

**THE FINNISH FOUNDATION
FOR ALCOHOL STUDIES**

REPORT ON ACTIVITIES 2016

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THE FINNISH FOUNDATION FOR ALCOHOL STUDIES

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GENERAL OVERVIEW

In 2016, the projects funded by the Finnish Foundation for Alcohol Studies resulted in the publication of three academic doctoral dissertations, 24 original peer-reviewed articles in international and three original peer-reviewed articles in national scientific journals. Sixteen other papers were published.

Alcohol and drug research received 281.963 euro in support for projects. In addition, 177.718 euro was granted to projects on gambling. 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 following members: four 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 seven external experts.

The Foundation's Research Director *Tomi 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

PhD dissertations supported by the Foundation

Haghighi Poodeh, Saeid: Novel pathomechanisms of intrauterine growth restriction in fetal alcohol syndrome in a mouse model

Fetal alcohol syndrome (FAS) is a pattern of anomalies in affected children due to maternal alcohol administration at vulnerable stages of fetal development. Intrauterine growth restriction and facial malformation are the presenting phenotypes of FAS. In this investigation, novel pathomechanisms of intrauterine growth restriction and facial malformation were the primary aims. We found by a FAS mouse model that AceCS1 gene expression and polyamines are the immediate targets of fetal alcohol exposure. The AceCS1 product is a precursor for lipid synthesis and protein acetylation and possibly, for polycation acetylation. We cloned the *Mus musculus* nuclear-cytosolic AceCS1 gene, and showed that its expression is developmentally regulated with a dynamic localization in the cytosolic and nuclear compartment. The enzyme plays an essential role in de novo synthesis of acetyl Coenzyme A. Fetal alcohol administration targets nutrient supplying networks, which are localized at critical barriers. The main findings were reduced surface of the labyrinthine zone, destruction of gap junctions in the hemotrichorial placenta, reduced syncytiotrophoblastic cell layers and loosening of interaction between cell layers and embryo endothelial cells, reduced Reichert's membrane thickness with discontinued Reichert's trophoblast and loss of interaction by Reichert's-parietal cells, reduction of capillary network and reduced vascularization in the brain area, and perturbed neural crest migration and formation of neural tube defect. Alteration of angiogenesis-regulating proteins such as VEGF, PlGF, PECAM was detected in FAS, with no significant changes in placental angiogenesis of the labyrinthine zone, but up-regulation of VEGF/PlGF caused permeability changes in the placenta and yolk sac. On the other hand, the PECAM pool in embryos' brain was reduced, which in turn led to decreased angiogenesis and vascularization. *Acta Universitatis Oulensis, D Medica* 1381. Oulu University Press, Oulu 2016. ISBN: 978-952-62-1316-3, ISSN: 0355-3221.

Räsänen Tiina: Health in game: Adolescents' gambling and its association with risk-taking

Gambling has become an ordinary way to spend leisure time among Finns. Adolescents are also participating in gambling even though it is forbidden by law for those under 18 years of age. According to research examining gambling among Finnish, up to 37 per cent of 15-17-year-olds respondents had gambled during the past 12 months. Gambling is indeed in many different ways present in the life of the youth. Gambling games are available in several places and advertisements can be seen from the living room couch as well as in grocery stores. In spite of the abundant availability and visibility of gambling games, there have been fairly few studies on adolescents' gambling behavior in Finland. Therefore, one of the main emphases of this study was to produce new information on gambling among Finnish adolescents. In the study it was examined whether gambling frequency (how often one participates in gambling) was associated with adolescents' risk behavior or poorer health. Risk behavior meant adolescent problem behavior and health risk-taking. Problem behavior, in turn, was activity that threatens well-being of young, is against the norms, or is even illegal. It was also examined how social support from parents, friends, school, as well as parents and friends gambling affect adolescents' gambling, as well as associations between risk behavior and health. On the other hand, we were interested in seeing what kind of gambling behavior is linked to problem gambling and risk behavior. Three different national surveys were used in the study: School Health Promotion Study from years 2010 and 2011 (N=102,545), Adolescent Health and Lifestyle survey from year 2011 (2,812) and Youth Gambling 2006 survey (N= 5,000). Furthermore, several different statistical methods were utilized. By multinomial logistic and

negative binomial regression analysis the association between gambling frequency, gambling related harms and risk behavior was studied. ROC analysis was used to examine the gambling behavior limits for problem of gaming. Gambling behavior thresholds were tested using logistic regression. Using latent class analysis teenagers were grouped into categories based on their problem behavior and path analysis was used to study the effect of social support on the associations between gambling, risk behavior and health. The study showed that gambling frequency was associated with risk-taking behaviour and with poorer health. Among girls, even gambling occurring as rarely as monthly was already associated with problem behaviour, and gambling 1–2 times per week showed increased risk taking behavior as well as poorer health when compared to non-gamblers. Among boys, gambling less often than once a month was linked with substance use. Physical symptoms and health risk-taking appeared mainly on boys who gambled on a daily basis. Social support from school and parents decreased the probability of gambling, but social support from friends increased the probability of gambling frequency among boys but decreased it among girls. However, social support explained only weakly the associations between gambling and problem behaviour and between gambling, health risk-taking and poor health. The risk of problem gambling increased with higher frequency of gambling, higher amount of gambling games played during the year, and with higher amount of money invested in gambling. Gambling that took place more often than 2–3 times a month, and/or in which the money that was used for gambling exceeded two euros in a week, the biggest sum that had been used for gambling was more than 8 euros and participating in more than two different games per year, were associated with problem gambling among 12–14-year-old adolescents. Among 15–17-year olds, gambling more often than once a week, spending more than four euros per week, gambling on more than two different games per year and spending sums larger than 12 euros on gambling, were linked with problem behaviour. Studies concentrating on gambling frequency and its association with health have been limited in Finland as well as internationally, since the main emphasis has been on gambling problems. These study results of links between gambling, poorer health and other risk behavior, as well as gambling limits form the basis for youth gambling research and development of preventive work. The results can also be used to support gambling policy-making, when considering whether or not adolescents' gambling should restrict even further. Acta Universitatis Tamperensis; 2222, Tampere University Press, Tampere 2016. ISBN 978-952-03-0256-6, ISSN 1455-1616.

Salonsalmi A: Alcohol drinking, health-related functioning and work disability

Alcohol drinking is a major potentially preventable risk factor for health and wellbeing worldwide. Alcohol drinking has increased markedly from the late 1960s in Finland until 2007. Alcohol-related causes of death and morbidity are common, especially among the working-age population. The majority of Finnish heavy drinkers are employed and there is a need to assess the contribution of alcohol drinking to health-related functioning and work disability using longitudinal data including several drinking habits. The aim of this study was to examine the associations between alcohol drinking, health-related functioning and work disability among ageing municipal employees. This study is part of the Helsinki Health Study. The baseline data were collected in 2000–02 among 40- to 60-year-old employees of the City of Helsinki (n=8960, response rate 67%). A follow-up survey was conducted in 2007 (n=7332, response rate 83%). The survey data were linked with sickness absence data, derived from the employer's personnel register, and with data on disability retirement, derived from the Finnish Centre for Pensions, among 78% and 74% of participants consenting to internal and external data linkages. Alcohol drinking was measured by weekly average drinking, frequency of drinking, binge drinking and problem drinking assessed by the CAGE scale. Logistic regression, Poisson regression and Cox regression were used in analysing the data. Heavy weekly average drinking, binge drinking and problem drinking were all associated with poor mental functioning, whereas concerning physical functioning associations were

found for problem drinking only and non-drinkers also had an increased risk. Heavy weekly average drinking, binge drinking and problem drinking were associated with both self-certified and medically confirmed sickness absence from work with the exception of binge drinking among men. The association between weekly average drinking and medically confirmed sickness absence was U-shaped, both non-drinkers and heavy drinkers having increased risks compared to moderate drinkers. Working conditions had no major contributions to the associations, although psychosocial working conditions somewhat attenuated the associations, especially among men. When studying changes in alcohol drinking, associations were found for self-certified sickness absence more often than for medically confirmed sickness absence, as associations for the latter were mainly explained by health and other health behaviours. Also, reduced alcohol drinking and previous problem drinking increased the risk of sickness absence. Alcohol drinking was strongly associated with disability retirement due to mental disorders, whereas no associations were found for musculoskeletal diseases. Throughout the study, alcohol drinking showed the strongest associations with poor mental health. Problem drinking was the drinking habit with the most widespread associations with poor health-related functioning and work disability. The results of the study indicate that alcohol drinking is a risk factor for poor health-related functioning and work disability in the middle-aged working population. Heavy drinking, binge drinking and problem drinking were all associated with poor health-related functioning and work disability, but problem drinking showed the strongest and most widespread associations. The study suggests that problem drinking should be assessed in addition to the overall amount of drinking in future studies and clinical settings. The study highlights the importance of alcohol drinking for poor mental health and calls for recognition and early prevention of heavy alcohol drinking among both the occupational and primary health care systems. *Dissertationes Scholae Doctoralis Ad Sanitatem Investigandam Universitatis Helsinkiensis*. Helsinki University Press: Helsinki 2016. ISBN:978-951-51-2700-6, ISSN 2342-3161.

Research contracts and collaborative projects

221 *Polydrug use related deaths: trends, prescription drug abuse and regulation of risks.*

Drug situation in Finland has been rather stable past 10 years. Exception to this are drug-related deaths which increased to a new level in the first decade of 2000s. 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 is a part of process called pharmaceuticalisation by health sociologists. This dissertation study explores drug related deaths and mortality a) by describing association between prescription drugs and polydrug deaths, d) by exploring how prescription drugs alter the dynamics of drug use scenes, c) by examining how hard drug users perceive overdose and other health risks, and d) by comparing drug related mortality across diverse social characteristics. The results of the study have so far been published in two peer-reviewed articles, third one is accepted for publication and the fourth one is to be finalised.

Researcher: *Sanna Rönkä*, University of Helsinki. (sanna.ronka@helsinki.fi)

222 *The role of opioidergic receptors in the development of alcohol addiction.*

Due to the negative consequences of alcohol on health, alcohol addiction has been vastly studied. The reinforcing and rewarding effects of alcohol are believed to be the cause of alcohol addiction. Several different neurotransmitter systems participate in mediating the effects of alcohol, of which the opioidergic systems have shown to be central players. Especially the activation of the opioidergic systems within brain areas associated with the reward tract, such as in the nucleus accumbens and ventral pallidum, are in a significant role in controlling alcohol intake. The aim of the present study is to clarify the role of the μ - and κ -opioidergic systems in controlling alcohol intake. In these studies the alcohol preferring AA (Alko Alcohol) line of rats is used.

Research suggests that different opioidergic systems have an opposing role in alcohol addiction. The μ -opioidergic system participates in mediating the rewarding effects of alcohol. However, as addiction progresses and alcohol intake becomes chronic, the role of the μ -opioidergic system may decrease and the role of the κ -opioidergic system may increase. The κ -opioidergic system is thought to mediate the anhedonic effects of alcohol and it may also have a role in relapse.

The acute role of the μ -opioidergic system in controlling alcohol intake is supported by our recent results. μ -Opioid receptor agonists and antagonists administered intra-accumbally were able to acutely modify alcohol intake. These results were recently published in *Alcoholism: Clinical and Experimental Research* (Uhari-Väänänen et al. 2016). In addition, our results suggest that pallidal μ -opioid receptors may also have an acute role in controlling alcohol intake. The results were presented this November in the Society for Neuroscience conference in San Diego.

Our previous results suggest that κ -opioid receptor antagonists can have a prolonged effect on decreasing alcohol intake when administered both systemically and intra-accumbally. Therefore, in our on-going study we are testing the ability of κ -opioid receptor antagonists on being able to prevent relapse to alcohol. These studies aim at a Doctoral Thesis.

Researcher: *Johanna Uhari-Väänänen*, University of Helsinki & National Institute for Health and Welfare. (Johanna.uhari@helsinki.fi)

224 *Effects of gestational alcohol exposure on epigenome, gene regulation and the development of embryo.*

We hypothesize that early ethanol exposure disrupts the epigenetic reprogramming of embryo, which leads to alterations in gene regulation and embryonic development. Our aims are

to reveal the molecular mechanisms, which lead to the phenotypic characteristics of fetal alcohol spectrum disorder (FASD) and to find biomarkers for FASD diagnosis as well as to develop new diagnostic criteria. Because prevention of FASD is often impossible, early diagnosis and appropriate support for development have an important role in the therapy of FASD children. We are using a mouse model of gestational alcohol exposure of which we have published a study in spring 2015 (Marjonen et al. PLoS One) as well as human samples in epi-FASD-project. In a co-operation with University Hospital we have collected 42 samples of alcohol-exposed, 12 smoking-exposed and 100 control newborns so far. Due to the restricted growth resulted from gestational alcohol exposure, we have explored the effects of alcohol exposure on *Insulin-like growth factor 2 (IGF2)/H19* locus in human placenta. This locus is imprinted, epigenetically regulated, and crucial for normal placental and embryonic growth. Our results are highly interesting: we observed association between a single nucleotide polymorphism at this locus and genotype-specific placental DNA methylation, gene expression as well as head circumference of alcohol-exposed newborns. Our finding emphasizes the significance of genetic variation in the etiology of alcohol-induced developmental disorders and introduces the first genetic factor behind the complex FASD phenotype. Researcher: *Nina Kaminen-Ahola*, University of Helsinki. (nina.kaminen@helsinki.fi)

226 *Young people and a changing culture of crime control – policing alcohol drinking, delinquency and the use of public space.*

While general trust in the police is high in Finland, young people's encounters with the police can be problematic. The starting point for the study was the observation that the police control and social control of young people has intensified, although youth delinquency and alcohol use have not increased. Furthermore, the rapid rise of private security in many Western countries has changed the social control landscape. There is, however, a lack of research on the role of private security in policing young people. This study examined adversarial encounters between young people, the police and private security guards. It focused on social control directed towards youth delinquency, alcohol use and the free time activities of young people. The primary objective was to study how trust is constituted between young people and the police and private security guards. This study drew on sociological and criminological approaches (e.g. labelling theory and procedural justice theory). It consists of 4 articles and a summary article. The primary research aims of the substudies were to find out: firstly, if public and private policing of young people targets some social groups selectively. Secondly, how do young people perceive fair and unfair encounters in situations where policing agents intervene in alcohol use? Thirdly, what differences there are in young people's trust and confidence in the police compared to private security guards? The study drew on a Finnish self-report delinquency survey (N=5826, ages 15 to 16) and on nine focus group interviews with 31 young people (ages 14 to 17). The findings based on quantitative data indicated that police and security guard interventions were highly prevalent among young people. Furthermore, the study examined which factors increase the likelihood of police interventions (substudy I) and security guard interventions (substudy II). The findings showed that heavy drinking and delinquency increased the likelihood of both types of interventions. Furthermore, police and security guard interventions disproportionately targeted lower class city youths and those from non-nuclear families, even when differences in offending were taken into account. While boys were more likely to experience police interventions, there were no gender differences in security guard interventions. Sub-study III analysed fictional and personal stories of fair and unfair encounters where police and security guards intervene in underage alcohol use. The study found that intervening itself in underage alcohol use did not challenge trust. Instead, the key difference between situations perceived as fair and unfair was related to how policing agents treated young people. Fair narratives highlighted friendly and peaceful interactions and mutual respect whereas unfair narratives described aggressive and impolite treatment. Furthermore, emotional aspects, such as policing agents being empathetic and controlling their negative

emotions, were important. Sub-study IV found that young people had more trust and confidence in the police than in security guards. Perceptions of trust were formulated in face-to-face encounters and based on general assumptions. Young people considered the police more educated, professional and their actions more legitimate and respectful. The security guards were perceived to exceed their legal rights and to act unfairly. However, the findings also suggest that private security guards have gained some legitimacy, and they were not conceptualized as private actors. On a positive side, the young people felt they can ask police and security guards for help. However, sometimes when there was alcohol used they did not want to ask for help because they were concerned about the consequences. The study highlights that, in particular within the context of this new form of public-private social control, there is a need to understand the positive and negative effects of policing in a broad sense. Unfairly perceived encounters can have broad societal effects: they can affect young people's trust in other people in society and their sense of social belonging. Furthermore, the study also revealed possibilities for developing good relations and trust between young people and policing agents. Researcher: *Elsa Saarikkomäki*. (elsa.saarikkomaki@alumni.helsinki.fi)

227 *Association between parental substance abuse problems and their children's cumulative risk factors for social deprivation at adolescence.*

This sociological dissertation study examines from different perspectives disadvantage that is related to parental substance abuse, and the intergenerational transmission of disadvantage from parents to 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 1990's. Harmful parental substance use in the child's living environment can significantly affect the child's wellbeing, and it can also become entangled with other problems, such as parental mental health disorders and the family's financial 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 disadvantage from birth to 20 years of age. The study is based on an extensive administrative register data of a total birth cohort of 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 2016 two articles were published: "A typology of families with parental alcohol or drug abuse", *Addiction Research & Theory* and "Mental disorders and harmful substance use in children of substance abusing parents", *Drug and Alcohol Review*. Also the third article manuscript was written. Results of the research project were presented at the KBS Thematic Meeting on alcohol's harm to others in Helsinki on September 16, 2016 with the title "Effect of parental substance abuse on educational attainment of children". Researcher: *Marke Jääskeläinen*, University of Helsinki. (marke.jaaskelainen@thl.fi)

229 *Neuroinflammation in mouse models of alcohol consumption.*

Immune system has been shown to modulate acute and chronic effects of alcohol, and neuroinflammation might be important also in development of alcoholism. Immune system related genes display expression changes in *postmortem* brains of alcoholics. Recent preclinical research shows a connection between neuroimmune signaling and alcohol consumption. For example, knockout mouse models of immune system genes show changes in alcohol consumption. Our aim is to investigate how strengthening of this immune signaling influence ethanol consumption and sensitivity, and how it modifies brain reward system. We have utilized lipopolysaccharide (LPS) for inflammation challenge, a model that has been shown to increase long term free-choice alcohol consumption in C57Bl/6J mice. However, we found that LPS-treatment reduced ethanol consumption at highest ethanol concentrations in a similar 24-h 2-bottle free-choice drinking test in contrast what was reported earlier by others. Therefore, we tested the effect of LPS also in a drinking in the dark (DID) -model. Utilizing this

model with 4-h restricted drinking for 4 days a week, we did not observe significant enhancement of alcohol consumption in tests with 15% or 20% ethanol. Our results indicate that the model of increased alcohol consumption by LPS-inflammation challenge requires further development and verification by other laboratories. Utilizing the DID model, we have observed decreasing effects of naltrexone and minocycline on ethanol consumption. However, it was evident that at least a part of the decreasing effect on alcohol consumption by minocycline was caused by a general decrease in liquid, also water, intake. It is clear, that better tools are needed for *in vivo* studies of alcohol-neuroinflammation interaction. In the future, we will study the effect of neuroinflammation on ethanol reward in conditioned place preference tests and changes in brain reward thresholds will be analyzed with intracranial self-stimulation method. This PhD thesis aiming research began in April 2013. Researchers: *Mira Lainiola* and *Anni-Maija Linden*, University of Helsinki. (mira.lainiola@helsinki.fi), annamaija.linden@helsinki.fi)

231 *Role of GDNF in incubation of alcohol craving.*

Withdrawal from alcohol often leads to relapse even after long periods of abstinence. It is known that there can be intense craving for alcohol and that craving can last long periods. Drug craving methods are well established with laboratory rats. In rats, it has been observed that rat's response to cues increases over time after withdrawal from cocaine and heroin self-administration. The phenomenon is termed incubation of drug craving. The first aim of our study was to set up and validate a novel method to study alcohol craving in mice by using IntelliCage in a social environment. The use of fully automated IntelliCage is a new approach to studying addiction-related behavior in mice. Self-administration, following extinction and relapse paradigms in mice, are still not well developed. Mice still pose an enormous possibility for studies that cannot be conducted in rats. It is good to remember that gene modifications are much more diverse in mice as well as they are rather cost efficient. We have studied differences in alcohol, alcohol and sweetener, sweetener, and water on drinking-related behavior in mice, as well as extinction responses on withdrawal days 1 and 10. We have found that there is increased craving in using sweetened alcohol as compared to alcohol, sweetener alone or to water control on withdrawal day 10. We have further analyzed the role of glial cell line-derived neurotrophic factor (GDNF) in alcohol craving using this method. GDNF is a protein that has survival promoting properties in dopamine neurons and effects on dopamine neurotransmission. We have found that increasing GDNF signaling in the ventral tegmental area there is decreased craving for alcohol on withdrawal day 10. Researchers: M.Sc. Maryna Koskela. Docents Vootele Voikar, T. Petteri Piepponen, Jaan-Olle Andressoo & Mikko Airavaara. (Mikko.airavaara@helsinki.fi)

234 *Substance Abuse in the Family – Children's Experiences of Inequalities and Ambivalent Family Relations.*

In this post doc -study, interest lies in the experiences of family relations, inequalities and social class of children and young people in problem-drinking families. For the qualitative part of the study, interview data (N=30) of children and young people who have a problem-drinking parent was collected. Also interviews of adult sons of problem-drinking fathers (N=21) are used in the study. In addition, national 1987 -cohort data will be utilized in the study.

During 2016, analyses and writing up the results have continued. Interviews of children and young people, collected in 2014 for the research project "Growing up in the Finnish Drinking Culture" have been analyzed as well as the quantitative national 1987 -cohort data, into which data from different sources has been combined. By the end of 2016, articles Pirskanen, H. (2015) "Sons of Problem-Drinking Fathers: Narratives on the Father-Son Relationship" (in *Family Science*); Pirskanen, H. et al. (2015) "Researching Children's Multiple Family Relations: Social Network Maps and Life-Lines as Methods" (in *Qualitative Sociology Review*),

and a book chapter Simonen, J., Pirskanen, H., Kataja, K., Holmila, M. & Tigerstedt, C. (2016) "Kun vanhempi juo liikaa – nuorten kokemukset ja voimavarat" in Holmila, Raitasalo & Tigerstedt (eds.) Sukupolvien sillat ja kasvamisen karikot, have been published. An article Orjasniemi, T. & Pirskanen, H.: "Seksuaalinen väkivalta päihdeperheessä tyttöjen kokemana ja näkemänä" is ready and awaiting publication in a book Kiuru, H. & Strömberg-Jakka, M. (eds.) Seksuaalisuuden tabut suljetuissa yhteisöissä. In 2017, three more articles will be finished and sent to review process before publication.

In 2016, the researcher has also presented her work in national and international seminars and congresses. Researcher: *Henna Pirskanen*, University of Jyväskylä / National Institute for Health and Welfare. (henna.pirskanen@jyu.fi)

235 *Immune response to alcohol metabolites.*

Antigenic protein adducts are formed in our body due to alcohol metabolism. Proteins are modified by acetaldehyde and the lipid peroxidation product malondialdehyde. Antibodies that bind to these adducts are found in humans. In the presence of alcohol, the lipids in the body are also altered. Phosphatidylcholine in our lipid membranes is modified with ethyl-group producing phosphatidylethanol. We have found antibodies binding to this lipid molecule in plasma samples of mice and humans. Our aim is to study the genetic background and the binding specificity of the antibodies binding to phosphatidylethanol. By using mouse and human monoclonal cell lines we are studying mutations in variable region sequences responsible for the binding specificity of the antibodies. We are investigating cross reactivity with structurally related molecules using purified antibodies to understand the specificity and the source of these antibodies. Natural antibodies are formed in the body without pre-exposure of immune system to exogenous antigen. Characteristic to these antibodies is that there are only a few mutations in variable region sequences compared with germ-line sequences. Natural antibodies binding to malondialdehyde-acetaldehyde adducts are reported recently in the literature. We are analyzing the immunoglobulin sequences of the monoclonal phosphatidylethanol antibodies in terms of natural antibody characteristics. Natural immunity to alcohol metabolites may be involved in pathogenesis of alcohol-related illness.

Researcher: *Antti Nissinen*, Research Unit of Biomedicine and Research Unit of Internal Medicine, University of Oulu. (antti.nissinen@oulu.fi)

236 *The Homeless in Finland – Morbidity, Mortality and Service Use.*

There is very little research on the health of homeless in Finland. From international studies we know that homelessness is associated with increased morbidity, especially in addiction disorders, liver disease, dermatological conditions, psychiatric disorders, neuropathology and infectious disease. The use of health care services is also bigger among the homeless compared to the general population, especially the use of emergency health care services.

In November 2013 there were 7500 homeless persons, out of 4100 resided in Helsinki. The majority of those registered as homeless stay with family-members or friends, only the most disadvantaged stay in shelters or sleep rough. Since June 2009 there has been only one shelter in Helsinki; Hietaniemenkadun palvelukeskus. The shelter offers free accommodation for one night at a time, as well as health care and social services and provides assistance in finding permanent housing solutions when necessary. Hence, the homeless population using the services of Hietaniemenkadun palvelukeskus is a natural starting-point when studying the situation of the homeless in Finland. The experience from five years of clinical work with homeless in Hietaniemenkadun palvelukeskus has shown that the health problems typical for homeless that is described in international literature, are also prevalent in Helsinki. We've also observed that the so called "easy homelessness", resulting from financial difficulties, is rare and usually taken cared of, but the long-term homeless that remain in shelter for longer almost always have severe psychiatric and/or addiction problems, and their situation reveals the weaknesses and problems in the Finnish welfare system.

The purpose of the dissertation research is to for the first time in Finland broadly and systematically study and describe the morbidity, mortality and service use of the homeless as well as the effect of health status in sustaining housing. The study is a register based follow-up study. The sample consists of all homeless individuals (n=836) that stayed in Hietaniemenkadun palvelukeskus during one year (1.9.2009-1.9.2010), the control group is a sex and age matched sample from population registry (n=1647). For the mortality study we use the population that stayed in the Herttoniemen asuntola, the shelter that preceded Hietaniemenkadun palvelukeskus, in the year of 2004 (n=628) with an age and sex matched control group from the population registry (n= 1254). The registers analysed are the primary health care patient records, the social services client register and patient records from substance abuse services in the City of Helsinki, the specialized care and hospital registers (HILMO), the causes of death from Statistics Finland and the medication and pension data from social insurance institution of Finland. The study period is 2004-2017. Researcher: Agnes Stenius-Ayoade, university of Helsinki. (Agnes.stenius@helsinki.fi)

237 *Equal services for all? Effectiveness analysis and modeling to help of designing substance abuse services in the treatment system reforms.*

The study describes intoxicant related cases and the use of services in social and health care services and special services for substance abusers in South Karelia, Kymenlaakso and Lapland. The study is based on survey data on intoxicant-related cases in the Finnish health care and social services gathered on a single day in 2015.

There are regional differences in the availability of substance abusers' services in Finland. One of the main goals of ongoing health and social services reform is to reduce the supply of services in regional disparities and to ensure equal access to the treatment, regardless of the place of residence. This study will provide information to support the reform.

The research project started in January 2016. The data processing, analysis and article writing have progressed according to the plan during the year. The study answers the following questions: 1) How many intoxicant-related cases there were in the research provinces, 2) In what social welfare and health care units those intoxicant-related cases took place and for what reasons and 3) Who were reached by services and what kind of services they received. In addition to answering research questions the detailed data analysis was made for non-responding social welfare and health care units.

The preliminary results of the study were presented in the Alcohol and drugs units' research meeting in National Institute for Health and Welfare on September 2016. Provincial results were presented in professional meetings between September and December 2016. For all meetings there were invited at least one professional from the social welfare services, health care services and special services for substance abusers. Semi-structured interviews were recorded, and the material has been used to interpret the results. In addition, material has brought important information on the survey as a data collection method now and in the future.

The results of the study are presented in Finnish article "Equal services for all? Substance abusing clients in social and health care services in areas of south-eastern Finland and Lapland". The article will be completed in January 2017, after which the article is expected to be submitted for publication. Researcher: *Hanna Samposalo*, National Institute for Health and Welfare. (hanna.samposalo@thl.fi)

238.1 *Maternal substance abuse and child's emotional, cognitive and physical development in school age.*

Maternal substance abuse including alcohol and drug-abuse form a considerable risk for children's well-being and development. Our knowledge is predominantly from infancy: the teratological effects of maternal drug-exposure predict problems or delays in cognitive, motor and socioemotional development (Salo & Flykt, 2013). Research is scarce on possible longitudi-

nal effects of early maternal substance abuse on children's development and mental health. Mother's drug exposure can cause subtle neurobehavioral deficits in infancy, which in turn deteriorate children's regulatory abilities such as attention, arousal and emotion regulation (Kaltenbach, 2013). This study attempted to understand why and how early maternal substance abuse would associate with children's wellbeing in school age, and what can be done to prevent or diminish negative effects.

Therefore, our longitudinal study aimed (1) to explore in depth the effects of maternal substance abuse on child development on cognitive, social, emotional and neurophysiological domains; and (2) to test the hypothesized neurophysiological and emotional underlying mechanisms for later developmental or mental health problems among drug-exposed children, and (3) to examine which intervention and treatment modules tailored for substance-abusing mothers are effective in preventing negative effects of drug exposure on children's mental health and development.

The sample are substance abusing mothers with their children (N=50), and non-using comparisons (N=50), the former is from dependency treatment specializig open-clinics and the latter from a maternity care unit. The women participated first in their 2nd and 3rd trimester (T1), then with their infants at four (T2) and twelve (T3) months. The assessments included maternal mental health, nature of substance abuse, emotion processing, mental reflection and representations of the infant and motherhood, infant-mother –interaction, and infants' sensomotor and emotion regulation characteristics. A follow-up data collection was when children were 7-12-year-olds. The participation rate was 48% from the T1. The assessents involved self-reports, testing for cognitive capacity, laboratory tools for emotion regulation, and hair-samples for cortisol levels.

Primary results show that (1) early maternal substance abuse predicted children's dysfunctional emotion regulation at school age, specifically regulation of anger and fear. (2) The early infant-mother interaction (emotional availability) and maternal representations predicted children's later emotion regulation, but mother's substance abuse was a more prominent predictor. (3) Maternal substance abuse formed a risk for problematic mother-child relationship at school-age, as sensitivity, structuring, and non-hostility were at lover level in the substance abusing than in comparison dyads.

The funding has enabled extensive international and Finnish cooperation, e.g., with Kathy Kerns in Kent University, USA, Zeynep Biringen, Colorado State University, USA, Nuno Sousa in University of Minho, Guimarães, Portugal, and with the Finn Brain research group. Two graduate and three bachelor's research are based on the data. The project has provided data for four students performing their research training within the education. The results have been presented Psychology 2016 congress in Finland, and will be in presented in congresses in the Netherlands and USA in 2017. The research group is organizing three trainign days and seminars for professionals working with risk families in child care in Espoo, Tampere and Lahti. Three peer-reviewed articles are in progress. Reserahers: *Professor Raija-Leena Punamäki* and *Kaisa Saurio*, University of Tampere. (raija-leena.punamaki@uta.fi)

238.2 *Early risk factors and the development of children's emotion regulation at school age: A Study of drug exposed children.*

The first years of a child's life are important for the later development of emotion regulation. The neural networks of the stress-response system develop during the early childhood. During this period parental sensitivity towards the child is crucial. Based on previous research we already know that children of sensitive mothers show better emotion regulation skills later in life. Maternal drug abuse can form a comprehensive risk for the child's development and interfere with the infant-mother interaction. On the other hand, good infant-mother interaction may protect children's development from the adverse effects of maternal drug abuse. However, longitudinal studies on this topic are rare.

The purpose of my dissertation is to study, how early drug exposure, infant-mother interaction and child-related factors predict the development of emotion regulation at school age.

The original study sample consisted of 101 mothers and their children, 51 with a history of drug abuse and a comparison group of 50 mother-child pairs. The drug abusing mothers participated in outpatient interventions targeting substance abuse and parenting. The study followed the families from pregnancy to school age. The data was collected when the child was 4 months (T2), 12 months (T3) and 7–12 years (T4) old. 49 families participated in the follow up, 19 with a history of drug abuse and a comparison group of 30 mother-child pairs.

The dissertation will consist of three articles. The results of the first study were presented at the Psykologia 2016 congress and will also be presented at EADP2017 –conference at Neatherlands. Researcher: Kaisa Saurio, University of Tampere. (Saurio.Kaisa.J@student.uta.fi)

242 *Adolescents and Alcohol: Effects of long-term alcohol use on neurophysiological functioning in adolescents.*

Alcohol use often begins in adolescence. Binge drinking in adolescence is known to be associated with subtle but significant deterioration in neurocognitive functioning. In functional magnetic resonance imaging studies, young heavy drinkers have shown changes in activation patterns during working memory tasks. In previous EEG studies, alcohol-associated differences in for example event-related potentials have been found in adolescent and young adult binge drinkers. This study is a part of the ongoing Adolescents and Alcohol project recording the health and alcohol use of Finnish adolescents using cutting edge technology. The aim of the project is to provide new information on the maturation of the adolescent brain under the influence of long-term alcohol use. This PhD dissertation consists of four articles. Neurophysiological functioning as well as the cognitive, psychosocial, and psychological functioning of the participants, are being targeted. The first article of this dissertation, considering the neuropsychological test results, was published in 2015 (Kaarre et al., hyperlink: http://www.psykiatriantutkimussaatio.fi/uploads/files/PF_2015/PF2015_ART7.pdf). No statistically significant differences were found in any particular field of the neuropsychological evaluations. The second article, exploring the TMS evoked EEG potentials after motor cortex stimulation was published in December 2016 (Kaarre et al.; *Addict Biol.* 2016 Dec 23. doi: 10.1111/adb.12486.). Most work during the year 2016 has focused on analyzing results of this part of the study and writing and revising this article. The main finding was a marked increase in the GABAergic N45 amplitude in alcohol users especially frontally. Also a positive correlation between the N45 amplitude and AUDIT-C-scores was observed. These findings suggest that long-term alcohol use in adolescence, even when not meeting the diagnostic criteria for a disorder, is associated with changes in connectivity and cortical excitability. The third article is currently being prepared. It explores the correlation between the N100 amplitude and performance in attention and working memory tasks. According to preliminary analyses, the N100 amplitude is statistically significantly correlated with performance in attention and working memory tasks. The future work aims to explore the correlations between cortical thickness and TMS-evoked potentials, as well as the results of the prefrontal cortex stimulation, exploring the functional and effective connectivity of the prefrontal areas.

Researcher: Outi Kaarre, Kuopio University Hospital and University of Eastern Finland. (outi.kaarre@kuh.fi)

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