014) (EA 14 25)

de Visser R O, School of Psychology, University of Sussex, Falmer, UK

The aim of this intervention study was to test the hypothesis that using glasses marked with standard UK alcohol "units" would improve adults' knowledge of unit-based alcohol intake guidelines, their motivation to employ these guidelines, and their subsequent alcohol intake.
The "intervention" group of adult drinkers was given unit-marked plastic glasses and asked to use them for one month. A second "control" group did not receive the glasses or any instructions related to their alcohol use.
The intervention was effective at producing changes in people's understanding of, and use of unit-based guidelines to monitor their drinking. The unit-marked glasses could have an impact at the individual level (on knowledge and attitudes) and at a broader level (by prompting discussion of alcohol use). The intervention did not result in significant changes in alcohol consumption.

Publications

De Visser RO, Brown C, Cooke R, Cooper G and Memon A (2016). Using Alcohol Unit-marked Glasses Enhances Capacity To Monitor Intake: Evidence From a Mixed-method Intervention Trial. *Alcohol and Alcoholism*, 52(2): 206-212.

Lifestyle, social media and alcohol consumption (2014) (EA 14 33)

Szmigin I, Birmingham Business School, University of Birmingham, UK

The study aimed to gain insight in the relation between alcohol consumption, social media, and lifestyle. The researchers discuss this relation in three categories: brand marketing, marketing venues, and individual young people. This was done by means of investigation of recent news reports and social media, discussions on Facebook, analysis of Twitter feeds and YouTube video's, and focus groups.

First, brand marketing mainly aims to encourage more frequent drinking. Brands try to find ways to relate any and every occasion at any time of the day to drinking. As social media is accessible 24/7, individuals can be exposed to social media advertisements 24/7, and thus be encouraged to drink all day, every day. Furthermore, brands often present alcohol as a reward and the marketing of cheap offers on social media may encourage young individuals to drink alcohol.

Second, marketing venues are highly sexualized. For example, social media advertisements regularly show scantily clad women drinking heavily. This sexualized presentation of women may lead to women being sexual harassed in bars, making women feel threatened. It is thought that it triggers aggressive sexual behaviour in men to women.

The third category is individual young people. Social media often presents risky behaviour around alcohol in a positive 'fun' and light-hearted manner. This media is mainly targeted at a young audience and may normalize drinking among young people. Especially taking into account that social media has a big impact on the lifestyle of young people and they feel pressure to use social media. In addition, a small group of young adults uses social media to show their alcohol misuse behaviour, which may also contribute to the normalization of drinking among young individuals.

Publications

Rogan, F., Piacentini, M., & Szmigin, I. (2016). Marketing "Raunch Culture": Sexualisation and Constructions of Femininity Within the Night-Time Economy. *ACR North American Advances*, 44:603-604.

The role of genetic markers of alcohol dependence, bitter taste perception, and alcohol tolerance in determining drinking patterns and the risk of breast and colorectal cancer (2015) (EA 14 39)

Simons C, Department of Epidemiology, University of Maastricht, The Netherlands

Within the Netherlands Cohort Study, two studies were conducted to investigate the association between alcohol consumption and the risk of colorectal cancer and breast cancer. Genetic variants, related to ethanol metabolism, were taken into account to assess whether they modify the associations between alcohol intake and cancer risk. The results show that alcohol is a risk factor for colorectal cancer in men across subsites and alcohol intake levels. For women, only colon cancer risk was increased at heavy intake levels. Alcohol was also found to be a risk factor for postmenopausal breast cancer in women. Additionally, genetic variants, related to ethanol metabolism, appear to have an effect on the association between alcohol and colon cancer in women, but not in men or in postmenopausal breast cancer in women.

Publications

Offermans NSM, Ketcham SM, van den Brandt PA, Weijenberg MP, Simons CCJM. (2018) Alcohol intake, *ADH1B* and *ADH1C* genotypes, and the risk of colorectal cancer by sex and subsite in the Netherlands Cohort Study. *Carcinogenesis*. 39(3):375-388.

Hahn, M, Simons, CCJM, Weijenberg, MP, van den Brandt, PA (2018). Alcohol drinking, *ADH1B* and *ADH1C* genotypes, and the risk of postmenopausal breast cancer by hormone receptor status: The Netherlands Cohort Study on Diet and Cancer. *Carcinogenesis*. [Epub ahead of print]

More is caught than taught: a ground-breaking study on the role of implicit parenting processes on adolescents' alcohol use (2014) (EA 14 41)

Koning I, Interdisciplinary Social Science, Youth Studies, Utrecht University, The Netherlands

This research investigated the relative effect of explicit and implicit parenting cognitions on adolescents' alcohol use. Explicit parenting cognitions refer to controlled, effortful, and intentional processes, while implicit cognitions are more automatic, more likely to occur outside of conscious awareness, and less intentional. The results suggest that both types of parenting cognitions have a different effect on adolescents' drinking behaviour over time. Stricter explicit parenting cognitions are more likely to predict a lower likelihood of ever having consumed alcohol six months later, while stricter implicit parenting cognitions predicted lower levels of weekly drinking. Moreover, these protective effects were particularly relevant for older adolescents. This means that implicit parenting cognitions are an important factor in the level of alcohol use among adolescents, even in predicting changes in behaviour over time. Strict parenting is effective in delaying the onset and reducing the amount of alcohol use even among older adolescents. We argue that the influence of parents is subject to change as a function of adolescents' age, with the prevailing role of automatic parenting over explicit parenting.

Publications

Koning, I. M., Spruyt, A., Doornwaard, S. M., Turrisi, R., Heider, N., & De Houwer, J. (2017). A different view on parenting: automatic and explicit parenting cognitions in adolescents' drinking behavior. *Journal of Substance Use*, 22(1): 96-101.

Koning, I.M., Doornwaard, S., Van der Rijst, V., De Houwer, J., & Vollebergh, W.A.M. A developmental perspective on parenting; Longitudinal effects of automatic and explicit parenting on adolescents' alcohol use. Submitted for publication.

Development and testing of a new alcohol attentional bias modification training paradigm: What are its neurocognitive mechanisms of action and how do they relate to real-life drinking behaviours? (2014) (EA 14 42)

Nikolaou K, Department of Psychology, Universiteit van Amsterdam, The Netherlands

This research aimed to validate a novel internet-based method of alcohol attentional bias re-training. With this method, participants are consistently trained to ignore stimuli associated with alcohol. This training would reduce attentional biases to alcohol-associated stimuli, and reduce alcohol consumption and craving. Results from a student population of social drinkers suggest that the training had a small effect on biases to alcohol related cues. Minor effects were found on alcohol drinking and alcohol craving. Additional analyses suggest that this type of training may be more beneficial to individuals with higher biases to alcohol cues, more severe alcohol use and higher levels of impulsivity before the start of the training. More research is needed to assess the effects of the training in bigger samples of patients with alcohol dependence.

Publications

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Effects of alcohol consumption on gut microbiota composition in adults (ALMICROBHOL) (2014) (EA 14 44)

Marcos A, Institute of Food Science, Technology and Nutrition (ICTAN), Spanish National Research Council, Madrid, Spain

The Almicrobhol study has been carried out by the Immunonutrition research group headed by Dr. Ascensión Marcos and Dr. Esther Nova. This study investigates whether the pattern of alcohol consumption (alcohol amount, frequency of consumption, binge- or regular-drinking) as well as the different types of alcoholic

fermented and distilled beverages influence the gut microbiota composition of healthy adult individuals. Participants were recruited in both Spain and Slovenia. 261 valid cases were included from Spain and 134 from Slovenia.
Gut microbiota composition from frozen faecal samples was analysed, centrally, through 16S rRNA sequencing and taxa identification by comparative rRNA taxonomy. The contribution of beer to alcohol consumption (8.4 g/d) was significantly higher than that of wine (2.8 g/d) in this population. The mean daily grams of alcohol consumption were positively associated with abundance of the genera *Borrelia*, *Erysipelothrix* and *Paraprevotella* (all, r=0,178; P=0,010). Daily grams of alcohol from beer were directly associated with *Chryseobacterium* and *Erysipelothrix* but no relevant association was found between amount of wine intake and the microbiota genera. Excessive weekend consumption was associated with a decrease in beta diversity. There were no differences among pattern consumption groups regarding the main phyla and genus analysed.
Conclusions: The amount of alcohol consumption may influence the abundance of minor genera in the microbiota and beer intake was related to some of the changes observed.

Publications

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Health effects of the ethanol and polyphenol content in beer: Evaluation of the effects of moderate beer consumption on cardiovascular system. A metabolomic approach. (2015) (EA 15 17)

Medina-Remon A, Department of internal Medicine, Hospital Clinic, University of Barcelona, Spain

This research consisted of a randomized controlled trial including 33 males between 55 and 75 years old. Participants underwent three interventions including beer, non-alcoholic beer, and gin, in a random order for four weeks for each intervention. The researchers performed an metabolomic analysis in urine and found two potential new biomarkers for beer and non-alcoholic beer consumption. Additionally, the results suggest that a regular and moderate beer and non-alcoholic beer consumption may increase fatty acid oxidation.

Publications

Quifer-Rada, P., Chiva-Blanch, G., Jáuregui, O., Estruch, R., & Lamuela-Raventós, R. M. (2017). A discovery-driven approach to elucidate urinary metabolome changes after a regular and moderate consumption of beer and nonalcoholic beer in subjects at high cardiovascular risk. *Molecular nutrition & food research*, 61(10), 1600980.

Quifer-Rada P, Martínez-Huélamo M, Lamuela-Raventos RM. (2017) Is enzymatic hydrolysis a reliable analytical strategy to quantify glucuronidated and sulfated polyphenol metabolites in human fluids? *Food & Function,* 8(7):2419-2424.

A study on young drinking behaviour-evaluation the relationship between taste reactivity and special beer consumption (2015) (EA 15 45)

Salanta L-C, University of Agricultural Sciences and Veterinary Medicine, Cluj-Napoca, Romania

This research aimed to evaluate the role of sensory characteristics in the perception, preference and consumption of low- and non-alcoholic beer among university students from Romania. The results show that students' perception of low- and non-alcoholic beer quality was based on a complex mix of expectations, which are generally associated with some sensory attributes such as colour, foam, flavour and aroma, mouthfeel and aftertaste.

95% of university students have consumed low-alcoholic beer, and 8.8% of them declared that they do not like it. Non-alcoholic beer was consumed by 84% of the student, and 38% indicated that they do not like it because of poor flavour profile of non-alcoholic beer.

Students who liked the low- and non-alcoholic beers were attracted by flavour and aroma (79.4%), low concentration of alcohol (11%) and colour (0.9%) of the beer. Students who indicated that they did not like the beer, claimed a poor aroma, CO_2, taste and foam.

Obtaining low alcohol content via interrupted fermentation is accompanied by low contents of aroma and flavour compounds, and their products are often characterized by worty off-flavours. This research indicates that flavour appears to play an important positive role for students. Additionally, anticipated emotions and feelings associated with beer consumption is also a motivation for their choice.

Publications

Salanță LC, Tofana M, Pop C, Pop A, Coldea T, Mihai M (2018). Risk Factors Associated with Alcohol Consumption Among Romanian University Students- Preliminary Research. *Bulletin UASVM Food Science and Technology*, 75(1): 86-89.

Salanță LC, Tofană M, Pop C, Pop A, Coldea T, Mudura E (2017). Beverage Alcohol Choice Among University Students: Perception, Consumption and Preferences. *Bulletin UASVM Food Science and Technology*, 74(1): 23-30.

Salanță LC, Tofana M, Mudura E, Pop C, Pop A, Coldea T (2016) The alcoholic beverage consumption preference of university students: a preliminary Romanian case study. *Bulletin UASVM Food Science and Technology*, 73(1): 31-39.

RESEARCH STILL UNDERWAY

Changing lifestyle may prevent or revert pulmonary arterial hypertension (2014) (EA1423)
Negrao R, Faculty of Medicine, University of Porto, Porto, Portugal

Alcohol and bleeding in the general population (2014) (EA1437)
Tolstrup SJ, National Institute of Public Health, University of South Denmark, Copenhagen, Denmark

Evaluation of moderate daily intake of beer in reducing menopausal symptoms. Estrogenic effect of hop prenylflavanoids (2015) (EA1514)
Tresserra Rimbau A, Deptartment of Nutrition and Food Science, School of Pharmacy, University of Barcelona, Barcelona, Spain

Risks and benefits of moderate beer intake (with and without alcohol) on osteoporosis in postmenopausal women (2015) (EA1515)
Lamuela-Raventos RM, Deptartment of Nutrition and Food Science, School of Pharmacy, University of Barcelona, Barcelona, Spain

Activation of the human innate immune system and anticancer properties mediated by hop-derived prenylflavonoids naturally enriched in beer (2015) (EA1528)
Ventruelli S, Department of Internal Medicine, University Hospital of Tuebingen, Tuebingen, Germany

Peer influence and alcohol cognitions: Understanding the interaction between implicit processes and peer context (2015) (EA1549)
Larsen H, Department of Psychology, University ofAmsterdam, Amsterdam, The Netherlands

Dissociating Impulsivity and Reward Processing Endophenotypes of Alcohol Misuse Patterns (2015) (EA1550)
Whelan R, Institute for Neurosciences, Trinity College Dublin, Dublin Ireland

Alcohol consumption in daily life: A mobile ecological momentary assessment study in a general population sample (2016) (EA1634)
Jacobs N, Faculty of Psychology and Educational Sciences, Open University, DL Heerlen The Netherlands

To consider the health effects arising from the components of beer (brewed at large and small scale) in particular, to investigate the effect of folate and vitamin B 6 content of beer on serum homocysteine and the cardiovascular system (2016) (EA1617)
Bertuzzi T, Catholic University of the Sacred Heart, Milan, Italy

Binging on alcohol and social stress in adolescence: a translational research in Sicily (BASTA) (2016) (EA1642)
Cannizzaro C, Department of Sciences for Health Promotion and Mother and Child, University of Palermo, Italy

Less spirit, more wine and beer: predictors, mediators and health consequences of drinking patterns in contemporary Sweden (2016) (EA1645)
Möller J, Department of Public Health Science, Karolinska Institute, Stockholm, Sweden

Role of liver progenitor cells in the progression of alcoholic liver disease (2016) (EA1653)
Sancho-Bru P, Biomedical Investigation Centre, Barcelona, Spain

Moderate beer intake effects on the inflammasome pathway and TLR-mediated immunomodulation in humans (2016) (EA16 59)
Badimon L, Institute of Biomedical Research, Hospital of Santa Creu, Barcelona, Spain

Pharmacological characterization of the novel positive allosteric modulator of the GABAB receptor, COR659: focus on its "anti-alcohol" effects (2017) (EA1714)
Maccioni P, Neuroscience Institute, Section of Cagliari, National Research Council of Italy [*Consiglio Nazionale delle Ricerche* (CNR)], Cagliari, Italy

In vivo evaluation of the effects of alcohol exposure on cell proliferation (2017) (EA1719)
Toietta G, Department of Research, Advanced Diagnostic and Technological Innovation, Regina Elena National Cancer Institute, Rome, Italy

Testing an Internet-based guided self-help intervention to reduce alcohol misuse and co-occurring depression symptoms in students: Take Care of You (2017) (EA1720)
Huizink A, Faculty of Behavioral and Movement Sciences, Vrije Universiteit Amsterdam, The Netherlands

Investigating the role of long non-coding RNA in alcoholic liver disease (ALD) (2017) (EA1763)
Chokshi S, Foundation for Liver Research, London, UK

Biomarkers of subclinical ischemic damage and low-grade inflammation as possible mediators of association between alcohol intake and vascular risk (2017) (EA1767)
Costanzo S, Istituto Neurologico Mediterraneo NEUROMED, Pozzilli (IS), Italy

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