

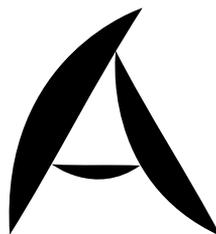
THE FINNISH FOUNDATION
FOR ALCOHOL STUDIES



REPORT ON ACTIVITIES

2012

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TABLE OF CONTENTS

GENERAL OVERVIEW	5
ADMINISTRATION	6
RESEARCH ACTIVITIES	7
RESEARCH CONTRACTS AND COLLABORATIVE PROJECTS	7
PUBLICATIONS	25

GENERAL OVERVIEW

In 2012, the projects funded by the Finnish Foundation for Alcohol Studies resulted in the publication of 8 academic doctoral dissertations, 29 original peer-reviewed articles in international and 4 original peer-reviewed articles in national scientific journals. Nine other papers were published.

Two new contract projects were launched. Senior researcher Vesa Huotari's project will explore the use of alcohol and attitudes towards alcohol in the internal security professions: the police, the fire department and the border control. Adjunct professor Anni-Maija Linden's project utilizes animal models to study the effect of neuroinflammation on alcohol consumption and immediate alcohol effects, with the role of receptor P2RX7 in focus. Seven ongoing research contract projects received additional funding. Ongoing contract projects will be described below under the title *Research activities*.

The Foundation kept its office at the National Institute for Health and Welfare (THL) in Helsinki.

ADMINISTRATION

The Board of the Foundation was composed of four members appointed by the Ministry of Social Affairs and Health, four appointed by the Federation of Finnish Scientific Societies, and one appointed by the Finnish Alcohol Retail Monopoly. The majority of the Board must consist of academically established scientists with special expertise in alcohol research. The Executive Committee was composed of four members of the Board and two external experts. The Gambling Research Committee was appointed by the Board and consisted of one Board member, the Research Director and six external experts.

The Foundation's Research Director *Tommi Lintonen* is the only full-time staff member. A contract between the Foundation and the National Institute for Health and Welfare (THL) provided administrative and technical support for the Foundation.

RESEARCH ACTIVITIES

The Foundation awards two types of grants: ordinary grants to support short-term projects proposed by the scientific community, and contract grants ensuring long term funding of projects deemed to be of major significance. The Foundation received 52 applications for alcohol research. Sixteen new grants were awarded. In addition, six contract grants were funded based on earlier commitments. The total amount of grants for alcohol research for the year 2013 was 365.000 euro. In addition, based on a funding agreement with the Ministry of Health and Social Affairs, the Foundation granted 277.440 euro for research on gambling harms.

This report reviews the contract grants included in the Foundation's research programme. It does not cover research funded by ordinary grants.

RESEARCH CONTRACTS AND COLLABORATIVE PROJECTS

The ongoing contract projects progressed as follows:

206 *Identification of Hazardous Drinkers by Biological Markers.*

Increased alcohol consumption is difficult to detect by a common interview and none of the current biomarkers is specific for a reliable detection of increased alcohol consumption. This is why our main aim in the present study is to search for new protein biomarkers which could be used for detecting and predicting hazardous drinking reliably. Network-based approaches are particularly useful in deciphering the connectivity between identified molecules and bridging them to cellular pathways. To extend our analyses on pathways affected by chronic alcohol consumption we utilized GeneMania (www.genemania.org), which indexes over 1400 association networks for approx. 150 000 genes from 7 different organisms, including rat. We first queried the identified rat proteins for their unique Gene identifiers to assign associations based on knowledge of physical and genetic interactions, structure homology, co-localization, shared protein domains, known cellular pathways and predictions derived from orthologous interactions. Utilizing equal weighting of the networks we connected 60 genes identified this way in chronic alcohol consumption rats (termed as AAakr) at 25 weeks of exposure, by 58 interactions. One of the most statistically enriched functional features in the network included peptidase activity, acting on L-amino acid peptides (GO:0070011, False discovery rate, FDR= 5.8E-4; with 8 identified genes in the network versus 209 ones in the rat genome). The second most enriched feature included regulation of homeostasis (FDR=5.8E-4; 8/211 genes). Similar analyses in rats with semichronic consumption of alcohol (termed as AAskr) pinpointed odorant binding (FDR=3.58E-2) and defense response (FDR=1.68E-1) as most enriched processes. Net-

work analysis of functional modules, which are affected in both chronic and semichronic alcohol consumption rats, identified ubiquitin-tagged degradation, response to oxygen radicals and actin assemblies as down-regulated functional modules, as compared to rats fed with water after 25 weeks of exposure. Comparative analyses of AA and ANA strains, after 25 weeks of chronic exposure to alcohol, distinguished several proteins and functional modules which differentiate them. Specifically, a class of peptidases can be pin-pointed in AAkr strain, with 4 proteases that differentiate it from alcohol avoiding ANAkr strain. This included: Gamma-glutamyl hydrolase, EC=3.4.19.9; meprin A, EC=3.4.24.18; Membrane alanyl aminopeptidase, EC=3.4.11.2; deoxyribonuclease I; EC=3.1.21.1. The most enriched functional processes characterizing both strains included enzyme inhibitor activity, FDR=2.78E10-8 and reactive oxygen species metabolic process, FDR=7.7E10-6. Researcher: *Marc Baumann*, Biomedicum, University of Helsinki. (marc.baumann@helsinki.fi)

209 *Precarious Pregnancies. Alcohol, Drugs and the Regulation of Risks.*

Since the 1970s alcohol and drug use by pregnant women has become a target of political, professional and personal concern. The present study focuses on prenatal substance use and the regulation of risks by examining different kinds of societal responses to prenatal alcohol and drug use. The study analyses face-to-face encounters between professionals and service users at a specialised maternity clinic for pregnant women with substance abuse problems, medical and political discourses on the compulsory treatment of pregnant women as a means of FAS prevention, and official recommendations on alcohol intake during pregnancy. Moreover, the study addresses the women's perspective by asking how women who have used illicit drugs during pregnancy perceive and rank the dangers linked to drug use. The study consists of five empirical sub-studies and a summary article. Sub-study I was written in collaboration with Dorte Hecksher and Sub-study IV with Riikka Perälä. Theoretically, the study builds, on the one hand, on the socio-cultural approach to the selection and perception of risks and, on the other hand, on governmentality studies which focus on the use of power in contemporary Western societies. The study is based on an ethnographic approach and makes use of the principles of multi-sited ethnography. The empirical sub-studies are based on three different types of qualitative data: ethnographic field notes from a maternity clinic from a period of 7 months, documentary material (medical journals, political documents, health education materials, government reports), and interviews from maternity clinics with clients and members of staff. The study demonstrates that the logic of the regulation of prenatal alcohol use in Finland is characterised by the rise of the emphasis on the foetus, a process in which the urgency of protecting the foetus has gradually gained a more prominent role in the discourses on alcohol-related foetal damage. An increasing unwillingness to accept any kinds of risks when foetal health is at stake is man-

ifested in the public debate on the compulsory treatment of pregnant women with alcohol problems, and in the health authorities' decision to advise pregnant women to refrain from alcohol use during pregnancy (Sub-studies I and II). Secondly, the study suggests that maternity care professionals have an ambivalent role in their everyday encounters with their pregnant clients: on the one hand, professionals focus on the well-being of the foetus, but on the other hand, they need to take into account the women's needs and autonomy. The professionals' daily encounters with their clients are thus characterised by hybridisation: the simultaneous use of technologies of domination and technologies of agency (Sub-studies III and IV). Finally, the study draws attention on how women understand the risks of illicit drug use during pregnancy, and shows that the understanding of risks differs from the bio-medical view. The study suggests that when pregnant women who use drugs seek professional help they can feel that their moral worth is threatened by the negative attitudes of the professionals, and this can make the use of these services challenging. The public defense of the PhD study took place in February 2012. Researcher: *Anna Leppo*, Finnish Foundation of Alcohol Studies.

210 *Drug induced Plasticity on Dopaminergic Pathway; Mechanisms and Meaning from Synaptic Level to Behaviour.*

Dopamine (DA) neurons of the ventral tegmental area (VTA) are involved at early phases of drug addiction. Various abused drugs induce glutamate receptor plasticity at the excitatory synapses of these neurons. Previously in the project it was found that benzodiazepines induce this similar plasticity, which could play a role in the benzodiazepine addiction. Also alcohol activates VTA DA neurons. However, its primary targets remain unknown. Recent findings suggest that extrasynaptic δ -subunit-containing GABA(A) receptors are sensitive to moderate concentrations of alcohol and could mediate the reinforcing effects. Gaboxadol (THIP) is a direct agonist at these receptors. THIP was used to study the role of the extrasynaptic GABA(A) system in the VTA DA neuron synaptic plasticity. A sedative dose of THIP to mice led to glutamate receptor plasticity in their VTA DA neurons that lasted at least 6 d after administration. In behavioral tests, no acute reinforcement was found in intravenous self-administration sessions with THIP in mice nor in baboons, nor was any place preference found after place-conditioning sessions in mice, but, surprisingly, a persistent aversion was found after THIP. The DA neurons of VTA seem to be organized anatomically depending where the neurons are projecting and these separate DA connections might mediate different aspects of motivation, positive or negative. Our findings provide proof also for VTA DA-mediated negative motivation, and this needs to be studied further. For this, an analysis was conducted of brain areas and neuronal populations that could mediate the THIP effect. C-Fos immunohistochemistry was used to map the neuronal activation induced by either THIP or amphetamine or saline as a control. THIP altered neuronal activity in a region-specific manner that differed

from the positively reinforcing amphetamine treatment. The activated areas led to a hypothesis that THIP-treated mice could actually exhibit anxious behavior after following acute drug administration, and several tests have been used to evaluate the relative anxiety status of mice (results pending). Also, the effects of ethanol on the VTA DA neurons have been studied. Voluntary alcohol consumption in mice was tested in order to correlate the increased motivation to consume ethanol to alterations in the gene expression profile of VTA DA neurons. Different paradigms of voluntary consumption in withdrawal after forced or voluntary ethanol experience have been now tried and the next set of experiments is being done after optimizing the protocol. After dividing the groups of high and low consumers, the VTA DA neurons are collected from the brain slices with laser microdissection method and the extracted RNA is used for gene expression profiling. Researchers: *Anne Panhelainen and Elena Vaschinkina*. Institute of Biomedicine, University of Helsinki.

211 *The Cultural and Structural Dimensions of Habitual Criminality. Drug Users and Police Interpretations of Habitual Criminality.*

The target group of this study consists of those regular drug users whose various types of recurring offences point to habitual crime. In the study, the motives behind and the attitudes linked to crime are considered as reflections of the lifestyle, values and self-identification of the offenders. Another focus is on police discretion, as well as on how the police perceives the role of drug-related law enforcement. The research material was gathered through interviews with police officers and drug users, through a survey made at Tampere Police Department, as well as using three different records of investigation and preliminary investigation files. This study draws on the concepts and viewpoints of cultural criminology to analyze the everyday nature of crime and the act of committing crimes as a way to seek experiences and excitement. From the viewpoint of lifestyle, the offences committed by drug-using habitual criminals are a reflection of their individual values and are carried out in the framework of dominant culture and subculture. Thus, the angle of lifestyle does not rule out economic deprivation or social exclusion. The study revealed that drug users were involved in various types of crime. Economic motives were not the only driving force behind offences committed by drug-using habitual criminals. Unlawful acts were also motivated by immaterial factors, such as seeking excitement and peer acceptance, as well as showing defiance towards authorities. Although offenders were branded as deviants by society, they still wanted to identify with the criminal peer group and earn the respect and recognition of fellow offenders. The data showed that police control was focused on certain known drug users, but this is likely to be a reflection of drug-related crime. In police rhetoric, controlling substance abuse was mainly a procedure to maintain public security and order. In police view, changing the social conditions leading to crime is not within the scope of their expertise and liability, but the role of social and health services. Besides the legal point of view,

the police see drug-related crime as a harmful, immoral and undesirable phenomenon, and they feel drug control is supported by the majority of people. Police discretion strategies are twofold: they must take into account both the concrete and symbolic effects of substance abuse control on the drug user, and also prioritize their actions according to the harms each criminal act will have on society. Researcher: *Tuula Kekki*, Finnish Foundation of Alcohol Studies.

212 *The Development of Alcohol Policy in Newly Independent Estonia.*

Changes in Estonian alcohol policy during the period 1991-2008 are analyzed through documents and interviews. The purpose of the interviews is to obtain new information which was difficult to grasp from the written documents, as well as to clarify and complement the information that emerged through the study of the written sources. There are three main topics that arise from the interviews: how respondents talk about the different problems and obstacles, decision making processes and external influences occurring when implementing alcohol policies. According to the analysis, some problems and difficulties in implementing alcohol policies are similar and valid throughout the period. For example, experience of Gorbachev's anti-alcohol campaign that created an unfavourable attitude towards all kinds of efforts to reduce alcohol consumption by political means, and which still prevails; domination of liberal right-wing parties since 1992 that brought about a hegemony of a liberal transition culture glorifying a minimalist state and a free market where alcohol-related problems were not much discussed; political and administrative instability which is due both to political turbulences that brought about twelve different government coalitions in office during the period of 1991-2008, and to a high yearly staff turnover rate of civil servants; the interests of alcohol producers have been favoured at the cost of social policy considerations, and alcohol producers had also been supporting political parties; and, in addition, weak civil society where citizens and NGOs have been consistently passive in policy forming processes. Other problems and difficulties in implementing alcohol policies are more specific and depend on the historical episode which I will discuss separately. (1) 1991-1994: "laissez-boire" politics - alcohol-related problems were not seen as important by the government. There was not much research done on alcohol consumption trends, either. Although problems related to illegal drugs only existed in a small scale in the beginning of the 1990s, thanks to the pressure from international organizations, these problems were considered primary. Many different problems had to be dealt with simultaneously, and there was no clear vision of what areas should be developed as a priority. Lots of problems were related to the control of the alcohol market, not only during the early 1990s but also later on. Likewise, surveillance over the law fulfillment was weak. (2) 1995-1999: increasing control - there were several problems and obstacles while implementing The Alcoholism and Drug Abuse Prevention Programme since 1997. Taken at face value, the programme

formed a basis for future action in both drug and alcohol policies. In practice, however, the implementation concentrated mostly on drug issues. Only in matters concerning information and education activities, including data collection (e.g. research), alcohol was seen as in line with tobacco and drug issues. Until today there is no separate action plan for alcohol-related harm in Estonia. (3) 2000-2004: years after the new legislation - intense preparations for accession to the EU and NATO. During the Estonian EU negotiations period, alcohol policy issues were not an important topic of discussion (like it had been for example in Finland and Sweden). Overall, we can note that NGOs and the civil society had become more active. Different organisations (womens, health related, parent, youth, religious and temperance organisations) had declared at various occasions their point of views on alcohol problems and demanding more severe restrictions. (4) 2005-2008: first years of the EU membership - the "institutional memory" of the civil servants has been short, because people working in the ministries tend to leave after few years working there and this makes it difficult to be consistent and systematic with achieving the objectives. How policy issues are handled and how successful they are seems to be dependant on the staff and administration capability. On the other hand, alcohol policy is a political issue and it is not possible to see it as separate from party politics. Alcohol has not been prioritized politically and alcohol producers have a strong power in Estonia. According to some respondents' view, they hinder all attempts on implementing more restrictive policies. The lack of a coordinated alcohol strategy is seen as one of the main obstacles why it has been so difficult to implement alcohol policy issues more from the health policy perspective. Researcher: *Kersti Kollom*, Tallinn University and Åbo Akademi, Department of Sociology. (kersti.kollom@gmail.com)

213 *The Role of Brain-derived Neurotrophic Factor in the Regulation of Alcohol Drinking.*

BDNF is a member of the nerve growth factor family of neurotrophins and has multiple tasks in central nervous system, such as neuronal survival and plasticity, learning, regulation of locomotor activity and appetite, and also in addiction. BDNF signals through TrkB- receptor and alcohol and other drugs are known to acutely induce them both. The aim of this study is to clarify the role of BDNF in the rewarding effects of alcohol and in the regulation of alcohol drinking. In the studies performed in the Institute of Health and Welfare we have seen dose-dependent and temporal region-specific changes in the levels of BDNF mRNA after acute alcohol exposure in the brains of wistar rats. Also, we have found that acute alcohol exposure alters the BDNF mRNA levels in AA and ANA rats in a similar manner as in wistar rats. Furthermore, we found a line-difference between AA and ANA rats in the basal levels of BDNF, as well as in the response to alcohol in the ventral tegmental area (VTA). This suggests that BDNF especially in the VTA may have a role in the different drinking preference of these rat lines. In the Autonomous Univer-

sity of Barcelona we have determined the effect of BDNF on dopamine synthesis and release in the rat striatum and found that BDNF decreases the synthesis of dopamine in the rat brain striatal miniprisms. I have presented these results in the annual science days of the Autonomous University of Barcelona and in the international congress "Global Questions on Advanced Biology" organized by SCB (Societat Catalana de Biologia, Catalanian Society on Biology) in Barcelona. Researcher: *Noora Raivio*, Department of Alcohol, Drugs and Addiction, National Institute for Health and Welfare, supervised by Kalervo Kiianmaa, and Institute of Neurosciences, Autonomous University of Barcelona, supervised by Jordi Ortiz and Josefa Sabrià. (noora.raivio@helsinki.fi)

215 *Diversity of Drinking Culture - The Examination of Intoxication, Drinking Practises and Drinking Situations of Women and Men.*

This sociological research investigates drinking habits from the gender point of view. Even though the differences in drinking between genders have been studied earlier, it is important to point out the differences inside a gender, as well. Therefore, the drinking practices, gender ideals and roles and the meanings related to drinking among women and men of different age are investigated in this research. By using the perspective of generation, the research also aims to clarify the changes in Finnish drinking culture. Especially by pointing out changes in drinking habits and drinking ideals among women of different generations, the research adds to the knowledge about the changes in drinking cultures in Finland in the last four decades. The main data of the research consists of focus group interviews collected in Finland (n=16) and Sweden (n=20). Women and men of four different age groups and two educational levels have been interviewed separately in both countries. The theoretical framework of the study applies theories which discuss gender as a part of self presentation and self expression. Therefore, gender is not only seen as a biological factor but as a social and cultural construction. The study is based on an assumption that in drinking situations, as in social life in general, gender is constructed by adopting, repeating and varying gender ideals and gender models which are considered normal and suitable. During the last year of the study two articles were published and two were accepted for publication. The dissertation summary is under finalization. The preliminary examination of the dissertation will take place in 2013. Researcher: *Jenni Simonen*, the Finnish Foundation for Alcohol Studies. (jenni.simonen@thl.fi)

216 *Teenagers' Images of Alcohol Use and Social Class Differences Related to Them in Finland and Italy.*

The study examines social class differences in drinking images among 14-16-year olds in Finland and Italy. The research provides novel insights for adolescent drinking cultures by utilizing comparative qualitative research methodology. The research applies a structured qualitative focus group methodology called The Reception Analytical Group Interview

(RAGI). The data of the research consist of group interviews among ninth graders in Helsinki, Finland (N=18) and Turin, Italy (N=10). In Helsinki the schools for the study were chosen according to the socioeconomic indicators of the area; In Italy the recruitment was also based on the area indicators as well as on the secondary school divisions. Franca Beccaria and her research team in Eclectica have been responsible for collecting the Italian part of the data. In both countries the participants were shown six film clips representing different kind of drinking behaviour and drinking settings. In 2012, two papers were presented in international conferences and an article was published in Finnish. Forthcoming articles compare Italian and Finnish adolescents' image of binge drinking and alcoholism. Researcher: *Anu Katainen*, University of Helsinki.

217 *The Division of Labour between Social Care health care, the Prison and the Police in the Handling of Intoxicant Related Harm.*

During 2012, the focus of the study has moved toward studying substance use among prisoners and the countermeasures applied by prison. Central data is derived from a prisoner health investigation (N=610) and prisoner register information. The point of departure for the study is the growing substance abuse problem in prisons and the ways that it is tackled by today's Finnish prison. The new act on imprisonment (767/2005) obligates prisons to make a plan for each sentence. It should be assessed which factors are central the prisoner's risk for reoffending and countermeasures should be targeted accordingly. On a theoretical level the study is connected to the risk debate in penology and the emergence of the risk concept in prisons. A central trait in the debate states that attention should be paid to structures and problems that prevent helpful elements from reaching the individual. The study provides new information on how the substance abuse problems among prisoners have changed since the 1980s. The research collaborated with an investigation that compared data from three prisoner health investigations conducted in 1985, 1992 and 2006, showing that abuse problems among inmates have increased enormously and that drug abuse has heavily supplemented alcohol abuse. It also relates this development to changes in the division of labour between the other main authorities that control the harm resulting from substance through days spent in institutions. For this register data the social and health authorities and the police authorities is additionally analysed and show that the role of the prison has grown. The study further analyses to what extent prisoners' abuse problems are noted in risk and needs assessments and sentence plans that are made in prisons, and what factors contribute to the problems being noted in them. Data on substance abuse from the prisoner health investigation from 2006 (N=610) is connected and compared to prisoner register information for the same persons. An article on this issue is currently being drafted. The data described above will also be used to investigate recidivism among prisoners who have been diagnosed with substance abuse problems, mental health problems, or who have a dual diagnosis. The study additionally analyses

what measures those prisoners whose sentence plans or risk and needs assessments states that they have problems with intoxicant abuse are subjected to. What factors contribute to countermeasures being taken and what do not? Data on prisoners who have been released (N=5448) in 2011 is used. During 2012 results from the study have been presented at THL to a meeting of experts on the intoxicant welfare system (VAHTI) and at the University of Helsinki to the Centre for Research on Addiction, Control and Governance (CEACG). Also, additional data has been gathered and work on the last three articles has started. The researcher has been on parental leave 15.9.2010-1.4.2012 Researcher: *Yaira Obstbaum*. (yaira.obstbaum@om.fi)

218 *Alcoholic Liver Cirrhosis: the Interaction between Genetic Factors and Gut Microbiota.*

The aim of this study is to find out how intestinal microbiota and genetic factors influence on the development of alcoholic liver cirrhosis. In Finland more than 90 % of cirrhosis is inflicted by alcohol. Heavy alcohol abuse leads to fatty liver and possibly to alcoholic liver cirrhosis. Our group has previously shown that CD14 polymorphism correlates with the risk of alcoholic liver cirrhosis. Endotoxin, a constituent of gram negative bacteria binds to the CD14 receptor in liver Kuppfer cells and can lead to activation of longterm inflammatory response which can cause alcoholic liver cirrhosis. Genetic variation of CD14 receptor has been studied in an autopsy material containing 1446 cases. We found out that all polymorphisms in the genes' regulation area did associate with the risk of alcoholic liver cirrhosis. The study is being expanded with multiple polymorphism sites and more samples. The reliability of post mortem samples has been evaluated. These results showed that post mortem samples can be taken for microbiological analyses if they are taken from liver or pericardial fluid within 5 days post mortem. Fecal samples (n=32), collected from autopsies, were compared to healthy volunteer fecal samples (n=7) in order to see whether they can be used in research purposes. Based on results, done with autopsy cecum and rectum samples, it can be said that autopsy fecal samples can be used reliably in investigation of intestinal microbiota, if they are taken before day 6 post mortem. The relative amounts of *Bacteroides* sp., *Bifidobacterium* sp., and *Clostridium* remained quite stable up to 5 day post mortem. Moreover the microbiota in autopsy rectum samples was similar to healthy controls (n=7), except there was slightly more *Bacteroides* sp. and less *Clostridium* sp. In autopsy cecum and rectum samples the bacterial DNA remained quite stable up to 5 day post mortem, after which it started to multiply in cecum. Manuscript has been sent to Forensic Science International. After the above-mentioned methodological research we are studying how intestinal microbiota and genetic factors influence on the development of alcoholic liver cirrhosis with autopsy samples and patient samples. Relative ratios of major commensal bacterial communities (*Bacteroides* sp., *Bifidobacterium* sp., *Clostridium* sp. and *Enterobac-*

ter sp. and *Lactobacillus* sp.) were determined using RT-qPCR in fecal samples of 7 male autopsies with alcoholic cirrhosis, 9 non-cirrhotic alcoholics and 7 non-alcoholic controls. Feces of 7 healthy male volunteers were used as controls. In addition to commensal bacteria, *Streptococcus* sp. and *Staphylococcus* sp. were determined by RT-qPCR in autopsy liver samples (n=25) and in 12 ascites from clinical alcoholic cirrhotics. Rectum samples of cirrhotics contained in mean >220-times more *Enterobacter* sp. compared to controls. Liver samples of cirrhotics and alcoholics contained more bacterial DNA compared to controls. The most common bacteria found in liver samples were *Streptococcus* sp., *Staphylococcus* sp., *Enterobacter* sp. and *Lactobacillus* sp. Bacterial DNA from streptococci followed by lactobacilli, clostridia and enterobacteria was found in 58 % of ascites samples of clinical cirrhosis patients. Manuscript is being written and it will be sent to Gastroenterology journal. Researcher: Sari Tuomisto, University of Tampere, Clinical School, Forensic Medicine. (Sari.Tuomisto@uta.fi)

219 *The Decisive Encounter – Process and Outcome Research of Initial Motivational Encounters at the A-clinic.*

This qualitative study focuses on the patterns of interaction in first client-counselor encounters in Finnish outpatient clinics for substance abusers. The aim is to identify those features of interaction that correlate with clients' engagement in treatment (=good outcome), and those which correlate with poor outcome. Poor outcome is defined as clients withdrawing from treatment or from contact with counselor, or even dropping out of the treatment. In 2012, the research was conducted part-time. The data consist of 38 audio taped initial encounters between counselor and client in 6 clinics in different parts of Finland. 12 counselors trained in MI were involved in producing the data. The audiotapes were transcribed and analyzed verbatim with conversation analysis (CA). CA describes the construction of conversation, focusing on the relation between consecutive turns. It describes the conversation as a mutual achievement of both participants. In 2012, research focused on two topics: 1) What happens after client's change talk (positive arguments on behalf of making a change)? 2) Ruptures / instances of discord in the interaction between client and counselor. For the research concerning the topic (1), the underlying hypothesis was that the counselors seek to identify change talk, evoke and elaborate it. This hypothesis is derived from the principles of Motivational interviewing, the prevalent counseling framework for substance abusers. However, the analysis revealed that in most instances counselors bypass clients' change talk. They very seldom recognize it immediately. In most of the cases in which counselors start to elaborate client's change talk, they do it in "a postponed fashion", a few moments after the moment of change talk. This has an effect on the contents of the initial encounter (what is the focus of the discussion), and therefore, also to the extent in which intrinsic motivation gets enhanced in the initial encounter. The results of this analysis have been reposted in a manu-

script: "What happens after clients' change talk? A qualitative analysis of interaction in initial encounters in outpatient clinics". It is currently being revised and will be sent to Behavioural and Cognitive Psychotherapy (BCP). The topic (2), ruptures / instances of discord in the interaction between client and counselor, emerged while analyzing the data for topic (1). The topic has been raised in the early phases of the research process as well. The underlying assumption for this research task is that alliance between client and counselors starts to build in the first encounter. The way mutual understanding is being built in the initial encounter may have an effect on the whole process. The analysis focuses on how participants identify instances of misunderstandings (mismatching communication /discord) and the different ways they solve the situations. The manuscript is being processed and it will be finished during spring 2013. Researcher: *Leena Ehrling*, V.T.T. (leena.ehrling@helsinki.fi)

220 *Mind, Body and Society in European Medical Thought on Alcohol c. 1790–1855.*

This study reconstructs a neglected tradition in the history of ideas on alcohol which emerged in European medical thought during the period from the late 18th to mid 19th century. At that time, alcohol-related diseases were established as an object of systematic clinical examination and classification. This study argues that an even further epistemological and ontological step was taken. By way of reasoning on the predisposing causes of alcohol-related diseases, many doctors extended their empirical interest from clinical considerations into inquiries of drinking as a socio-cultural phenomenon. Hence, the study argues, the doctors of the era brought forth a holistic understanding about the interconnections between alcohol, the individual and society. Their understanding about the physiological and pharmacological processes underlying the effects of alcohol on the mind and body interlocked with a view of drinking as a meaningful practice subject to historical and cultural variation. In addition, they rendered the very desire for alcohol as cultural, that is: not innate or natural. The emergence of the tradition is traced to the late 18th-century works of doctors who derived their intellectual outlooks from the hotbed of the Scottish Enlightenment medicine and moral philosophy, the University of Edinburgh. Especially the ideas of Thomas Trotter are highlighted. From there the study turns to the Continental tradition of clinico-pathological studies on alcohol-related diseases and the associated understanding about their societal antecedents in the first half of the 19th century. Here the focus is especially on the ideas of Magnus Huss. Based on the analysis and interpretation of an extensive corpus of primary sources the study contributes to discussion within the alcohol studies field as well as to the historiography of medicine and the social sciences more generally. The final report of the study is an article-based dissertation to be completed in 2013. In 2012, two article manuscripts were written for international peer-reviewed journals, and a thematic issue of the journal *Nordic Studies on Alcohol and Drugs* was co-edited (with

Michael Egerer). Also the editorial of the thematic issue 'Theories and Images of Addiction' (NAD 1–2/2013) was co-written. Three papers – including one plenary talk – were presented at international conferences. Since the beginning of the research project, fifteen international presentations have been given at intellectual history and alcohol/addiction studies conferences, symposia, and researcher meetings in e.g. Princeton, Victoria, Copenhagen and St. Petersburg. Other international activities include a research visit at the University of Edinburgh in 2010 and a lecture given at the University of Tallinn. Researcher: *Arto Ruuska*.

221 *Polydrug use related Deaths: Trends, Prescription Drug abuse and Regulation of Risks.*

Topic of this doctoral study is polydrug use related deaths. The prevalent paradigm in addiction research for the past decades has been a single substance driven orientation. Studies have concentrated on particular substances and harms they cause. However, empirically it is evident that polydrug use – concurrent or simultaneous use of licit or illicit substances - is very common. As research has concentrated on the use of single substances, polydrug use and its harms have not been studied much. Recent studies and statistics show that drug situation in Finland has been rather stable for the past 10 years. An exception to this trend is drug-related deaths which have increased since 2003. This has been explained by the increase of poisonings due to prescription opioids, especially buprenorphine, often in combination with other drugs. Finland is not alone in this development as the non-medical use of prescription drugs has increased rapidly in Western countries in the past decades. This PhD study will address these themes a) by examining the trends of polydrug use deaths in Finland, b) by comparing polydrug related mortality across diverse population groups, c) by describing association between prescription drugs and polydrug deaths, and d) by exploring the users' perceptions of risks related to polydrug use. In 2012, the data collection was finalized and research design refined. Analysis of two substudies was conducted and writing of article manuscripts has been started. Two manuscripts will be submitted to international peer-reviewed journals - one in the spring 2013 and one by the autumn 2013. A research visit was made to SoRAD, Stockholm University, in April-May. Researcher: *Sanna Rönkä*, University of Helsinki.

222 *The Role of Opioidergic Receptors in the Development of Alcohol Addiction.*

Alcohol dependence causes significant health related consequences that at present cannot be efficiently treated with current pharmacotherapies. Development of effective pharmacotherapies, however, relies on our understanding of the neurobiological mechanisms underlying addiction to alcohol. The opioidergic system has been shown to participate in mediating the effects of alcohol and in controlling alcohol consumption. The aim of this study is to clarify the role of the opioidergic system in regulating alcohol consumption using AA (Alco, Alcoholic) rat lines. The main

emphasis of this study is on the μ and κ opioid receptors in the nucleus accumbens and ventral pallidum, both of which are brain areas implicated in mediating the effects of alcohol. The experiments in this study are conducted with lentiviral vectors that either over- or underexpress μ or κ opioid receptor genes locally in the nucleus accumbens or ventral pallidum. Lentiviruses were chosen for this study because of their ability to integrate the transgene of interest into the genome of host cells and thus cause long-term transgene expression. During the course of this year the function of μ opioid receptor overexpressing virus vectors has been confirmed using in vitro cell experiments. In addition, alcohol drinking studies have been conducted with μ opioid receptor overexpressing viral vectors microinjected into the nucleus accumbens. In order to confirm overexpression of μ opioid receptors, morphine, a μ opioid receptor agonist, was used to induce locomotor activity and alcohol drinking in a time restricted alcohol drinking model. The tissue level effects of opioid receptor overexpression are analyzed using immunohistochemistry and Western blot analysis. Especially in the morphine induced alcohol drinking experiments, the animals treated with μ opioid receptor overexpressing vectors consumed more alcohol than control animals, which shows that the μ opioid receptors in the nucleus accumbens participate in controlling alcohol drinking. The κ opioid receptors may have a larger role in relapse to alcohol drinking than in maintaining alcohol drinking behavior. In order for the effects of κ opioid receptor gene overexpressing viral vectors to be measured reliably, we have started to implement a method that provides a reliable means to measure relapse to alcohol drinking. The studies aim at a Doctoral Thesis. Researcher: *Johanna Uhari*, University of Helsinki. (johanna.uhari@helsinki.fi)

223 *Interactions of Dopamine and Histamine in Alcohol Addiction.*

To study drinking behavior in mice, a new technique “Drinking in the dark” was launched and applied in 2011 to investigate the effects of histamine H3 receptor antagonists on alcohol drinking. This method was now extended to study cue-induced reinstatement of alcohol seeking in mice. The method was successfully applied to mice for the first time. We found that two different histamine H3 antagonist significantly attenuated lever pressing following cue reinstatement. The histaminergic system is thus not only involved in alcohol reward but also in seeking behavior. The result motivates related studies on human subjects, because H3 receptor antagonists are already in clinical tests for other indications. Since the histaminergic system is involved in alcohol reward and drinking, which are known to be associated with the dopaminergic system, we tested the hypothesis that histamine regulates expression of dopamine receptors or signaling proteins associated with these receptors. No differences were found in mRNA expression of D1 and D2 receptors, or the signaling proteins DARPP-32 or STEP61. The results were presented in a poster. In the presentation Histamine is not required in alcohol reward and stimulation the main message was that histamine is not required for

alcohol reward, but the effect of H3 receptor antagonists on reward cannot be seen in mice lacking histamine. Researcher: *Pertti Panula*, University of Helsinki. (pertti.panula@helsinki.fi)

224 *Environmental Effects on Developing Embryo: Epigenetic Changes in the Developing Brain caused by Ethanol Exposure.*

In our research we are aiming to understand the mechanism by which the environment affects the developing embryo and the role of epigenome in it. We will use mouse models of gestational ethanol exposure (FAS) and ethanol exposure before fertilization (EBF), developed during my post-doc period in Epigenetics Laboratory, QIMR Australia 2007-2009. The other aim of our research is to reveal the molecular mechanisms in the development of offspring, which lead to the phenotypic characteristics of fetal alcohol syndrome. We reveal these mechanisms by combining our studies of mouse genetics (mouse models of FAS and EBF) and human genetics (samples of ethanol-exposed individuals in Finland). Mouse model of FAS: In our work we are focusing on brain tissue. We are investigating changes in gene expression and epigenome in the brain of 28 days old gestationally ethanol-exposed mice. According to earlier studies of FAS phenotypes, corpus callosum, hippocampus, cerebellum and frontal cortex are the most interesting brain structures in the mouse to start with. We have used Affymetrix's microarrays (GeneChip® Mouse Exon 1.0 ST array) for mouse to interrogate ethanol-induced changes in gene expression on a genome-wide scale. We have established valuable collaboration with Docent Sampsa Hautaniemi's Bioinformatics Laboratory (Systems Biology Laboratory, Bioinformatics, University of Helsinki) to analyse our microarray data. Our expression array results from hippocampuses are encouraging. We have detected significant changes in the expression of several genes and some microRNAs in ethanol-exposed pups. In the ethanol group we can see changes in the expression of several epigenetically regulated olfactory receptor genes, which are normally expressed in a stochastic fashion in olfactory neurons. Interestingly, previous studies have shown that gestational ethanol exposure leads to abnormal olfactory bulb development, impaired odor discrimination and preference for the odor of ethanol later in life in rat studies, particularly during adolescence. After confirming the results in the main olfactory epithelium and olfactory bulb we will perform epigenetic, behavioral and structural studies. Professor Staffan Bohm from University of Umeå has trained us to dissect olfactory epithelium and olfactory bulbs. Results of the arrays are used to identify candidate genes for further analysis; the genes chosen will have CpG rich promoters, and will be assayed by bisulphite sequencing (DNA methylation) and chromatin immunoprecipitation (ChIP) followed by qPCR (histone modifications). In addition to RNA, we have extracted DNA for methylation analyses and collected brain, liver and kidney samples. Human studies, FAS: If the alcohol-induced molecular changes occur very early in the development prior to the differentiation of the three germ layers, they should be present in all tissue types including blood. To

confirm that the changes found in our mouse model can also be detected in human cells, we have established co-operation with Finnish clinicians and specialists. We have submitted our ethical approval in December 2012 to the ethical board and we are waiting for a permission to start collecting the human samples. We will start to collect the first set of blood samples of ethanol-exposed individuals in Finland in the year 2013. We hope that 100 pregnant women with an increased risk to deliver children damaged by gestational ethanol exposure are willing to participate to this study. In addition to 100 normal control women, we would like to include 50 women who are smoking during the pregnancy to this study. By using these “smoking controls” in our study, we aim to separate the epigenetic effects caused by smoking from the effects of ethanol. We will analyze genetic and epigenetic changes between three groups of samples (EtOH, smoking, controls). When children are at the age of 2-3 and 5-6, we will perform neuropsychological tests to determine the phenotype. In the end of the follow-up study our aim is to find potential correlation between epigenetic changes and the phenotype of the affected child.

Mouse model of EBF: The second mouse model involves 10% ethanol consumption for four days per week for five or ten weeks immediately prior to fertilization; a period that encompasses multiple cycles of oocyte maturation and ovulation. In our previous study we showed that ten weeks exposure increased transcriptional silencing and hypermethylation of the Avy allele in the offspring. In this study we want to clarify the mechanism that is probably different compared to the gestational ethanol exposure: the Avy allele is paternally derived and not present in unfertilized oocytes. We have collected samples of corpus callosum, hippocampus, cerebellum and frontal cortex from 28 days old offspring of dams who have consumed ethanol prior to fertilization as described above. We are establishing co-operation with Professor Rickard Sandberg’s research group (Karolinska Institute, Sweden) to perform single cell expression sequencing for the mature oocytes of ethanol treated dams. We hope that by combining the information from gene expression in oocytes and gene expression and epigenetic information of 28 days old offspring we can understand the effects of ethanol exposure before fertilization. I have worked as an independent project leader in the laboratory of Professor Juha Kere, in Research Program of Molecular Medicine (Biomedicum Helsinki). In the spring 2012 two skillful undergraduate students, Anna Nyman (genetics) and Heidi Marjonen (genetics, animal physiology), started to work with me, and both of them are continuing to the doctoral degree. In the beginning of the year 2013 I will be a principal investigator and establishing a research group of Environmental Epigenetics in Development in the Department of Medical Genetics (Haartman Institute), University of Helsinki. Due to the challenges with increasing bioinformatics data, I am planning to recruit a student of bioinformatics in this project. Docent Sampsa Hautaniemi and I will supervise him or her. In addition, I am willing to recruit a student to work with the human samples and the meconium analysing procedure. Researcher: *Nina Kaminen-Ahola*, University of Helsinki. (nina.kaminen@helsinki.fi)

225 *Molecular Mechanisms of Alcohol-Induced Birth Defects.*

Prenatal exposure to ethanol is an important cause of many birth defects such as central nervous system (CNS) damage, brain growth deficiencies, mental retardation, neurodevelopmental disorders and craniofacial anomalies. These symptoms and findings belong to the Fetal Alcohol Syndrome (FAS). We have studied FAS using a mouse model. Mice received two intraperitoneal injections of ethanol at 8.75 days post coitum (dpc). The fetus head, trunk, yolk sac and placenta were collected on 9.5 and 12.5 dpc. In 2012 we have published a report on placental malformations and malfunction. We have further explored some of the metabolic pathways that were affected by ethanol exposure in our animal experiments and DNA microarray analyses. We observed a total depletion of polyamines in the embryo head after ethanol exposure. This could explain CNS defects found in FAS children (manuscript "Ethanol-induced derangement in the polyamine metabolism - a potential cause of neural tube defect and intrauterine growth retardation in fetal alcohol syndrome" submitted). In addition, a manuscript "Alcohol consumption during pregnancy disturbs cholesterol synthesis and lipid metabolism in placenta" will be submitted during spring 2013. Saeid Haghighi Poodeh is preparing a thesis based on these publications and will have dissertation by the end of 2013. Researchers: *Markku Savolainen, Saeid Haghighi Poodeh, Jussi Vuoristo and Tuire Salonurmi*, University of Oulu, Institute of Clinical Medicine, Department of Internal Medicine. (markku.savolainen@oulu.fi)

226 *Young People and a Changing Culture of Crime Control – Policing Alcohol Drinking, Delinquency and the Use of Public Space.*

This sociological PhD research project examines adversarial encounters between young people, police and private security guards, in a changing culture of control. The purpose is to study in which kind of situations these contacts take place, how common they are, and whether they are biased or selective. The study investigates how and to what kind of delinquency, alcohol drinking and free time activities these interventions target. In addition, the project examines how youth themselves experience and perceive these encounters with police and security guards. The purpose is to provide information on diversity of youths' views on control of alcohol drinking and other youth activities, and the positive and negative effects of such interventions. The starting point for the study is an observation that crime control of young people has intensified and they are often seen as a threat or risk to security when they use public spaces. The study discusses on societal level what kind of youth activities and which kind of groups is seen as risks and what kind of societal reactions are produced. Thus, the study uses criminological labelling theory and the theory of societal reactions. In addition, it contributes to the (global and local) discussions in changes of social control, such as intensification of crime control, the emergence of risk governance, and privatisation of social control. As an example, first, police control of young people has

increased recently despite the fact that youth delinquency and their substance use habits have not changed significantly. Second, in many countries there has been a major transformation in crime control. Indeed, the private security sector has become larger and its general societal impact has increased. What follows is that adversarial contacts between young people, police and security guards are rather common. Despite these aspects of societal changes, empirical research on those who are targets of control interventions has been scarce. Particularly, the role of private security guards in controlling youth activities and alcohol drinking has been a neglected topic. The aims of the study are, on one hand, to describe the nature and likelihood of youths' encounters with police and guards and, on the other hand, to provide information on how young people perceive these encounters and how they conceptualise successful interventions. The study uses mixed methods. First, the study uses the nationally representative youth survey for youth aged 15 to 16 (self-report delinquency survey collected in 2008). The survey data analyses the nature, prevalence and the factors affecting the likelihood of adversarial police and guard contacts. It explores the effects of heavy drinking, delinquency, and socio-demographic characters. Alcohol use (in public space) is one essential factor that increases the likelihood for these contacts. Secondly, the qualitative part of the study consists of focus group interviews with youth aged around 15 to 18. The data is used to study the meaning of the adversarial contacts, which are linked to youths' free time activities and substance use. The study investigates how and what kind of drinking habits are officially reacted to, how youth perceive these situations and what kind of effects they have for instance on trust on authorities. The project began in 2011 and from May 2012 it continued as a research contract project. The plan is to publish four international articles and to include them in my doctoral thesis. During this period, the first article has been finalised and the second article manuscript has been under preparation. In addition, the focus group interview data has been designed and the first interviews were made in the autumn 2012. The first article 'Young People as Objects of Police Control in a Nordic Context: Who Are Socially Visible Targets?' has been submitted to an international journal in December. The second manuscript has been written, about policing young people - the role of private security guards. Both of the articles use the quantitative survey data. In addition, the preliminary findings of the second article have been presented in the conference of the British Society of Criminology. Researcher: *Elsa Saarikkomäki*. (elsa.saarikkomaki@helsinki.fi)

227 *Association between Parental Substance Abuse Problems and their Children's Cumulative Risk Factors for Social Deprivation at Adolescence.*

The sociological dissertation study examines, from different perspectives, the social deprivation which is related to parental substance abuse and the inheritance of parental problems to the children. The study is based on the findings of an increase in alcohol consumption in Finland

over the last forty years, especially among women who are at parenting age, and the more prevalent drug use and the stabilization of higher drug use level than before during the 1990s. Harmful parental substance use in the living environment of a child can significantly affect the child's wellbeing and it can also become entangled with other problems, such as parental mental health problems and the family's livelihood difficulties. The aim of this study is to find out associations between parental substance abuse and child's risk factors for health, social and economic deprivation, from birth to 20 years of age. The study is based on an extensive administrative register data of the children born in 1991 and their biological parents. The data allows the follow-up of the cohort until year the 2011. The methods applied in analysis are statistical analysis suitable for longitudinal data. In 2012, the study was conducted from July to December and was funded by the research contract. During this period, research permissions were applied for the extra data, and data requests were sent to the various register authorities. Preliminary analysis was conducted for the data and writing of the first article manuscript was started. The article will be offered to an international journal in March or April 2013. Researcher: *Marke Jääskeläinen*.

228 *Forensic Psychiatric Patients in a Welfare State.*

The research examines forensic psychiatric patients and their social background, social status and patterns of use of welfare services prior to committing criminal activities leading up to involuntary psychiatric admissions. The findings will be utilized as the basis for three articles. The first article will focus upon the patients' use of substance abuse services, psychiatric inpatient services and prison services. The second article will consider their parents' and their own history of substance abuse. The final article will examine the patients' social background and any issues they may have experienced in their parental home whilst growing up. The research materials consisted of psychiatric assessments and records relating to psychiatric inpatient treatment. In addition, extracts from criminal records in relation to prison sentences were examined. Methods of data analysis included statistical tests. The funding from The Finnish Foundation of Alcohol Studies was utilized to collect and analyze the data and to compile the first draft of the first article listed above. The researcher presented the research plan in the workshop titled "Mechanisms of Welfare and Inequality" during the Social Policy Days in Jyväskylä. Researcher: *Miisa Törölä*.

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