

Institute of  
Psychiatry

at The Maudsley

**KING'S**  
*College*  
**LONDON**

# PhD/MD(Res) Research Showcase Event 2011

Supported by the Graduate School Open Competition

**Friday 18th November**

**09:00 – 17:00 followed by refreshments**

**Wolfson Lecture Theatre and Seminar Rooms 1 & 2**

**Poster presentations and short talks by PhD and MD(Res) students**  
**All PhD, MD(Res) students and supervisors welcome**

## **INTRODUCTION**

---

Dear students, staff and guests

It gives me great pleasure to introduce the first IOP-wide showcase event for postgraduate research students. The IOP has one of the largest groups of PhD and MD(Res) students in Europe working in the area of mental health and neuroscience. However, you rarely have the opportunity to share your work with the wider body of fellow-students and learn about work going on elsewhere in the IOP. I hope that today's event will give us all a real sense of the breadth, depth and quality of work that is being done across the departments and different research groups. I am sure that the day will be an enjoyable, rewarding and informative one for us all, and the first in what I hope will become an annual event.

Richard Brown  
*Head of Graduate Studies (Research)*

November 2011

---

## TIMETABLE

---

- 09:00** Registration, tea/coffee, putting up posters
  - 09:30** Opening address by Professor Shitij Kapur (Dean)
  - 09:45** Platform presentations (10 min plus 5 min questions)
  - 10:45** Morning poster session (beverages available)
  - 11:45** Platform presentations (10 min plus 5 min questions)
  - 12:45** Lunch and poster change-over
  - 13:45** Platform presentations (10 min plus 5 min questions)
  - 14:45** Afternoon poster session (beverages available)
  - 15:45** Platform presentations (10 min plus 5 min questions)
  - 16:45** Buffet and presentation of prizes by Professor Susan Lea (Vice Dean of Education)
-

## ORAL PRESENTATIONS PROGRAMME

Abstract	Time	Name	Title
1	09.45	Abel, Olubunmi	Credibility Analysis of fALS Genes
2	10.00	Anderson, Greg W.	Cortically-Derived Human Neural Stem Cell Line as a Potential Tool for Neuropsychiatric Drug Discovery
3	10.15	Challacombe, Fiona L.	An investigation into the impact of Postnatal Obsessive-Compulsive Disorder
4	10.30	Cullen, Alexis E.	Temporal lobe volume abnormalities in children aged 9-13 years presenting putative antecedents of schizophrenia
5	11.45	Easton, Alanna C.	Establishment of cocaine-induced place preference is delayed in $\alpha$ CaMKII autophosphorylation-deficient mice
6	12.00	Hoang, Uy	Characterising recent trends in mortality for people with schizophrenia and bipolar disorder in England
7	12.15	Lazarus, Anisha	Understanding the experience of young carers of someone with a severe mental illness: a qualitative research project
8	12.30	Paraviainen, Lotta	The Role of Astrocytes in the Pathogenesis of Juvenile Form of Neuronal Ceroid Lipofuscinosis (JNCL)
9	13.45	Perera, Gayan	Prescribing dementia treatment medications in a routine clinical setting: a retrospective longitudinal study in South London, UK
10	14.00	Pidsley, Ruth	Disease-associated epigenetic changes in monozygotic twins discordant for schizophrenia and bipolar disorder
11	14.15	Shakoor, Sania	A prospective longitudinal study of children's theory of mind and adolescent involvement in bullying
12	14.30	So, Suzanne H.W.	Response of delusional dimensions, reasoning biases and emotions in the first 8 weeks of antipsychotic treatment
13	15.45	Stangl, Doris	Molecular mechanisms mediating dietary modulation of adult hippocampal neurogenesis and associated behaviour
14	16.00	Vorontsova, Natasha	Cognitive factors maintaining persecutory delusions in psychosis: the contribution of depression
15	16.15	Winton-Brown, Toby	What's so important about salience?
16	16.30	Woodhead, Charlotte	Impact of exposure to combat during deployment to Iraq and Afghanistan on mental health by gender

# ABSTRACTS FOR ORAL PRESENTATIONS

1

## Credibility Analysis of fALS Genes

Olubunmi Abel  
John Powell, Ammar Al-Chalabi  
*Departments of Clinical Neuroscience and Neuroscience, MRC  
Centre for Neurodegeneration Research*

**Background:** ALS is a neurodegenerative disease causing progressive paralysis and leading to death within 5 years. The short duration makes it a challenging disease. Despite this, ALS genetics researchers have discovered both familial and sporadic ALS genes. The derived genetic data are collated into online databases (ALSoD and ALSGene). As of October 2011 there are 100 ALS genes (sporadic ALS 78; familial ALS 20; Phenotype-modifying genes 2) in ALSoD (<http://alsod.iop.kcl.ac.uk>). However, the levels of evidence for ALS involvement can differ from overwhelming support to limited, and it is difficult for non-experts to know which genes have the highest credibility.

**Methods:** To explore this we developed a credibility score using publicly available data to rank genes based on evidence. 14 putative familial ALS genes were studied: ALS2, FUS, DAO, VCP, VAPB, ANG, DCTN1, FIG4, SETX, SOD1, TDP43, SPG11, NEFH, and OPTN. The database was updated with information from publications for patient data, mutation data, number of cases and controls used in the studies, number of countries replicating the mutation, LOD scores and predicted pathogenicity of mutations using bioinformatic tools, PANTHER, SIFT and PolyPHEN.

**Results:** Results generated from queries performed were summed and ranked to predict the credibility of a gene. Ranking based on this score was compared with the ranking from a selection of ALS experts. There was a high correlation between the automated method and the choices of experts.

**Conclusions:** We conclude that an automated method for assessing the credibility of new genetic discoveries is possible.

**Key words:** amyotrophic lateral sclerosis; motor neuron disease; genetics

2

## Cortically-Derived Human Neural Stem Cell Line as a Potential Tool for Neuropsychiatric Drug Discovery

Greg W. Anderson<sup>1</sup>  
Brenda P. Williams<sup>2</sup> and Maria J. Arranz<sup>3</sup>  
*<sup>1</sup>Psychosis Studies, <sup>2</sup>Neuroscience, <sup>3</sup>Psychological Medicine*

**Background:** Human neural stem cells (hNSC) represent a readily available, physiologically relevant model to screen for novel neuropsychiatric medicines. These are generally overlooked however in favour of cell lines that are rarely human or even neural in origin and often require artificial expression of the desired drug target(s). Recent advances in our understanding of neurotransmitter receptor pharmacology have highlighted the importance of using native cells to more faithfully reproduce drug-induced intracellular signalling. Our research seeks to develop a hNSC based platform for studying neuropsychiatric drugs.

**Methods:** We used cell-type specific markers to determine the ability of the cortical hNSC line CTXOE16/02 to generate different neural cell-types. RT-PCR, Ca<sup>2+</sup>-imaging and ERK phosphorylation assays were used to assess the presence and function of neurotransmitter receptors targeted by antipsychotic medicines. Response specificity was determined using receptor-specific agonists and antagonists.

**Results:** We found that CTXOE16/02 cells were capable of differentiation into different types of neurons and glia. Functional analysis revealed that neurons within these cultures were capable of responding to dopaminergic, serotonergic, cholinergic, glutamatergic and GABAergic agonists, indicating functional receptor expression at the cell surface. Importantly, while the effect of the antipsychotic, haloperidol, could not be measured when administered alone until reaching the mM range, effects could be detected in the pM range when added to cultures in the presence of dopamine concentrations mirroring physiological tone.

**Conclusions:** Differentiated hNSC cultures have the potential to provide a sensitive platform to screen for novel neuropsychiatric compounds and to study their mode of action.

**Key words:** human neural stem cells; antipsychotics; functional neurotransmitter receptors

## An investigation into the impact of Postnatal Obsessive-Compulsive Disorder

Fiona L. Challacombe<sup>1</sup>

Matt Woolgar<sup>2</sup>, Paul Salkovskis<sup>3</sup>

<sup>1</sup>Psychology, <sup>2</sup>South London & Maudsley NHS Foundation Trust, <sup>3</sup>University of Bath

**Background:** Obsessive compulsive disorder (OCD) has been termed a 'rare yet severe mental disorder' known to significantly impair sufferers' lives and burden those around them (Torres et al, 2006). Recent research suggests that pregnancy and the postnatal period may be a time of increased risk for developing OCD. However, the effects on parenting and the mother-infant relationship are not yet well described. This task may be complex given the heterogeneity of the disorder which postnatally commonly presents around fears of the baby becoming ill via contamination or thoughts of deliberate harm. Many women are deterred from seeking help for their difficulties due to fears about their disorder and the impact on their baby and what may be inferred about parenting and/or risk by professionals. Lack of detailed disclosure and misdiagnosis are common.

**Methods:** Mothers mental state, interactions and perceptions of parenting were assessed in detail when their infants were 6 months old. This was part of an ongoing study examining the impact of intensively delivered cognitive behaviour therapy on maternal symptoms and parenting variables.

**Results:** Data from the first 20 participants are presented. Mothers experienced moderate to severe OCD. Preliminary results indicate that mothers with a variety of OCD presentations report that everyday parenting tasks such as nappy changing, feeding and playing are impaired by the symptomatology of OCD. Reported behaviours include avoidance of touching the baby, preventing others touching the baby and delegation of everyday tasks. High levels of preoccupation are common.

**Conclusions:** OCD can cause disruption in everyday parenting tasks – identification and treatment of the disorder should be a priority.

**Key words:** obsessive-compulsive disorder; parenting; postnatal period

## Temporal lobe volume abnormalities in children aged 9–13 years presenting putative antecedents of schizophrenia

Alexis E. Cullen<sup>1</sup>

Stéphane A. De Brito<sup>1</sup>, Sarah L. Gregory<sup>1</sup>, Robin M. Murray<sup>2</sup>, Steve C. R. Williams<sup>3</sup>

Sheilagh Hodgins<sup>1,4,5</sup>, Kristin R. Laurens<sup>1,6,7</sup>

<sup>1</sup>Department of Forensic and Neurodevelopmental Sciences,

<sup>2</sup>Department of Psychosis Studies, <sup>3</sup>Centre for Neuroimaging Sciences, <sup>4</sup>Département de Psychiatrie, Université de Montréal, Montréal, Canada, <sup>5</sup>Department of Psychiatry, Heidelberg University, Heidelberg, Germany, <sup>6</sup>Research Unit for Schizophrenia Epidemiology, School of Psychiatry, University of New South Wales, Sydney, Australia, <sup>7</sup>Schizophrenia Research Institute, Sydney, Australia

**Background:** Structural brain abnormalities characterise individuals with first-episode schizophrenia. Regions of abnormality are present already, albeit less extensively, in individuals at ultra high-risk for psychosis, suggesting that some brain structure abnormalities precede the prodromal period. Using a novel community screening method, we identified children presenting multiple putative antecedents of schizophrenia (ASz) who may be in an early at-risk (pre-prodromal) phase of psychosis. We aimed to determine whether ASz children displayed brain volume abnormalities relative to typically-developing (TD) children with no antecedents.

**Methods:** Structural MRI scans from 20 ASz and 20 TD children aged 9–13 years (matched on age, sex, and IQ) were examined. Whole-brain differences in grey matter (GM) and white matter (WM) volume were determined using voxel-based morphometry methods.

**Results:** Relative to TD children, the ASz group showed significantly decreased GM volume in the right middle temporal gyrus and increased GM volume in the left superior-middle temporal gyri ( $p < 0.05$ , corrected). WM volume was significantly increased in ASz children relative to TD children in a cluster encompassing the left inferior parietal lobe, occipital lobe, and superior temporal gyrus.

**Conclusions:** ASz children aged 9–13 years present relatively localised GM and WM volume abnormalities in several regions characterised by abnormality in individuals with first-episode schizophrenia and ultra high-risk youth. These findings imply that an early at-risk (pre-prodromal) phase of psychosis may be characterised by volume abnormalities in the temporal lobe. Prospective studies that follow high-risk individuals from childhood through the age of risk for psychosis are needed.

**Key words:** psychosis risk; neuroanatomical abnormalities; superior temporal gyrus

## Establishment of cocaine-induced place preference is delayed in $\alpha$ CaMKII autophosphorylation-deficient mice

Alanna C. Easton<sup>1</sup>

Walter Lucchesi<sup>2</sup>, Gunter Schumann<sup>1</sup>, Cathy Fernandes<sup>1</sup>, K. Peter Giese<sup>2</sup>, Christian P. Muller<sup>1</sup>

<sup>1</sup>*Social, Genetic and Developmental Psychiatry Centre (MRC),*

<sup>2</sup>*James Black Centre*

**Background:** Cocaine is the most widely used illicit psycho-stimulant drug in the UK with an estimated 1,000,000 users. The underlying processes by which cocaine dependence is established are believed to involve molecular mechanisms of learning and memory. Alpha calcium/calmodulin dependent protein kinase II ( $\alpha$ CaMKII) is a major synaptic kinase, critical for memory formation. Upon autophosphorylation,  $\alpha$ CaMKII switches to an autonomous state of activity after calcium levels drop, preserving kinase activity.  $\alpha$ CaMKII autophosphorylation-deficient mice (Mt) show severe one-trial learning impairments which may be overcome by repeated training. We hypothesise that the behavioural and motivational properties associated with drugs of abuse will initially be attenuated in the Mt mice, diminishing after repeated treatment.

**Methods:** We tested cocaine's effects on the learning curve established in a conditioned place preference (CPP) paradigm.

**Results:** Mt mice were impaired in learning cocaine CPP, but after a 7 day period with no treatment or conditioning, Mt mice had the same level of preference as Ht and WT mice. Acute locomotor responses to cocaine and saline were identical between groups. We can therefore rule out to a great extent metabolism differences in these mice. There was a significant conditioned hyperlocomotion effect seen between genotype groups with cocaine, sensitising after 7 treatments. There were no saline effects. This suggests that the  $\alpha$ CaMKII autophosphorylation is not required for this type of learning.

**Conclusions:** This study supports the role of learning processes in the development of addictive behaviours. Data suggest an important, specific role for  $\alpha$ CaMKII autophosphorylation in the establishment of addiction related behavioural responses.

**Key words:**  $\alpha$ CaMKII; autophosphorylation; conditioned place preference; cocaine

## Characterising recent trends in mortality for people with schizophrenia and bipolar disorder in England

Uy Hoang

*Health Services and Population Research Department*

**Background:** Severe mental illness including schizophrenia and bipolar disorder have been described as 'life shortening conditions' with many studies showing that people with these conditions have higher mortality than the general population. In recent years there has been evidence that the rate of death from suicide in these groups has been declining in the UK, however recent trends in mortality rates more generally for these groups remains poorly characterized, particularly the relative contributions from natural and unnatural causes. In my research I aim to look at the recent trends in mortality for these groups, and answer the following questions 1) is the mortality gap decreasing, 2) what is the relative contribution of natural causes to the mortality risk for these groups 3) what proportion of these deaths is 'avoidable' by good public health intervention or 'amenable' to good medical intervention.

**Methods:** Record linkage study, using an English national database containing all hospital records for NHS patients in England between 1998 and 2010, and all death records over the same period.

**Results:** The mortality gap for these people is increasing, especially in the first year after discharge, compared with the national population (as recently described in our BMJ paper, with Rob Stewart and Michael Goldacre). Yet to report on avoidable and amenable mortality.

**Conclusions:** The issue of avoidable mortality in people with schizophrenia and bipolar disorder needs urgent attention, including more research to better characterize underlying causes and effective interventions.

**Key words:** schizophrenia; bipolar disorder; mortality

## Understanding the experience of young carers of someone with a severe mental illness: a qualitative research project

Lazarus, Anisha<sup>1</sup>

Vanessa Lawrence<sup>1</sup>, Elizabeth Kuipers<sup>2</sup>, Joanna Murray<sup>1</sup>

<sup>1</sup>*Health Services and Population Research Department,*

<sup>2</sup>*Department of Psychology*

**Background:** Although young carers are currently a much-discussed topic, there is limited evidence-based research in the UK on young carers who look after someone with a mental illness. Understanding their caring experiences will help to inform the development of interventions to support them.

**Methods:** 14 in-depth semi-structured interviews were conducted with a wide range of participants in addition to a focus group with 10 participants. The interviews were transcribed and analysed using thematic analysis, in which the data was first coded before building themes by meaningfully connecting the codes. Multiple methods were used to validate the coding framework.

**Results:** Building descriptive and latent themes from the data and constructing theoretical models enabled a deeper understanding of the experience of young carers looking after someone with a severe mental illness. The young carer's circle of support and experience of mental health services are some of the factors that contribute to the caring experience and its impact on his/her life. The role of the young carer can be very varied and it tends to be a process of learning.

**Conclusions:** The results have added to the current knowledge about this oft-hidden population. Using qualitative methods has enabled more detailed insight. The interventions suggested by participants as being likely to be helpful from their experience are being further researched and will inform the development and piloting of an intervention for this group.

**Key words:** young carers; mental illness; qualitative research

## The Role of Astrocytes in the Pathogenesis of Juvenile Form of Neuronal Ceroid Lipofuscinosis (JNCL)

Lotta Parviainen<sup>1</sup>

S. Dihanich<sup>1</sup>, S. Pope<sup>2</sup>, S. Heales<sup>2</sup>, H.M. Mitchison<sup>2</sup>,

J.D. Cooper<sup>1</sup>, B.P. Williams<sup>1</sup>

<sup>1</sup>*Pediatric Storage Disorders Laboratory, Department of Neuroscience, Centre for the Cellular Basis of Behaviour,*

<sup>2</sup>*Molecular Medicine Unit, Institute of Child Health, University College London, UK*

**Background:** The neuronal ceroid lipofuscinoses (NCLs, Batten disease) are fatal neurodegenerative disorders of childhood. In all forms of NCL, astrocyte activation occurs early in the disease and precedes neuronal loss. However, in the most common juvenile form (JNCL), caused by mutations in the *Cln3* gene, this astrocyte response appears to be compromised. Since astrocytes are crucial for the functioning and survival of neurons, such deficits in astrocyte biology could have a significant impact on JNCL pathogenesis.

**Methods:** We are comparing the biology of healthy astrocytes with those isolated from a well-characterised mouse model of JNCL (*Cln3* deficient mice). We use a combination of immunofluorescence, western blotting and ELISA to compare the ability of astrocytes to respond to stimulation, by analysing changes in morphology, proliferation, protein synthesis and secretion. Co-cultures are used to explore the potential impact of mutant glia on neuronal survival and function.

**Results:** We have shown that *Cln3* deficient astrocytes have an impaired ability to change morphologically and divide upon stimulation. We have also revealed different protein secretion profiles in both basal and stimulated *Cln3* deficient astrocytes. In addition, mutant astrocytes secrete markedly reduced levels of glutathione, one of the most important brain antioxidants. Most importantly, we have observed that *Cln3* deficient glia have a negative impact on the survival of both healthy and mutant neurons *in vitro*.

**Conclusions:** Our data indicate an active role for astrocytes in JNCL pathology, and suggest that these cells are not only functionally compromised but have the potential to cause neurodegeneration.

**Key words:** astrocyte (s); JNCL; neurodegeneration



## Prescribing dementia treatment medications in a routine clinical setting: a retrospective longitudinal study in South London, UK

Gayana Perera<sup>1</sup>

Robert Stewart<sup>1</sup>, Mizanur Khondoker<sup>2</sup>, Matthew Broadbent<sup>3</sup>, Gerome Breen<sup>3</sup>

<sup>1</sup>*Epidemiology section, Health Services and Population Research*, <sup>2</sup>*Biostatistics Department*, <sup>3</sup>*SLAM BRC Nucleus*

**Background:** Acetylcholinesterase inhibitors (AChEIs) are given to patients with cognitive impairment including Alzheimer's disease. Previous studies in routine clinical practice have shown cognitive improvement in some groups of patients after given the drug. However, longitudinal cognitive change for patients who were given AChEIs from before prescription has never been described before.

**Objectives:** The objective of this study was to describe the longitudinal cognitive outcome for those who were given AChEIs before and after prescription among patients who had contacts with a South London hospital, UK during 2003 and 2010.

**Method:** A non-randomised, retrospective longitudinal study of 1843 patients who were prescribed with AChEIs were obtained from the SLAM BRC case register. Cognitive outcome was measured using mini mental health state examination score (MMSE). Longitudinal cognitive change was modelled using non-linear semi parametric methods. Linear MMSE score change was modelled using three-piece linear mixed models.

**Results:** Overall, rate of cognitive improvement was 3.2 MMSE scores (95% CI 2.5 to 3.9) from one year before given the drug and up to 6 months after given the drug. This effect was greater if baseline MMSE was between 0- 20 with an improvement in score by 4.7 (95% CI 3.6 to 5.8). On average patients maintained their baseline MMSE score for average 10 months (95% CI 8 – 12 months) before it declines to less than baseline MMSE score.

**Conclusion:** In this naturalistic routine clinical practice study, as shown in randomised controlled trials, the response to AChEIs were proven to be better during first 6 months of the study especially for those who had a MMSE score between 0 to 20 at the time of prescription. This also demonstrated that there was no cognitive improvement for those who had a MMSE score over 24 at the time when AChEIs were given.

**Key words:** acetylcholinesterase inhibitors (AChEIs); mini mental health state examination score (MMSE); observational study

## Disease-associated epigenetic changes in monozygotic twins discordant for schizophrenia and bipolar disorder

Ruth Pidsley<sup>1</sup>

Emma L Dempster<sup>1</sup>, Leonard C Schalkwyk<sup>1</sup>, Sheena Owens<sup>2</sup>, Anna Georgiades<sup>2</sup>, Fergus Kane<sup>2</sup>, Sridevi Kalidindi<sup>2</sup>, Marco Picchioni<sup>2,3</sup>, Eugenia Kravariti<sup>2</sup>, Timothea Touloupoulou<sup>2</sup>, Robin M Murray<sup>2</sup>, Jonathan Mill<sup>1</sup>  
<sup>1</sup>*MRC Social, Genetic and Developmental Psychiatry Centre*, <sup>2</sup>*Psychosis Studies*, <sup>3</sup>*St Andrew's Academic Centre, Northampton*

**Background:** Studies of the major psychoses, schizophrenia and bipolar disorder, have traditionally focused on genetic and environmental risk factors, although more recent work has highlighted an additional role for epigenetic processes in mediating susceptibility. Since monozygotic (MZ) twins share a common DNA sequence, their study represents an ideal design for investigating the contribution of epigenetic factors to disease etiology.

**Methods:** We performed a genome-wide analysis of DNA methylation on peripheral blood DNA samples obtained from a unique sample of MZ twin-pairs discordant for major psychosis.

**Results:** Numerous loci demonstrated disease-associated DNA methylation differences between twins discordant for schizophrenia and bipolar disorder individually, and together as a combined major psychosis group. Pathway analysis of our top loci highlighted a significant enrichment of epigenetic changes in biological networks and pathways directly relevant to psychiatric disorder and neurodevelopment. The top psychosis-associated differentially methylated region, significantly hypomethylated in affected twins, was located in the promoter of *ST6GALNAC1* overlapping a previously reported rare genomic duplication observed in schizophrenia. The mean DNA methylation difference at this locus was 6%, but there was considerable heterogeneity between families with some twin-pairs showing a 20% difference in methylation. We subsequently assessed this region in an independent sample of post-mortem brain tissue from affected individuals and controls, finding marked hypomethylation (>25%) in a subset of psychosis patients.

**Conclusions:** Overall, our data provide further evidence to support a role for DNA methylation differences in mediating phenotypic differences between MZ twins and in the etiology of both schizophrenia and bipolar disorder.

**Key words:** epigenetics; monozygotic twins; psychosis

## A prospective longitudinal study of children's theory of mind and adolescent involvement in bullying

Sania Shakoor<sup>1</sup>

Sara R Jaffee<sup>1</sup>, Lucy Bowes<sup>1</sup>, Isabelle Ouellet-Morin<sup>1</sup>,  
Francesca Happé<sup>1</sup>, Terrie E. Moffitt<sup>1,2</sup>, Louise Arseneault<sup>1</sup>  
<sup>1</sup>MRC Social, Genetic and Developmental Psychiatry Centre,  
<sup>2</sup>Departments of Psychology and Neuroscience, Psychiatry and  
Behavioural Sciences and Institute for Genome Sciences and  
Policy, Duke University, Durham, USA

**Background:** Theory of mind allows the understanding and prediction of other people's behaviours based on their mental states (e.g. beliefs). It is important for healthy social relationships and thus may contribute towards children's involvement in bullying. The present study investigated whether children involved in bullying during early adolescence had poor theory of mind in childhood.

**Methods:** Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally-representative sample of 2,232 children and their families. We visited families when children were 5, 7, 10 and 12 years. We assessed theory of mind when children were 5 years using eight standardized tasks. We identified children who were involved in bullying as victims, bullies and bully-victims using mothers', teachers' and children's reports when they were 12 years.

**Results:** Poor theory of mind predicted becoming a victim ( $d=0.26$ ), bully ( $d=0.25$ ) or bully-victim ( $d=0.44$ ) in early adolescence. These associations remained for victims and bully-victims when child-specific (e.g., IQ) and family factors (e.g., child maltreatment) were controlled for. Emotional and behavioural problems during middle childhood did not modify the association between poor theory of mind and adolescent bullying experiences.

**Conclusions:** Identifying and supporting children with poor theory of mind early in life could help reduce their vulnerability for involvement in bullying and thus limit its adverse effects on mental health.

**Key words:** theory of mind; bullying involvement; child development

## Response of delusional dimensions, reasoning biases and emotions in the first 8 weeks of antipsychotic treatment

Suzanne H.W. So<sup>1</sup>

Philippa Garety<sup>1</sup>, Emmanuelle Peters<sup>1</sup>, Shitij Kapur<sup>2</sup>  
<sup>1</sup>Department of Psychology, <sup>2</sup>Psychological Medicine

**Background:** Delusions are characterised by dimensions such as conviction, preoccupation, distress and disruption. Negative affect and reasoning biases, "jumping to conclusions" style and lack of belief flexibility in particular, have been shown to be important in the development and maintenance of delusions. This study examined changes of delusional dimensions, affect, and reasoning biases at the initial phase of antipsychotic treatment.

**Methods:** Patients with delusions were interviewed five times in the first 8 weeks of their antipsychotic treatment. Measures included interview-based and self-reported questionnaires, Beads task and Card task.

**Results:** The sample consisted of 40 individuals with a high level (80%) of delusional conviction. All four delusional dimensions improved together over 8 weeks of antipsychotic treatment. The hypothesis that conviction reduces in a slower or lesser degree was not supported. Change in dimensions was the greatest in the earlier weeks, and reduction in the first 2 weeks predicted subsequent improvement. There was an improvement in belief flexibility and cognitive biases, but not in "jumping to conclusions" (JTC) style. Anxiety, depression, and subjective distress did not change. Baseline reasoning biases did not predict change in conviction, although individuals with belief flexibility at baseline had a lower level of conviction.

**Conclusions:** In contrast with the traditional view that delusions are persistent and unchanging, our findings suggest that delusional dimensions and cognitive biases underlying delusions, including belief flexibility and appraisals, are capable of improving after only 8 weeks of antipsychotic treatment, despite JTC remaining prevalent.

**Key words:** delusion; reasoning biases; antipsychotics

## Molecular mechanisms mediating dietary modulation of adult hippocampal neurogenesis and associated behaviour

Doris Stangl

B. Morisse, S. Ahmet, S. Thuret

*Neuroscience*

**Background:** It is now well established that during adulthood, new neurons are generated from adult neural stem cells residing in the dentate gyrus of the hippocampus, a region important for memory and learning function as well as mood in rodents and humans. In the rodent, an increase of neurogenesis in the hippocampus is associated with improved memory and learning abilities, whereas a decreased neurogenesis is associated with symptoms of depression. The level of adult hippocampal neurogenesis can be regulated by factors such as enriched environment, physical activity, aging, and stress but also by diet.

**Methods:** In vivo: Animal mouse model; In vitro: human embryonic hippocampal progenitor cell line.

**Results:** We first present dietary parameters responsible for adult hippocampal neurogenesis and learning/memory as well as mood regulation. We show that meal frequency, independently of calorie intake, affects adult neurogenesis, learning/memory and mood.

We next identified possible molecular mechanisms mediating the effects of diet on adult hippocampal neurogenesis. We show that the ageing suppressor gene *Klotho* is highly expressed in the hippocampus and its expression is up-regulated by 2 fold upon diet-induced increased adult hippocampal neurogenesis. Immunocytochemical analysis of the cells upon *Klotho* knockdown showed a decrease in proliferation, differentiation, gliogenesis while apoptosis is increased. We will further present data on the same cell line conditionally over expressing the secreted form of *Klotho*.

**Conclusions:** Our data suggest that diet modulates adult hippocampal neurogenesis through *Klotho* regulation, and underline a central role for *Klotho* in regulating hippocampal neurogenesis.

**Key words:** adult neurogenesis; diet; *Klotho*

## Cognitive factors maintaining persecutory delusions in psychosis: the contribution of depression

Natasha Vorontsova

Daniel Freeman, Philippa Garety

*Psychology*

**Background:** Persecutory delusions are one of the most common and distressing symptoms of psychosis (e.g. Appelbaum et al., 1999; Sartorius et al., 1986). Development of better treatments requires an improved understanding of the mechanisms which maintain paranoid beliefs. Many studies indicate an association of persecutory delusions with depression (e.g. Smith et al., 2006). A direct role for depression-related cognitive factors in the maintenance of persecutory delusions has not been systematically examined, despite such processes being implicated in a cognitive model (Freeman et al., 2002).

**Methods:** In this talk the initial findings from an ongoing project will be presented. This project examines, over time, the cognitive processes associated with depression and their contribution to the persistence of persecutory delusions over six months in a sample of 60 patients. We hypothesise that negative schematic beliefs, memory bias, rumination and problem-solving difficulties lead to the persistence of paranoid fears. A longitudinal design will enable hypothesis-driven tests of maintenance factors.

**Results:** N/A

**Conclusions:** N/A

**Key words:** psychosis; depression; delusions

## What's so important about salience?

Toby Winton-Brown<sup>1</sup>

Philip McGuire<sup>2</sup>, Shitij Kapur<sup>2</sup>

<sup>1</sup>*Dept of Psychosis Studies, <sup>2</sup>Psychological Medicine*

**Background:** Despite alterations in 'salience processing' being central to current theories of psychosis, addiction and depression there is little consensus on what 'salience' in this context means. The aim of the present study is to use fMRI to compare behavioural and neurophysiological responses to putative elements of salience, namely reward prediction, novelty and emotion and their interactions.

**Methods:** 30 healthy adults participated in a MRI scanning session where behavioural and neurophysiological responses to novel, reward predicting and emotional stimuli were compared.

**Results:** Significant differences were found between the processing of rewarding emotional and novel stimuli evident at a behavioural (RT, delayed recall) and neurophysiological (fMRI activation) level.

**Conclusions:** Reward prediction, prediction error, emotion and novelty contribute to the detection and processing of salient stimuli in healthy subjects.

**Key words:** salience; fMRI; emotion

## Impact of exposure to combat during deployment to Iraq and Afghanistan on mental health by gender

Charlotte Woodhead

*King's Centre for Military Health Research*

**Background:** Interest in the mental health of women deployed to modern military campaigns is increasing, though research examining gender differences is limited. Little is known about experiences women have had on these deployments, or whether men and women respond differently to combat exposure.

**Methods:** The current study uses data from a representative sample of UK Armed Forces personnel to examine gender differences among those deployed to Iraq and Afghanistan (n=432 women, n=4554 men) in three measures of experience: 'risk to self', 'trauma to others' and negative appraisals of deployment. The impact of such experiences on post-deployment symptoms of PTSD, symptoms of common mental disorder (CMD) and hazardous alcohol use is examined.

**Results:** After adjustment, men reported more exposure to 'risk to self' and 'trauma to others' events and more negative appraisals of their deployment. Among both genders, all measures of combat experience were associated with symptoms of PTSD and CMD (except 'risk to self' events on symptoms of CMD among women) but not with alcohol misuse. Women reported higher PCL-C scores among those exposed to lower levels of each experience type but this did not hold in the higher levels. Women reported greater symptoms of CMD and men reported greater hazardous alcohol use across both levels of each experience type. Examining men and women separately suggested similar responses to exposure to adverse combat experiences.

**Conclusions:** The current findings suggest that while gender differences in mental health exist, the impact of deployment on mental health is similar among men and women.

**Key words:** combat; gender; mental health

## POSTER PRESENTATIONS – MORNING SESSION

- 1 **Alharthy, Basma** - Pharmacokinetic and pharmacodynamics of methadone drug response: The significance of drug-drug interactions
- 2 **Ashwood, Karen** - Quantitative Analysis of Emotion Recognition in Autism Spectrum Disorder (ASD) and Attention Deficit Hyperactivity Disorder (ADHD)
- 3 **Azadi, Bahare** - Antisaccades in individuals with ADHD and autism using the gap/overlap paradigm
- 4 **Birken, Mary** - Development of an intervention to improve occupational performance post discharge from an acute psychiatric ward
- 5 **Bonnington, Oliver** - Experience of stigma and discrimination amongst people with a Borderline Personality Disorder diagnosis
- 6 **Borschmann, Rohan** - The effectiveness of joint crisis plans for people with borderline personality disorder: an exploratory randomised controlled trial
- 7 **Burdett, Howard** - Mental Health and Social Wellbeing of Ex-Service personnel: the resettlement process
- 8 **Cattrell, Anna** - Investigating the neurobiological and genetic basis of Empathic Resonance and the Manipulation of Other Minds in Adolescence
- 9 **Chantiluke, Kaylita** - Pharmacological fMRI on the effects of Fluoxetine on functions of impulsiveness, cognitive flexibility and working memory in children with Attention Deficit Hyperactivity Disorder and High Functioning Autism Spectrum Disorders
- 10 **Chaplin, Eddie** - Piloting a guided self-help pack called the SAINT for adults with intellectual disabilities
- 11 **Lee, JongSun** - The effect of Cognitive Bias Modification on Emotional Vulnerability: Comparison of delivery schedules
- 12 **Chou, Chung-Hsing** - Distinguishing contact-mediated effects from soluble factors of human endothelial cells on the differentiation of clinical-grade human neural stem cell lines
- 13 **Chua, Kia-Chong** - Response shift and the measurement of change in health-related quality of life
- 14 **Clark-Papasavas, Chloe** - Establishing the Neuropsychological Profile of Psychosis in Alzheimer's Disease
- 15 **Cross, Sean** - The challenges of calculating incidence rates of self-poisoning presentations across ethnic groups in two London boroughs
- 16 **Crossley, Nicolas** - Integrating published functional neuroimaging studies with graph analysis
- 17 **Cubillo, Ana** - Task-dependent drug-specific upregulation effects of Methylphenidate and Atomoxetine on brain function in medication-naïve children with ADHD
- 18 **Daley, Stephanie** - What are implications of recovery for older people with mental health problems, including those with dementia?
- 19 **Das-Munshi, Jayati** - Born into adversity; the intergenerational factors accounting for the 'transmission' of mental health inequalities in second generation Irish children growing up in Britain
- 20 **De Simoni, Sara** - Understanding the central effects of ketamine on brain function: a combined functional magnetic resonance imaging blood oxygen level dependent, cerebral blood flow and subjective ratings approach
- 21 **Dickson, Hannah** - Face emotion processing in children aged 9-14 years presenting putative antecedents of schizophrenia
- 22 **Emilsson, Brynjar** - The R<sup>2</sup>R2 ADHD programme for adults: A randomized controlled study
- 23 **Fernandes, Alinda** - Lentiviral mediated gene delivery reveals distinct roles of nucleus accumbens dopamine D2 and D3 receptors in novelty- and light-induced locomotor activity

- 24 Gayer-Anderson, Charlotte** - Gender differences in the association between childhood adversity, social support and psychosis
- 25 Grayton, Hannah** - Behavioural characterization of the NRXN1/2 knockout mice: A functional study on susceptibility genes for neurodevelopmental disorders
- 26 Harris, Stephanie** - Facial affect recognition in patients with schizophrenia and a history of violence
- 27 Heslin, Margaret** - The Epidemiology of Psychotic Depression
- 28 Hung, Chi-Fa** - Monoamine oxidase A gene polymorphism and suicide: An association study and meta-analysis
- 29 Huo, Yuanyuan** - Distinguishing Social Anxiety from Persecutory Delusions: Testing the Aetiological Role of Interpretative Biases
- 30 Jarrett, Manuela** - At Risk Mental State: Prevalence and correlates among male prisoners
- 31 Keeling, Mary** - Marital Relationships Among Military Personnel
- 32 Kepa, Agnieszka** - Role of brain-specific transcription factor MYT1L in neural development
- 33 Khalid, Farah** - Aggressive behaviour and psychosis in a clinically referred child and adolescent sample
- 34 Knightsmith, Jodi** - "We just don't know how best to help" Staff experiences of Eating Disorders in UK Schools
- 35 Kolliakou, Anna** - Why do patients with psychosis use cannabis and are they ready to change their use?
- 36 Lee, William** - Quantifying Errors in the relationship between alcohol use and mortality
- 37 Leung, Rufina** - Plasma Inflammatory Markers Correlate with Severity in Alzheimer's Disease
- 38 Lievesley, Kate** - Examining factors associated with Chronic Fatigue Syndrome in adolescence
- 39 Lin, Hsuan-Hwai** - Neuronatin promotes the neural development of mouse embryonic stem cells via regulation of intracellular calcium concentration
- 40 Lysenko, Laura** - Environmental stress predicts methylation of CRHR1 but does not predict subsequent antisocial behaviour
- 41 Mantzari, Eleni** - The effectiveness of financial incentives for smoking cessation during pregnancy: Is it from being paid or from the extra aid?
- 42 Marlow, Sally** - The validity of the Alcohol Use Disorders Identification Test ("AUDIT") to detect alcohol misuse in populations of women, and the optimum cut-off points for identification of alcohol misuse: A systematic literature review and meta-analysis
- 43 Martinez Medina, Lourdes** - Use of lentivirus-mediated gene delivery to investigate the role of the brain specific transcription factor Myt1l *in vivo*
- 44 Merwood, Andrew** - The shared aetiology of ADHD symptoms and Cloninger's temperament dimensions: an adult twin study

## POSTER PRESENTATIONS – AFTERNOON SESSION

- 1 **Mifsud, Mario** - The identification of two designer drugs, 1-benzylpiperazine (BZP) and 1-(3-chlorophenyl)piperazine (mCPP): implications for users
- 2 **Miller, Jack** - Exome capture in Amyotrophic Lateral Sclerosis
- 3 **Mowbray, Fiona** - Risk Perception, Precautionary Behaviour and Public Health Education for Tick-Borne Disease Risks
- 4 **Musiat, Peter** - Trait focused internet-based prevention of common mental health problems in university students
- 5 **Nam, Kie Woo** - Resting state functional connectivity in an executive control network in young adults who were born very preterm
- 6 **Nellums, Laura** - The Impact of Migration and Stressful Life Events on Women's Mental Health and Quality of Life
- 7 **Niblock, Michael** - The Molecular Relationship Between TDP-43 and Tau Pathology
- 8 **Nicholls, Francesca** - Validating exogenous labels for cell transplantation
- 9 **Nicholson, Tim** - Life events in Conversion Disorder: timing and nature of psychological precipitants
- 10 **Nottage, Judith** - Extracting the high frequencies from the EEG
- 11 **Nymberg, Charlotte** - MAOA genotype protects against hyperactivity through the inhibition of caudate activity during reward anticipation
- 12 **O'Hara, Caitlin** - Anorexia nervosa and the motivation to restrict food intake: the effects of acute dopamine precursor depletion
- 13 **Osborne, Sarah** - Major depressive disorder in pregnancy and the hypothalamic-pituitary-adrenal axis
- 14 **Page, Nicholas** - Imagery Rescripting For Obsessive Compulsive Disorder: A Pilot Study
- 15 **Papanastasiou, Evangelos** - The Genetics of Metabolic Syndrome in Schizophrenia
- 16 **Pararajasingham, Jennifer** - Prenatal Tobacco Exposure and Intrauterine Growth: A Gene-Environment-Wide Interaction Study of Foetal Genetic Modifiers
- 17 **Patel, Yogen** - Measures of global DNA methylation in post-mortem Alzheimer's disease brain
- 18 **Pauls, Astrid** - Working memory in postpartum psychosis (PP)
- 19 **Perfect, Leo** - Monoallelic gene expression in human neural stem cells
- 20 **Phillips, Thomas** - Systematic review of screening tools and procedures to identify hazardous drinking and alcohol use disorders in adult attendees in emergency departments (ED)
- 21 **Pick, Susannah** - Dissociation in individuals diagnosed with Dissociative Seizures (DS): a study of psychological and somatoform symptoms relative to a healthy control group<sup>1</sup>Susannah Pick
- 22 **Pinto, Rebecca** - The separation of ADHD inattention and hyperactivity-impulsivity symptoms: specific pathways from genes to cognitive impairments and symptoms
- 23 **Plant, Dominic** - Maternal Childhood Trauma Predicts Maternal Psychopathology In Pregnancy And Offspring Outcome At 11 Years
- 24 **Powell, Timothy** - The effects of early stressful life events on gene expression in the brain
- 25 **Price, Annabel** - Mental capacity assessment for terminally ill patients requesting assisted suicide in England and Wales: how concepts of knowing the patient impact upon process and outcome
- 26 **Radua, Joaquim** - Effects of the COMT x 5-HTTLPR genetic interaction on brain grey matter volume

- 27 Rane, Lena** - Psychological and physiological consequences of caring for patients with treatment resistant depression
- 28 San José Cáceres, Antonia** - Effects of social (mis) understanding on IQ in Autism Spectrum Disorder
- 29 Sapara, Adegboyega** - Neural Correlates of insight in psychosis investigated with fMRI of working memory
- 30 Sharpe, Helen** - Growing up with body confidence: A qualitative study of young people's views on appearances and dieting
- 31 Skirrow, Caroline** - Mood instability in adults with Attention Deficit Hyperactivity Disorder (ADHD): characterization, relationship to ADHD symptoms, and response to treatment
- 32 Smith, Lindsay** - Care-giving processes in Adulthood
- 33 Sood, Poonam** - Views and Experiences of physical health in First Onset Psychosis: a qualitative study
- 34 Stilo, Simona** - Cumulative Impact of Social Disadvantage in a Sample of First Episode Psychosis Patients
- 35 Stoica, Radu** - Amyotrophic Lateral Sclerosis-associated proteins TDP-43 and FUS disrupt the ER-mitochondria interaction
- 36 Suzuki, Akiko** - Title of presentation here (bold) The development of a new paradigm to clarify the role of childhood trauma in emotional processing of depressed individuals
- 37 Trzaskowski, Maciej** - Stable genetic influence on anxiety ratings across middle childhood
- 38 Tseng, Huai-Hsuan** - A study of Audiovisual Emotional Integration
- 39 Tye, Charlotte** - Shared and distinct Neurophysiological markers of Attention and Inhibition in Children with ASD and ADHD
- 40 Velayudhan, Latha** - Smell identification test as a progression marker in Alzheimer's disease
- 41 Wastling, Stephen** - Improving the Quality of Brain Images for Functional Magnetic Resonance Imaging Applications
- 42 Watermeyer, Tamlyn** - Emotional Processing and Social Cognition in Amyotrophic Lateral Sclerosis / Motor Neurone Disease
- 43 Willson, Rob** - Imagery re-scripting for body dysmorphic disorder
- 44 Wong, C. Peng** - Profiling DNA methylation in human Period 1 and negative life events in adolescents



## POSTER ABSTRACTS – MORNING SESSION

1

### Pharmacokinetic and pharmacodynamics of methadone drug response: The significance of drug-drug interactions

Basma Alharthy<sup>1</sup>

Kim Wolff<sup>1</sup>, Leon Barron<sup>2</sup>

<sup>1</sup>Addictions, <sup>2</sup> Pharmaceuticals/ Forensic science and drug monitoring

**Abstract:** Methadone is usually administered orally as a racemic mixture although it exists as a chiral molecule. In heroin dependence, methadone is acknowledged as an effective pharmacological substitution treatment. However, the drug response can be affected by various drug-drug interactions. The optimal dose of methadone can vary highly across individual patients, but is nevertheless important in enabling a successful methadone maintenance treatment (MMT) outcome (Lehotay et al., 2005). Factors affecting reaching an optimum dose including pharmacokinetics and pharmacodynamics factors have been studied however; the research is incomplete and further investigation on factors influencing reaching an optimum dose especially in a population likely to receive multimедication (antidepressants and antipsychotics) such as MMT patients.

The aim of this study is to investigate the steady-state pharmacokinetic of methadone and its metabolites in MMT using analytical methods that could also be applied for therapeutic drug monitoring. Drug-drug interactions influence the pharmacokinetic and/or pharmacodynamic of methadone when prescribed to heroin addicts. Therefore the study will also investigate drug-drug interactions between methadone and alcohol, benzodiazepines and antipsychotic medication and to determine whether these interactions influence the drug response in MMT. It will also attempt to investigate treatment outcomes when drug-drug interactions are a consistent problem.

**Conclusions:** N/A

2

### Quantitative Analysis of Emotion Recognition in Autism Spectrum Disorder (ASD) and Attention Deficit Hyperactivity Disorder (ADHD)

Karen Ashwood<sup>1</sup>

Bahare Azadi<sup>2</sup>, Sally Cartwright<sup>1</sup>, Philip Asherson<sup>2</sup>, Patrick Bolton<sup>2</sup>

<sup>1</sup>Child and Adolescent Psychiatry, <sup>2</sup>Social Genetic Developmental Psychiatry

**Background:** There is ongoing debate about whether ASD and ADHD can be conceptualised as continuous traits or discrete categories. Although emotion recognition deficits have been observed in both clinical populations, few studies have evaluated whether there is an association between ASD and ADHD traits and emotion recognition, preferring instead to adopt a categorical approach.

**Methods:** 113 males between the ages of 7 and 16 took part in the study. Included were individuals who, according to the DSM-IV, fulfilled the diagnosis of an ADHD (n=33) or ASD with (n=39) and without (n=17) comorbid ADHD symptoms and healthy controls (n=24) with an IQ>70. Both SCQ and Conners questionnaire scores provided a measure of parent-reported ASD and ADHD traits for all participants. Facial affect recognition was assessed using labeling and same/different discrimination computer tasks, with negative emotions (sad, angry, fear, disgust).

**Results:** Fewer ASD traits were associated with more accurate performance on the labeling task ( $r=-.29$ ,  $p=.001$ ), but not the discrimination task ( $p\geq.10$ ). The same pattern of results was shown for both inattentive traits ( $r_s = -.21$ ,  $p = .02$ ) and hyperactive/impulsive traits ( $r_s = -.25$ ,  $p = .01$ ). However, after controlling for FSIQ only the association between ASD traits and emotion labeling ability remained significant.

**Conclusions:** The findings support a selective association between ASD traits and emotion labeling ability which may suggest a fundamental problem in identifying and processing emotion, independent of general cognitive ability.

**Key words:** emotion recognition; ASD; ADHD

## Antisaccades in individuals with ADHD and autism using the gap/overlap paradigm

Bahare Azadi<sup>1</sup>

Ulrich Ettinger<sup>1,2</sup>, Philip Asherson<sup>1</sup>, Karen Ashwood<sup>1</sup>, Sally Cartwright<sup>1</sup>, Patrick Bolton<sup>1</sup>

<sup>1</sup>*Social, Genetic and Developmental Psychiatry Centre (MRC),*

<sup>2</sup>*Ludwig-Maximilians-University Munich*

**Background:** Saccadic reaction time (SRT) is a good index of visual attention pattern. “Gap/overlap paradigm” is supporting the idea that state of attention (engaged/disengaged) influences the SRT toward stimulus. In “overlap”, fixation point (FP) and target overlap; while in “gap”, FP is extinguished before target onset. 200ms gap is associated with reduced RT compared with the overlap (“gap effect”).

**Methods:** Boys aged 7-16, with diagnosis of ADHD, ASD or comorbid ASD+ADHD (FSIQ>70) were tested on antisaccades and prosaccades under gap, overlap, and step conditions.

**Results:** Data were available for 17 ASD, 35 ADHD, 38 comorbid, and 22 controls. For SRT, a significant condition effect was observed ( $p<.001$ ) reflecting an increase in latency from gap to step to overlap conditions.

No significant between-group differences were obtained for the antisaccade error rate ( $p=.56$ ); however, analyses on the correction rate showed a significantly higher rate of correction in the control group than the ASD ( $p=.05$ ), ADHD ( $p=.002$ ) and comorbid ( $p=.03$ ) groups.

**Conclusions:** No impairment in engagement and disengagement of visual attention was found in the clinical groups relative to controls. However, it was evident that the saccade metrics like amplitude and velocity were different in the clinical groups from controls. Therefore, even though individuals with ASD, ADHD or comorbid ASD-ADHD could engage and disengage their attention with no difficulties, they were still not able to generate saccades with the same magnitude and speed as the controls. Even though the clinical groups did not show higher direction errors, they corrected fewer errors compared to controls, which is indicative of impairment in response monitoring, an important function of frontally driven cognitive control.

**Key words:** ADHD; autism; antisaccade

## Development of an intervention to improve occupational performance post discharge from an acute psychiatric ward

Mary Birken<sup>1</sup>

Mike Slade<sup>1</sup>, Claire Henderson<sup>2</sup>

<sup>1</sup>*Section for Recovery, Health Service & Population Research Department,* <sup>2</sup>*Section for Community Mental Health, Health Service & Population Research Department*

**Background:** There are a range of consequences of having a diagnosed psychotic disorder. This study is concerned with the consequences relating to carrying out activities of daily living, at a stage of transition of the person's life, following discharge from hospital. Despite the well documented evidence that the consequences of having a psychotic disorder greatly effect activities of daily living for the individual there is a paucity of evidence regarding effective interventions to address this. This presentation aims to describe the development of an intervention to improve occupational performance of self care and leisure for people with a diagnosed psychotic following discharge from hospital.

**Methods:** The Medical Research Council Framework for Developing and Evaluating Complex Interventions 2008 is used to guide the study design. A systematic review of interventions, literature review of theory and studies of occupational performance, and focus groups with service users and clinicians, were carried out to provide best evidence on which to base the intervention.

**Results:** The synthesis of results found evidence regarding theoretical framing of the problems of occupational performance and theory based interventions to improve occupational performance in the occupational therapy and occupational science literature. The synthesis overall found no intervention specifically to address problems of occupational performance as identified by service users in focus groups.

**Conclusions:** The newly developed intervention is being piloted in phase two of the study. This study will add to the body of knowledge regarding interventions to prevent long term disability and support recovery for people with a psychotic disorder.

**Key words:** psychosis; activities of daily living; intervention

## Experience of stigma and discrimination amongst people with a Borderline Personality Disorder diagnosis

Oliver Bonnington

Diana Rose, Joanna Murray

*Health Service & Population Research Department*

**Background:** Schizophrenia and depression have been the main focus of mental illness stigma research. Such research has typically taken a quantitative approach and surveyed public opinion rather than the subjective experiences of people with psychiatric diagnoses. The experiences of stigma and discrimination amongst people who have been given a diagnosis of borderline personality disorder have been under-researched. Also, little is known about the ways gender, age and ethnicity affect stigma experience. In order to redress this imbalance, this wholly qualitative study investigated the experiences of stigma and discrimination amongst people with a diagnosis of borderline personality disorder.

**Methods:** In-depth interviews were conducted with individuals who self-reported a diagnosis of borderline personality disorder. All participants self-defined their ethnicity as White, Black African or Black Caribbean. Participants were recruited via mental health charities and participant networking. Issues explored included anticipated and experienced stigma and discrimination, the impact of discrimination on different areas of everyday life and ideas about how stigma and discrimination could be reduced. Fieldwork was audio recorded, transcribed and subjected to Thematic Analysis with the aid of NVivo 8 software.

**Results:** Emerging findings from 15 individual in-depth interviews will be presented. Preliminary results indicate that many people with a borderline personality disorder diagnosis experience or anticipate stigma and discrimination in a range of contexts, but especially healthcare settings.

**Conclusions:** The means of reducing stigma and discrimination, as well as some of the potential difficulties inherent in this, will be discussed.

**Key words:** stigma, discrimination, borderline personality disorder

## The effectiveness of joint crisis plans for people with borderline personality disorder: an exploratory randomised controlled trial

Rohan Borschmann

*Health Services & Population Research Department*

**Background:** Borderline Personality Disorder (BPD) is a common mental disorder associated with raised mortality, morbidity and substantial economic costs. Although complex psychological interventions have been shown to be useful in the treatment of BPD, such treatments are expensive to deliver and therefore have limited availability and questionable cost-effectiveness. Less complex interventions are required for the management of BPD. A Joint Crisis Plan (JCP) is a record containing a service user's treatment preferences for the management of future crises and is created by the service user with the help of their treating mental health team. JCPs have been shown to be an effective way of reducing compulsory treatment in people with psychosis. This exploratory trial will examine whether use of a JCP is an effective and cost-effective intervention for people with BPD for reducing self-harm.

**Methods:** In this single blind exploratory randomized controlled trial, approximately 120 participants (age >18 years with a primary diagnosis of DSM-IV BPD) will be recruited from community mental health teams and assigned to one of two conditions: (1) a JCP plus treatment as usual, or (2) treatment as usual. Those allocated to the JCP condition will take part in a facilitated meeting, the purpose of which will be to agree the contents of the plan. Following the meeting, a typed version of the JCP will be sent to the patient and to any other individuals specified by the participant. All participants will be followed-up at 6 months. The primary outcome measures are: any self-harm event, time to first episode of self-harm and number of self-harm events over the follow-up period. Secondary outcome measures include cost, working alliance, engagement with services, perceived coercion, quality of life, social impairment and satisfaction with treatment.

**Results:** Data collection is ongoing.

**Conclusions:** Results of this trial will help to clarify the potential beneficial effects of JCPs for people with BPD and provide information to design a definitive trial.

**Key words:** borderline personality disorder (BPD); self-harm; joint crisis plan (JCP)

## Mental Health and Social Wellbeing of Ex-Service personnel: the resettlement process

Howard Burdett

*The King's Centre for Military Health Research*

**Background:** At some point in their lives, all those serving in the Armed Forces must leave and re-enter civilian life. In the UK, this is facilitated by the government-mandated "resettlement" process. Studies of the consequences and effectiveness of resettlement are few and limited. The KCMHR cohort contains data on over 1,700 Service leavers including a variety of health, wellbeing, labour market and social exclusion variables.

**Methods:** Statistical analysis will be performed using the software package STATA (version 11). Frequencies and cross tabulations of variables will provide descriptive statistics. Univariable associations between outcome variables and resettlement utilisation, as well as in-Service and pre-enlistment factors, will be investigated by logistic regression.

**Results:** Taking resettlement is associated with post-Service employment, as well as having some protective effect on common mental disorders. PTSD, alcohol misuse, housing, and legal difficulty do not seem to be affected by taking resettlement. Intriguingly, vocational training does not seem to affect any outcome (except legal difficulty).

**Conclusions:** While resettlement does have the expected effect on re-employment after leaving the Armed Forces, other forms of socio-economic exclusion and mental health difficulty may not be affected. The lack of effect of vocational training may have policy implications.

**Key words:** military personnel; mental welfare; social exclusion

## Investigating the neurobiological and genetic basis of Empathic Resonance and the Manipulation of Other Minds in Adolescence

Anna Cattrell

Eva Loth, Francesca Happé, Gunter Schumann  
*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** Behavioural and neuroimaging work has shown that two fundamental aspects of social cognition, namely empathy and theory of mind, are disrupted in developmental disorders (e.g. autism and conduct disorder). We are unaware of any other projects that have investigated both traits in the same study, and aim to establish the extent to which these traits might influence development in healthy adolescents and potentially serve as risk factors for the development of psychopathology.

**Methods:** Based on personality information from 1700 typically developing adolescents from the IMAGEN project we have (i) developed two scales to assess empathy and manipulation; (ii) conducted a preliminary validation study of the two scales; (iii) investigated the relationship between empathy and manipulation and a clinical measure of conduct disorder (CD) and (iv) investigated the relationship between the two scales and a conduct disorder working with individuals with extreme scores (e.g. high manipulation and low empathy).

**Results:** In our extreme group work we have found that the combination of low empathy and high manipulation was related to a higher rate of CD traits; this group also contained more individuals at risk for a possible/probable diagnosis of CD and these results were significantly higher than rates for the three other extreme groups.

**Conclusions:** Our extreme group work has shown that neither high manipulation nor low empathy traits are sufficient to predict CD but that in a population based adolescent sample CD traits are best predicted by a unique combination of high MOM and low ER.

**Key words:** empathy; conduct disorder; adolescence

## Pharmacological fMRI on the effects of Fluoxetine on functions of impulsiveness, cognitive flexibility and working memory in children with Attention Deficit Hyperactivity Disorder and High Functioning Autism Spectrum Disorders

Kaylita Chantiluke<sup>1</sup>

Anna Smith<sup>1</sup>, Vincent Giampietro<sup>2</sup>, Nadia Barrett<sup>3</sup>, Declan Murphy<sup>4</sup>, Katya Rubia<sup>1</sup>

<sup>1</sup>*Child and Adolescent Psychiatry*, <sup>2</sup>*Centre for Neuroimaging*, <sup>3</sup>*SLaM - NHS*, <sup>4</sup>*Forensic and Neurodevelopmental Sciences*

**Background:** Genetic and biochemical studies have shown that serotonin (5-HT) dysregulation may play a pivotal role in both Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorders (ASD). Serotonin agonists such as the serotonin-reuptake inhibitor (SSRI) Fluoxetine reduce symptoms in both disorders and modulate ventrolateral prefrontal activation in healthy adults which is structurally and functionally abnormal in both disorders. However no studies have investigated the neurofunctional effect of serotonin agonists in children with ADHD or ASD.

**Methods:** Twenty boys with the clinical DSM-IV diagnosis of ADHD (combined sub-type) and 20 with that of high functioning ASD, aged 10-17, IQ < 70 will undergo two structural and functional magnetic resonance imaging scans (s/fMRI) (four weeks apart), either under placebo (peppermint water), or a single clinical dose of Fluoxetine (titrated to weight), in a double-blind, cross-over design. fMRI will use 4 tasks, i.e. a working memory NBack task, a Stop Task measuring motor inhibition, a Temporal Discounting task to measure reward-related decision making and a Reversal Learning task. We will test for normalisation effects by comparing patients with age and IQ matched controls. Disorders will also be compared in f/sMRI at placebo.

**Results:** We hypothesise that Fluoxetine will increase activation in inferior and orbital frontal brain regions in both groups, but with a more pronounced effect in ASD patients. Differences in laterality are expected with potential normalisation in left ventrolateral frontal dysfunction in ASD and right inferior frontal dysfunction in ADHD. Disorder-specific structural and functional deficits are expected for the placebo-between patient comparisons.

**Conclusions:** N/A

**Key words:** attention deficit hyperactivity disorder (ADHD); autism spectrum disorders (ASD); serotonin; functional magnetic resonance imaging

## Piloting a guided self-help pack called the SAINT for adults with intellectual disabilities

Eddie Chaplin

Nick Bouras and Tom Craig

*Health Service & Population Research Department*

**Background:** The present study is currently piloting the Self Assessment and Intervention SAINT; a unique guided self-help tool for people with intellectual disabilities (ID). Previously we developed the SAINT and investigated its main psychometric properties and are now in the pilot phase. This study aims to examine proof of concept of this intervention for people with ID. The SAINT was developed in consultation with clinical and service user experts and was tested for reliability and validity against validated measures specific to this population i.e. the GDS-LD and GAS-ID, producing promising results.

**Methods:** A mixture of Delphi and focus groups were used to develop the SAINT. With a number of correlation based statistics to examine reliability against established measures (GDS-LD, GAS-ID). Single Case Experimental Design (SCED) has been used for the pilot.

**Results:** (n=46 unless stated) We have seen high internal consistency at 0.868 and 0.821-0.853 for any item deleted. The SAINT was significant at the 0.01 level (2-tailed) with the GDS-LD. Test retest reached significance ( $r = 0.914$ ,  $p < .01$ ) (n=14)

**Conclusions:** The SAINT study is now in its final stage has shown to have good internal consistency. Currently the SAINT is being piloted using a SCED.

**Key words:** guided self help; intellectual disability; SAINT

## The effect of Cognitive Bias Modification on Emotional Vulnerability: Comparison of delivery schedules

JongSun Lee<sup>1</sup>

Andrew Mathews<sup>2</sup>, Sukhi Shergill<sup>1</sup>, Jenny Yiend<sup>1</sup>

<sup>1</sup>*Department of Psychosis Studies, <sup>2</sup>Department of Psychology, University of California, Davis, US*

**Background:** Changing cognitive bias has been considered a powerful therapeutic mechanism for psychiatric disorders. Recently, Cognitive Bias Modification (CBM), a new experimentally based therapeutic program, has shown the promise of therapeutic benefit for some clinical patients (e.g., anxiety). Recent work has shown that CBM improves emotional vulnerability to stress and promotes clinical symptom reduction (e.g., Mathews, Ridgeway, Cook, & Yiend, 2007). The current study tested differential effects of a novel computerized CBM-Error training on mood and cognition change and emotional vulnerability to stressor, by comparing four different schedules of individual learning sessions.

**Methods:** Depressed individuals (N=80) were recruited from the community. Participants were randomized to one of four groups. Three groups received CBM and one was a 'no training' control group. The CBM groups (N=20 each) compared an Expanded Interval Schedule (EIS; 4 sessions one on each of day 0, 2, 6 and 15) with a Uniform Interval Schedule (UIS; 4 sessions one on each of day 1, 5, 10, 15) and a Massed Schedule (MS; the 4 sessions presented together all on day 0).

**Results:** After the cognitive error modification intervention, expanded and uniform schedules showed better outcomes on depressive mood compared to control group. After training, both expanded and uniform groups were less emotionally distressed by unpleasant film clips, compared to controls.

**Conclusions:** After changing interpretations using our cognitive error modification procedure, we found that participants reported reduced susceptibility to stressful effects of unpleasant emotional stressors. This research will contribute towards developing a more cost-effective and easily-accessible intervention to treat affective disorders.

**Key words:** Cognitive Bias Modification; depression; cost-effective intervention

## Distinguishing contact-mediated effects from soluble factors of human endothelial cells on the differentiation of clinical-grade human neural stem cell lines

Chung-Hsing Chou

Mike Modo

*Centre for the Cellular Basis of Behaviour, Department of Neuroscience*

**Background:** The vascular compartment plays an intricate role within the neurovascular niche, where neurogenesis and angiogenesis are considered coupled processes. Endothelial cells, together with astrocytes and pericytes, form the blood-brain-barrier, and they are certainly involved in cerebrovascular events, such as stroke, in which the neurovascular unit is disrupted. Transplantation of neural stem cells (NSCs) within this environment can affect angiogenesis, but conversely, angiogenesis can also affect the fate of NSCs. To develop a better therapeutic use of NSCs, we therefore investigated how the neurovascular microenvironment can influence the fate of NSCs in the co-culture systems.

**Methods:** Human NSCs: CTX0E03 and STROC05 cell lines. Human cerebral microvascular endothelial cells (HCMECs): D3 cell line. Human umbilical vein endothelial cells (HUVEC). Immunocytochemistry: phenotypic characterization of neural lineage and endothelial cells in co-culture systems with or without direct contact (e.g. stem cell marker, Nestin; astrocyte marker, GFAP; neuronal marker, MAP2)

**Results:** Soluble factors of HUVECs increased GFAP expression in differentiated NSCs, but also maintained the expression of Nestin at the level of undifferentiated cells. These changes were the result of the emergence of a subpopulation of cells co-expressing Nestin and GFAP. D3 cells formed tube-like structures during blood vessel morphogenesis when cultured with NSCs directly. Differentiation of NSCs was affected by D3 cells as well.

**Conclusions:** These studies will potentially provide evidence as to how the neurovascular microenvironment can influence the fate of NSCs and indicate the optimal cell ratio between ECs and NSCs in a combined transplantation therapy.

**Key words:** neural stem cell; endothelial cell; neurovascular niche

## Response shift and the measurement of change in health-related quality of life

Kia-Chong Chua

Sube Banerjee, Renee Romeo

*Mental Health & Ageing, Health Services & Population Research*

**Background:** Response shift is a phenomenon in which illness adaptation evokes a change in one's internal standards, or perceptions of health-related quality of life (HRQL). An assessment of change might lose its meaning if the meaning of HRQL differs between assessments. Consequently, the measurement of change may not reflect true treatment effects.

**Methods:** HRQL data from clinical trial of antidepressant in dementia (HTA SADD) were analysed using structural equation modelling. Specifically, the analyses focused on the HRQL model parameters at baseline and follow up to assess whether the meaning of HRQL has changes. The analysis will assess the nature and extent of response shift and derive an adjusted estimate of change.

**Results:** Changes in factor loading patterns, actual factor loading values, and/or item means suggest the potential presence of re-conceptualisation, re-prioritisation, and re-calibration. Preliminary findings will be presented.

**Conclusions:** Response shift is a potentially relevant phenomenon among people with dementia in face of the devastating impact of progressive global decline in cognitive functioning. The impact of illness adaptation on HRQL appraisal warrants further research to minimize the prospect of positive effects of a treatment being overlooked or negative effects being missed.

**Key words:** response shift; health-related quality of life in dementia; structural equation modelling

## Establishing the Neuropsychological Profile of Psychosis in Alzheimer's Disease

Chloe Clark-Papasavas

*Department of Old Age Psychiatry*

**Background:** Psychotic symptoms (delusions and/or hallucinations) occur in 40-60% of people with Alzheimer's Disease (AD) and are associated with considerable morbidity in patients and carers. Positron Emission Tomography (PET) imaging data on people with AD has shown increased striatal dopamine D2/3 receptor availability to be associated with psychotic symptoms, and in addition was associated with cognitive (attentional) and motor (latency) function. This study aims to test the hypothesis that performance on neuropsychological tests showing a demonstrated relationship with dopamine function differ between psychotic and non-psychotic groups, and to establish a comprehensive neuropsychological profile of psychotic symptoms in AD.

**Methods:** One hundred participants with mild to moderate AD (50 with psychotic symptoms, 50 without) will be compared on a neuropsychological test battery which includes measures of memory, attention, visuospatial perception, language, motor speed and executive functioning. The Neuropsychiatric Inventory (NPI), a carer-rated scale, will be used to determine the frequency and severity of psychotic symptoms. When 70 participants (35 in each group) have been recruited, preliminary statistical analyses will be conducted using multiple analysis of covariance models (MANCOVA) to control for potential confounding variables.

**Results:** 30 participants (15 [50%] males; mean age = 79.7±5.6; MMSE = 21.1 ±6.1) have been recruited to the study thus far. Carers reported delusions in 13(44.8%) and hallucinations in 1(3.4%) of the sample.

**Implications:** If it can be established that performance on certain neuropsychological tests differ between the two groups, it is possible that these tests could act as markers of psychotic symptoms or treatment response in AD.

**Key words:** Alzheimer's disease: delusions; psychotic symptoms; neuropsychological test

## The challenges of calculating incidence rates of self-poisoning presentations across ethnic groups in two London boroughs

Sean Cross

*Dept Liaison Psychiatry, SLAM*

**Background:** This project forms part of a wider MD (Res) project entitled 'Self-poisoning across ethnic groups in SE London'. The project is a mixed methods study in which both quantitative and qualitative methods are being employed to investigate the salience of ethnicity in a common care pathway. Numerator and denominator calculations across different ethnic groups in this pathway face several challenges. The former requires use of both local and neighboring acute trust and mental health trust record systems and the latter requires local population data in ethnically diverse and changing inner city London boroughs. In addition both numerator and denominator require a reconciling of different classification systems for ethnicity that occur in health and local authority systems. These are based on ONS categories but vary from them in some important ways relevant to the local populations in Lambeth and Southwark.

Self-harm cases account for over 1% of Emergency Department presentations nationally. Locally in Lambeth and Southwark this translates to approximately 2000 presentations to St Thomas' and King's College Hospitals. Self-poisoning (also known as overdose) accounts for the majority of these presentations at over 70%. This is therefore a common presentation in which there are challenges in providing a high quality care pathway given the complex physical and psychological needs of those who present. In addition to the healthcare needs of each individual presentation there are two important associations which make this an important area: a high repetition rate (15% at 1 year and up to 40% eventually) and an association with completed suicide which sees this cohort 100x more likely to die in this way when compared with the background population.

The salience of ethnicity in this pathway in a variety of ways has been little investigated. Accurate measurement of local incidence rates is an initial step towards addressing this.

**Methods:** Measurement of self-poisoning presentations in 2009 has occurred (with one part still remaining). This has required use of a range of different systems: Guy's and St Thomas' NHS Foundation Trust and King's College Hospital NHS Foundation Trust A&E record systems through collaboration with Department of Clinical Toxicology at GSTT; St George's NHS Healthcare Trust A&E record systems and a number of different recording systems within South London and Maudsley NHS Foundation Trust. A range of different steps in different institutions with regard to data protection permission were taken. A survey of different ethnicity monitoring systems has occurred and can be discussed.

**Results:** In line with guidelines below this potential presentation is focusing on the background and methods. Preliminary results and discussion can occur if requested by the organizers of the showcase day.

**Conclusions:** N/A

**Key words:** self-poisoning; suicide prevention; ethnicity



## Integrating published functional neuroimaging studies with graph analysis

Nicolas Crossley

Andrea Mechelli, Philip McGuire

*Psychosis Studies*

**Background:** Functional neuroimaging studies such as PET and fMRI have helped us to understand the functioning of the brain. Typically, a subject is scanned while performing a cognitive task, allowing us to see the brain areas that are “active”. Although it gives us detailed information about the biological underpinnings of that cognitive task, so far it has been difficult to integrate different tasks and activations to shed light into the overall cognitive structure of the brain. We propose to use elements of network science to overcome this problem. Specifically, we suggest the use of 2-mode networks to display and analyze results from several functional neuroimaging studies.

**Methods:** We used the freely available database brainmap.org, which collects peak activation coordinates from fMRI studies. All studies in the database were grouped according to types of tasks used, and summaries of the activations of similar studies were obtained with ALE meta-analysis. A 2-mode network was then built using task as one mode, and brain regions as the other, drawing links between them if the task activated that region. Characteristics of the published literature and of cognitive networks can be obtained from the analysis of this 2-mode network using methods such as clique analysis.

**Results:** Preliminary results demonstrating the feasibility of the method and its potential will be shown.

**Conclusions:** Network analysis can be used to analyze meta-data of neuroimaging studies. This method can also be used to integrate functional neuroimaging studies of pathological states.

**Key words:** functional; meta-analysis; graph analysis

## Task-dependent drug-specific upregulation effects of Methylphenidate and Atomoxetine on brain function in medication-naïve children with ADHD

Ana Cubillo<sup>1</sup>

Anna Smith<sup>1</sup>, Nadia Barrett<sup>1</sup>, Vincent Giampietro<sup>2</sup>, Andrew Simmons<sup>2</sup>, Katya Rubia<sup>1</sup>

<sup>1</sup>*Department of Child and Adolescent Psychiatry, <sup>2</sup>Department of Neuroimaging*

**Background:** The psychostimulant Methylphenidate (MPH) enhances fronto-striatal function in ADHD patients, while effects of the non-stimulant Atomoxetine (ATX) are unknown. We compared the neurofunctional effects of both drugs in medication-naïve ADHD boys.

**Methods:** 20 medication-naïve boys with ADHD were scanned in fMRI after a single dose of MPH (0.3g/kg), ATX (1mg/kg) or placebo during 3 tasks (Stop, Working Memory and Time Discrimination) in a double-blind, randomized, crossover design.

**Results:** During time perception, MPH improved performance and upregulated anterior cingulate, right inferior prefrontal cortex (IFC) and parietal activation compared with ATX and placebo. ATX compared with MPH and placebo upregulated right IFC activation during motor inhibition. Both drugs deactivated the posterior cingulate (PCC) during working memory (WM). Interaction effects of WM load by drug condition showed that during high WM load, ATX relative to MPH showed stronger upregulation effects in the IFC and stronger deactivating effects in the PCC.

**Conclusions:** ATX and MPH have dissociated, task-specific effects on brain activation in ADHD. ATX has a drug-specific upregulation effect on right IFC during motor inhibition and stronger upregulation effects in this region during WM. MPH on the other hand has a drug-specific effect on right IFC-parieto-cingulate time perception networks.

**Key words:** ADHD; Methylphenidate; Atomoxetine; fMRI

## What are implications of recovery for older people with mental health problems, including those with dementia?

Stephanie Daley

Mike Slade, Joanna Murray, Sube Banerjee

*Health Service & Population Research Department*

**Background:** Whilst the impact of the recovery philosophy upon mental health services for working age adults has been substantial, similar developments have not yet taken place in older people's mental health services and research in this area is under-developed. This study aims to

- Identify which components of recovery are valued by older people with mental health problems, including those with dementia
- To identify whether there are components of recovery which are specific to dementia, and if so, whether these change as the illness progresses

**Methods:** Qualitative interviews have been carried out with 28 users of older peoples' mental health services and 10 carers in order to develop a framework for recovery and older people. These interviews have been analysed using grounded theory methodology.

**Results:** The experience of recovery for users of older peoples' mental health services differs in that it appears to be primarily concerned with maintaining or regaining a sense of pre-illness identity. Key coping strategies appear to relate to the continuity and adaptation of existing social supports, valued social roles and meaningful activities. For people with dementia, the subjective experience of recovery changes over time, and spousal carers having a pivotal role in facilitating or hindering the opportunities for recovery to take place.

**Conclusions:** Personal recovery does have resonance for older people, including those with dementia. There are substantial practice implications arising from these findings for older peoples' mental health services, which differ significantly from those which affect working age adult services.

**Key words:** recovery; older people; continuity

## Born into adversity; the intergenerational factors accounting for the 'transmission' of mental health inequalities in second generation Irish children growing up in Britain

Jayati Das-Munshi<sup>1</sup>

C. Clark<sup>2</sup>, M.E. Dewey<sup>1</sup>, G. Leavey<sup>3</sup>, S.A. Stansfeld<sup>2</sup>, M.J. Prince<sup>1</sup>

<sup>1</sup>*Section of Epidemiology, Department of Health Services Research & Health of Populations,* <sup>2</sup>*Department of Psychiatry, Queen Mary, University of London,* <sup>3</sup>*University College London (UCL), Northern Ireland Association for Mental Health (NIAMH)*

**Background:** Despite relative improvements in socioeconomic circumstances, Irish people living in Britain experience elevated mortality and morbidity. This has persisted into the second generation. The reasons for this are unknown. We conducted analyses of two prospective datasets to assess how far migration and settlement-related experiences might account for excess psychological morbidity in childhood.

**Methods:** Data from two British birth cohorts which surveyed 17,000 babies born in 1958 and in 1970 were used. Second-generation Irish children formed 6% of each cohort. Odds ratios were calculated using multivariate logistic regression.

**Results:** Relative to non-Irish children, second generation Irish children grew up in circumstances of marked material hardship. Irish-born mothers were more likely to be depressed when their child was 5 (OR: 1.47 (95% CI: 1.17, 1.86; p=0.002)), or 10 (OR: 1.44(95% CI: 1.13, 1.84; p=0.004)), and Irish-born parents reported more chronic health problems than non-Irish parents (OR: 1.29; 95% CI: 1.08-1.54; p=0.005). Second generation Irish children had greater emotional and behavioral problems at age 7, 11 and 16, which diminished after accounting for material hardship and mother's mental health.

**Conclusions:** We conclude that second generation Irish children growing up in 1960s and 1970s Britain experienced significant emotional and behavioral morbidity but the excess was accounted for through adverse material circumstances and mother's mental health. As childhood adversity and psychological health are implicated in the aetiology of adult morbidity and mortality, the findings suggest life-course mechanisms for the intergenerational 'transmission' of health inequalities.

**Key words:** migration; life-course epidemiology; childhood emotional and psychological health

## Understanding the central effects of ketamine on brain function: a combined functional magnetic resonance imaging blood oxygen level dependent, cerebral blood flow and subjective ratings approach

Sara De Simoni<sup>1</sup>

O.G. O'Daly<sup>1</sup>, F.O. Zelaya<sup>1</sup>, A.J. Schwarz<sup>2</sup>, S. Stephenson<sup>1</sup>, S.C.R. Williams<sup>1</sup>, M.A. Mehta<sup>1</sup>

<sup>1</sup>Neuroimaging, <sup>2</sup>Eli Lilly Pharmaceuticals

**Background:** fMRI relies on the blood oxygen level dependent (BOLD)<sup>1</sup> signal as an indirect measure of neuronal activity whereas continuous arterial spin labelling (cASL) provides an absolute measure of regional cerebral blood flow (rCBF). Both are imaging techniques used to describe separable facets of central drug responses. In the present study we characterised the reliability and anatomical profile of the cASL and BOLD responses to low-dose ketamine infusion, known to induce symptoms similar to schizophrenia at higher doses.

**Methods:** Data were acquired from 10 right-handed healthy male participants at rest on two separate occasions, before and during ketamine infusion. Reliability of the brain networks and subjective ratings sensitive to ketamine was calculated using the intra-class correlation coefficient [ICC(3,1)]<sup>2</sup>.

**Results:** Robust responses to ketamine were observed in subjective ratings, cASL and BOLD data across both sessions. Many regions within the induced network showed good reliability (BOLD cingulate region (ICC=0.74); cASL subgenual region (ICC = 0.76)). Reliability for some subjective rating subscales was high (cognitive disorganisation ICC=0.87), but others were less reliable (derealisation ICC=0.39).

**Conclusions:** Low dose ketamine infusion produced changes consistent with previous studies<sup>3</sup>. Although differences in the spatial distribution of the BOLD and rCBF changes were evident both possess suitable properties to act as objective markers of the ketamine effect, which is relevant for repeated measures studies of novel treatments for schizophrenia which may modulate this effect.

[1] Schwarz et al. (2004) *Synapse* 54(1): 1-10.

[2] Caceres et al. (2009) *NeuroImage* 45(3) 758-68.

[3] Deakin et al. (2008) *Arch. Gen. Psych.* 65(2) 154-64.

**Key words:** blood oxygen level dependent; continuous arterial spin labeling; reliability

## Face emotion processing in children aged 9-14 years presenting putative antecedents of schizophrenia.

Hannah Dickson<sup>1</sup>

Monica Calkins<sup>2</sup>, Christian Kohler<sup>2</sup>, Sheilagh Hodgins<sup>1</sup>, Kristin. R. Laurens<sup>1,3</sup>

<sup>1</sup>Department of Forensic and Neurodevelopmental Sciences,

<sup>2</sup>Schizophrenia Research Centre and Brain Behaviour

Laboratory, Department of Psychiatry, University of

Pennsylvania School of Medicine, USA, <sup>3</sup>Research Unit for

Schizophrenia Epidemiology, School of Psychiatry, University of New South Wales, Australia

**Background:** Deficits in face emotion processing are observed in individuals with schizophrenia and in “high-risk” young relatives of schizophrenia patients (Eack et al., 2010; *Schizophrenia Bulletin*, 36, 1081-1088). We have established a novel questionnaire method of identifying children who present multiple putative antecedents of schizophrenia (ASz) who may bear elevated risk of developing the disorder (Laurens et al, 2007, *Schizophrenia Research*, 90, 130-146). The current study aimed to determine whether ASz children show deficits in face emotion processing compared to typically-developing (TD) children who do not present with the antecedents.

**Methods:** 33 ASz (10 female; mean age 12 years 1 months) and 33 TD children (14 female; mean age 12 years 7 months) completed the Penn Emotion Recognition Task, comprising 40 colour photographs of happy, sad, angry, scared, or neutral emotions presented serially. Participants selected the emotion label that most accurately reflected the emotion portrayed on the face.

**Results:** Analyses indicate that, when compared to TD children, ASz children make more emotion recognition errors overall ( $p < 0.001$ ), and were significantly more likely to misidentify (label) other emotions as neutral ( $p < 0.01$ ) and sad ( $p < 0.05$ ) expressions. ASz children also committed more neutral face misattributions than TD children, with the majority of these constituting neutral expressions being mislabelled as sad expressions ( $p < 0.01$ ).

**Conclusions:** Children presenting multiple putative antecedents of schizophrenia show similar face emotion processing deficits to young relatives at familial high-risk for schizophrenia. Only longitudinal follow-up of ASz children will establish whether these deficits are a potential marker for schizophrenia.

**Key words:** at-risk; schizophrenia; face emotion recognition

## The R&R2 ADHD programme for adults: A randomized controlled study

Brynjar Emilsson<sup>1,2</sup>

Gisli Gudjonsson<sup>1</sup>, Susan Young<sup>2</sup>

Jon F. Sigurdsson<sup>3</sup>, Halldora Olafsdottir<sup>3</sup>, Gisli Baldursson<sup>3</sup>,  
Emil Einarsson<sup>3</sup>

<sup>1</sup>Psychiatry, <sup>2</sup>Forensic and Neurodevelopmental Science,

<sup>3</sup>Landspítali - The National University Hospital of Iceland

**Background:** Few randomized controlled studies on psychological treatments for adults with ADHD have been published. These studies have showed promising results but there is a need for continued developments in new treatment models and studies on their effectiveness. This study aimed at measuring the efficacy of a novel CBT model for adults with ADHD, the R&R2 ADHD programme. The primary measurements were ADHD symptoms and severity of illness and secondary outcome measures were co-morbid disorders. It was hypothesised that those who received the psychological treatment would show significantly more improvement on the selected outcome measures than those who did not and that this difference would be maintained at three month follow-up.

**Methods:** This study was conducted at an outpatient clinic at the Landspítali National University Hospital of Iceland. 54 adults with ADHD and residual symptoms were randomly allocated to an experimental (CBT/MED) treatment condition (n = 27) and a 'treatment as usual' (TAU/MED) control condition (n = 27) that did not receive the CBT intervention. Both treatment conditions received specific ADHD medication treatment throughout the study phase. The outcome measures were obtained after treatment and at three month follow-up, and included self-reports and ratings by independent assessors.

**Results:** The results show medium to large treatment effects on measures of ADHD symptoms at the end of treatment. Significant and large treatment effects were noted on all the measures at follow-up.

**Conclusions:** The results give support for the growing evidence for the effectiveness of CBT interventions for adults with ADHD. The implications are that the benefits of R&R2ADHD are multifaceted and that combined psychopharmacological and CBT based treatments will add to and improve pharmacological interventions.

**Key words:** ADHD; R&R2; RCT

## Lentiviral mediated gene delivery reveals distinct roles of nucleus accumbens dopamine D2 and D3 receptors in novelty- and light-induced locomotor activity

Alinda Fernandes

Sylvane Desrivieres, Alanna Easton, Christian Müller,  
Gunter Schumann

Social, Genetic and Developmental Psychiatry Centre (MRC)

**Background:** Functional studies investigating effects of alteration of the dopaminergic system lead to changes in cognitive and motor functions. Although the roles of specific dopamine receptors in behaviour have been extensively investigated using pharmacological agents and knockout mice, non-specificity of ligands and compensatory molecular adaptations in mutated animals restrict the interpretation of the results.

**Methods:** We used lentivirus-mediated gene knockdown and overexpression to specifically and locally manipulate expression levels of these genes in the rat nucleus accumbens (NAcc), a brain area important for motor response. Lentiviruses, inducing expression of rat D2R or D3R, or efficient knockdown of either receptor by small hairpin (sh)RNAs were stereotaxically injected into the NAcc. Novelty- and light-induced locomotor activities as well as anxiety-related behaviours were measured.

**Results:** Knockdown of either receptor significantly reduced spontaneous locomotor activity in a novel, but not in a habituated environment. While D2R knockdown increased, while D3R knockdown decreased light induced locomotor activity in this test.

**Conclusions:** Altogether, our findings suggest that D2R and D3R, expressed in the NAcc, have both, shared and non-overlapping roles in locomotor activity.

**Key words:** gene silencing; lentivirus; behaviour

## Gender differences in the association between childhood adversity, social support and psychosis

Charlotte Gayer-Anderson<sup>1</sup>

Robin Murray<sup>2</sup>, Craig Morgan<sup>1</sup>

<sup>1</sup>*Health Service and Population Research, <sup>2</sup>Psychosis Studies*

**Background:** Several recent studies have demonstrated gender differences in the association between childhood adversity and psychosis, whereby reports of severe childhood physical and sexual abuse are associated with psychosis in women, but not men. Social support has also been shown to be a protective factor in the onset and course of the disorder. Thus our aim was to investigate whether current social support moderated the relationship between severe childhood physical and sexual abuse separately in men and women.

**Methods:** The sample consisted of 199 first-episode psychosis cases and 266 population-based controls who were assessed with the Significant Others Scale (SOS) and the Childhood Experiences of Care and Abuse Questionnaire in South London and Nottingham as part of the AESOP (Aetiology and Ethnicity of Schizophrenia and other Psychoses) study. The analysis of this data has informed the development of the hypotheses and methods of my PhD study.

**Results:** Women who were sexually or physically abused as a child were generally more likely to be a case if they reported currently having lower perceived support, lower emotional support and fewer significant others, compared with women who weren't abused as a child, following adjustment for potential confounders. In contrast, current social support did not modify the odds of being a case in men who had experienced childhood abuse.

**Conclusions:** Social support appears to moderate the relationship between childhood adversity and risk of psychosis in women but not in men.

**Key words:** psychosis; childhood adversity; social support

## Behavioural characterization of the NRXN1/2 knockout mice: A functional study on susceptibility genes for neurodevelopmental disorders

Hannah Grayton<sup>1</sup>

Cathy Fernandes<sup>1</sup>, Markus Missler<sup>2</sup>, David Collier<sup>1</sup>

<sup>1</sup>*Social, Genetic and Developmental Psychiatry Centre,*

<sup>2</sup>*Institute of Anatomy and Molecular Neurobiology, Westfälische Wilhelms-Universität, Münster, Germany*

**Background:** Copy number variations (CNVs) are emerging as an important genomic cause of several common neurodevelopmental disorders, including autism, mental retardation, epilepsy and schizophrenia (Walsh et al, 2008; Mefford et al, 2008; Stefansson et al., 2008). Deletions within the neurexin 1 gene (NRXN1; 2p16.3) have been found in cases with autism, mental retardation and schizophrenia (Kirov et al., 2008; Feng et al, 2006; Zahir et al, 2007), and recently, a truncating mutation in the NRXN2 gene (11q13) has also been seen in a patient with autism and a family history of schizophrenia (Gauthier et al, 2011). Neurexin1 $\alpha$  and 2 $\alpha$  knockout mice (Nrnx1<sup>tm1Sud</sup>; Nrnx2<sup>tm1Sud</sup>) already exist and the Nrnx1<sup>tm1Sud</sup> mouse has been used to analyse the role of neurexins in synapse formation and some behaviours (Etherton et al., 2009). Full behavioural analysis has, however, not yet been carried out.

**Methods:** The behavioural phenotype of Nrnx1<sup>tm1Sud</sup> and Nrnx2<sup>tm1Sud</sup> mice will be assessed using a battery of tests that span the behavioural domains known to be affected in neurodevelopmental disorders, such as anxiety, cognition and social behaviour (Kas et al, 2007).

**Results:** Results suggest such deletions may cause alterations in the behaviour of the mice, such as changes to anxiety levels and long-term memory.

**Conclusions:** These initial results are very promising and suggest that a second much larger study with a diverse behavioural test battery will enable us to fully explore the behavioural consequence of such a deletion, revealing a possible impairment in the traits related to neurodevelopmental disorders.

**Key words:** copy number variation; neurexins; neurodevelopmental disorders

## Facial affect recognition in patients with schizophrenia and a history of violence

Stephanie Harris<sup>1</sup>

Clare Oakley<sup>1</sup>, Avi Reichenberg<sup>2</sup>, Declan Murphy<sup>1</sup>, Simon Surguladze<sup>3</sup>, Marco Picchioni<sup>1</sup>

<sup>1</sup>*Department of Forensic and Neurodevelopmental Sciences,*

<sup>2</sup>*Department of Psychosis Studies,* <sup>3</sup>*Cygnnet Health Care*

**Background:** There is a robust association between schizophrenia and an increased risk of violence. Evidence suggests that disrupted emotional processing impairs the regulation of social emotional cues, increasing the chances of violence. Affective empathy deficits exist both in those with psychopathy and violent offenders, particularly for negative emotions. Patients with schizophrenia also experience facial affect recognition deficits. We hypothesised that patients would show decreased affect recognition accuracy for negative emotions compared to happiness.

**Methods:** Males with schizophrenia and a history of violence completed a computerised facial affect recognition task (FAR) comprising emotions of anger, fear, happiness and sadness. Emotional intensity was experimentally manipulated (0%, 25%, 50%, 100%) along with stimulus duration (500ms, 2000ms).

**Results:** Patients made significantly fewer total errors in the identification of happy faces compared with the other emotions. Of the four emotions, patients were worse at accurately identifying sad expressions, both overall and at high intensity. At 50% intensity, participants were significantly better able to recognise happiness and fear, which in turn did not differ significantly. No differences between emotions were found at low intensity; however patients were more likely to identify neutral faces as sad, compared with other emotions.

**Conclusions:** Our data suggest that violent patients with schizophrenia are worse at accurately recognising negative emotions, particularly sadness and are more likely to misattribute sadness to neutral expressions. Patients are better able to identify expressions of happiness. Consistent with previous findings, this lends tentative support to the proposed relationship between violence and an inability to accurately evaluate 'restraint producing' emotional cues.

**Key words:** schizophrenia keyword; violence; affect recognition

## The Epidemiology of Psychotic Depression

Margaret Heslin

Tom Craig, Craig Morgan

*Health services and population department*

**Background:** The point prevalence for psychotic depression varies depending on the setting, with general population community settings at approximately 4 in 1000 people (0.4%) in Western Europe, with slightly higher rates for the UK at 0.5% (Ohayon M, Schatzberg A., 2002). Despite this high prevalence, psychotic depression is still relatively under researched. Here we outline a proposed study to investigate the onset, course and outcome depressive psychosis.

**Methods:** All patients with a first episode of psychosis (codes F20–29 and F30–33 in ICD–10) who presented to secondary services within tightly defined catchment areas in London and Nottingham over a 2 year period were enrolled into the study. Exclusion criteria were age under 16 years or over 65 years; evidence of psychotic symptoms precipitated by an organic cause; and transient psychotic symptoms resulting from acute intoxication as defined by ICD–10. No patient included in the study had an IQ of less than 65. Information was collected at baseline and 10-year follow-up on clinical and sociodemographic characteristics and a range of risk factors for onset and relapse.

**Results:** We will present the outline for the study as well as preliminary baseline differences in sociodemographics between patients diagnosed with psychotic depression, manic psychosis and non affective psychosis.

**Conclusions:** This study will provide the largest and most comprehensive characterisation so far of the epidemiology of depressive psychosis. This will allow us to assess whether current assumptions about the disorder are warranted and will have the potential to inform clinical practice.

**Key words:** epidemiology; psychosis; depression

## Monoamine oxidase A gene polymorphism and suicide: An association study and meta-analysis

Chi-Fa Hung

*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** Abnormalities in brain monoamine transmission have been implicated in the pathogenesis of suicidal behaviour. Studies examining the association between *monoamine oxidase A (MAOA)-uVNTR* polymorphism and suicide revealed inconsistent findings. This study aims to evaluate the possible association between the *MAOA-uVNTR* polymorphism and suicidal behaviours by examining our own subjects and conducting a meta-analytic review.

**Methods:** 373 unrelated psychiatric patients were genotyped for the *MAOA-uVNTR* polymorphism. A meta-analysis was then performed by pooling data from seven case-control association studies by random effects model.

**Results:** Our results indicate that there is no association between the *MAOA-uVNTR* polymorphism and suicide attempts in both genders. It also reveals that there is no association with violent suicide attempts. In the meta-analysis, there is no association between the polymorphism and suicidal behaviours. There is no difference in the allelic distribution between psychiatric patients with and without suicidal behaviours.

**Conclusions:** Our study is the first one to use meta-analysis in exploring the role of the *MAOA-uVNTR* polymorphism in suicidal behaviour in psychiatric patients. No significant association was found in our study, suggesting *MAOA-uVNTR* polymorphism is unlikely to contribute significantly to suicide behavior. Further studies investigating the gene-environment interaction or focusing on the genetic risk factors of endophenotypes of suicidal behaviours are warranted.

**Key words:** monoamine oxidase A (MAOA); Suicide; association study

## Distinguishing Social Anxiety from Persecutory Delusions: Testing the Aetiological Role of Interpretative Biases

Yuanyuan Huo<sup>1</sup>

Michael William Eysenck<sup>2</sup>, Jenny Yiend<sup>3</sup>

<sup>1</sup>*Department of Psychosis Studies, <sup>2</sup>Department of Psychology, Roehampton University, UK, <sup>3</sup>Department of Psychosis Studies*

**Background:** Social anxiety and persecutory delusions are highly comorbid, especially in the prodromal phase. Both are associated with cognitive biases in interpretation but this has not been systematically investigated either in terms of process or content.

**Methods:** Participants were assessed at time 1, and 6 months later, at time 2. Self-report questionnaires were used to measure their emotion traits. Three cognitive experimental tasks were used to measure interpretation biases for socially threatening information, versus paranoia relevant information.

**Results:** We anticipated that only “negatively evaluative” interpretation style would predict level of social anxiety. Conversely, only the “harmful intent” interpretation style should predict paranoia.

**Conclusions:** If the results are as expected, we will conclude that an interpretation manner that assumes “harmful intent” contributes to eliciting paranoia, whereas, interpretations biased towards “negative evaluation” are more likely to lead to social anxiety. The potential implications of these data include the development of cognitive models of paranoia, appropriate targets for cognitive-behavioural therapies, and new directions for early intervention in the prodromal phases of psychosis.

**Key words:** interpretation bias; social anxiety; paranoia

## At Risk Mental State: Prevalence and correlates among male prisoners

Manuela Jarrett

*Health services and Population Research Department*

**Aim and Objectives:** To establish feasibility of introducing the OASIS service to London male prison. To determine prevalence of At Risk Mental State (ARMS) among new receptions to the prison and to identify social, demographic and behavioural factors associated with ARMS in this population.

**Background:** Previous published literature about at risk mental states in psychosis has focused on community help seeking samples. There have been no studies examining at risk mental states among prisoners. This is despite the higher prevalence of psychosis among prisoners and the potential for early detection and treatment.

**Method:** A two phase sampling design is being used. All new receptions from court aged 35 yrs or under with no psychiatric history are screened for prodromal symptoms. Those who screened positive were asked to participate in a further assessment to establish whether they met criteria for ARMS.

**Results:** We are currently in the second year of recruitment. Over 800 prisoners have been screened and over 300 have undergone further assessments. We have found an ARMS prevalence rate of 6% and a (3%) prevalence of first episode psychosis. Funding has been obtained to establish an early detection service in the prison and this stage is currently underway.

**Conclusions:** N/A

**Key words:** early detection; psychosis; prisoners

## Marital Relationships Among Military Personnel

Mary Keeling

Nicola Fear, Simon Wessely

*Psychological Medicine; King's Centre for Military Health Research*

**Background:** Military lifestyle can have a negative impact on the personal relationships of military personnel. Research from the US indicates relationship difficulties can have a detrimental effect on military personnel's job performance and on re-enlistment. Reports from the US suggest increased marital dissolution rates since operations began in Iraq and Afghanistan. However, other US research does not support these claims. Current literature focuses on investigating the impact of deployment on relationships and has not looked at the personal relationships of military personnel more generally i.e. the distribution of marital status and satisfaction and the associated socio-demographic and military characteristics. The aim of this research was to examine UK military personnel's relationships (regardless of deployment status) and the different socio-demographic and military characteristics that are associated with relationship status and satisfaction.

**Methods:** Using data from the King's Centre for Military Health Research's (KCMHR) cohort study, relationship status and satisfaction was investigated using multinomial and logistic regression analysis.

**Results:** The majority of UK military personnel are in a relationship and satisfied with their relationship. Relationship dissatisfaction is associated with childhood adversity, being an officer, being a reserve, being married and discussing divorce or separation in the last year. Discussing divorce or separation in the last year is related to having more childhood adversity, being deployed, co-habiting or being in a long term relationship opposed to being married and not having children.

**Conclusions:** Being dissatisfied with one's relationship and leaving the relationship are not necessarily associated. This finding is discussed in relation to social exchange theory.

**Key words:** military personnel; relationships; social exchange theory



## Role of brain-specific transcription factor MYT1L in neural development

Agnieszka Kepa

Sylvane Desrivières

*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** Abnormalities in brain development and maladaptive plasticity are thought to underlay a range of neurodevelopmental and neurological disabilities and disorders, such as autism spectrum disorders, schizophrenia and learning disability. One transcription factor, the myelin transcription factor 1-like (MYT1L) gene product specifically expressed in the central nervous system, has recently been shown to be one of three factors sufficient to transform fibroblasts into neurons, suggesting a central role for this protein in neural cell function. We hypothesize that, as a transcription factor, MYT1L must interact with other proteins or protein complexes that might modulate its function to ensure that gene expression is properly controlled. The number of potential MYT1L target genes identified in our laboratory, suggest that MYT1L functions by regulating expression of genes involved neurodevelopment.

**Methods:** We aim at validating this hypothesis and identifying direct downstream targets of MYT1L. Since the fundamental steps in neural development and the MYT1L gene are highly conserved in vertebrates, we anticipate that interference with its function will result in obvious phenotypes. To understand the role of MYT1L in neuronal cell function and vertebrate brain development, we investigate the consequences of its down-regulation in vitro, using human neural stem/progenitor cell lines as a model for neural differentiation, and in the developing zebrafish, as a model for vertebrate brain development

**Results:** We report these approaches and present preliminary findings.

**Conclusions:** Further results are expected to provide a greater understanding of normal brain development and have important implications by identifying genes and pathways that might be altered in neurodevelopmental and neurological disorders.

**Key words:** MYT1L; brain development; transcription factor

## Aggressive behaviour and psychosis in a clinically referred child and adolescent sample

Farah Khalid<sup>1</sup>

Tamsin Ford<sup>2</sup>, Barbara Maughan<sup>1</sup>

<sup>1</sup>*Social, Genetic and Developmental Psychiatry Centre (MRC),*

<sup>2</sup>*Institute of Health Services Research, Peninsula Medical School, University of Exeter*

**Background:** Despite evidence of an increased risk of violence among adults suffering from psychosis, very little is currently known about the relationship between early-onset psychosis and aggressive behaviour. We aimed to identify and examine overlaps between aggressive behaviour and psychosis in a referred child and adolescent sample to assess whether potential risk factors and other associated features of this co-occurring pattern can be identified at a young age.

**Methods:** Standardized item sheet data on young people referred to the Child and Adolescent Department of the Maudsley Hospital between 1973 and 2004 were used to contrast 3 groups: 1. *Aggressive-only* (n=1346), 2. *Psychosis-only* (n=173), and 3. *Co-occurring aggression and psychosis* (n=39) on a range of comorbid symptoms and potential risk factors.

**Results:** Co-occurring cases presented with elevated rates of depersonalisation/derealisation and restlessness, and were more likely to have received past treatment compared to both psychosis-only and aggressive-only cases. Although co-occurring cases resembled the psychosis-only group in many domains including socio-demographic background and rates of emotional symptoms, they differed from 'pure' psychosis cases in having high levels of irritability, special educational needs, non-aggressive antisocial behaviours as well as increased contact with police and child care authorities.

**Conclusions:** Our findings suggest it is possible to identify early risk factors for aggression in individuals with psychosis.

**Key words:** adolescence; aggression; psychosis

## “We just don’t know how best to help” Staff experiences of Eating Disorders in UK Schools

Jodi Knightsmith

Ulrike Schmidt, Janet Treasure

*Eating Disorders Unit, Department of Psychological Medicine*

**Background:** A significant proportion of the UK’s school-aged population suffers from eating disorders. There are no current qualitative studies of UK school staff experiences of eating disorders.

**Methods:** 42 UK School-staff took part in focus groups exploring their experiences of EDs at school. The key issues highlighted by these focus groups were explored using questionnaires completed by a further 800 staff. Teachers, school nurses and pastoral staff working in UK primary, secondary and special schools participated. Responses were categorised according to focus then compiled into working papers exploring key themes highlighted by respondents.

**Results:** Key issues highlighted were:

- Eating disorders are often a taboo subject in schools
- Parents can be difficult to approach and can act as a barrier when trying to help a child
- Many staff do not have even a basic understanding about eating disorders but would like to learn
- Many schools do not have an eating disorder policy but would welcome one
- Staff are unsure how to support students suffering or recovering from eating disorders
- Reintegration of students is only successful when adequate support and guidance is given.

**Conclusions:** School staff would welcome support and training on how best to support students at risk of or suffering from eating disorders. The results of this research will be used to develop eating disorder prevention and early intervention training programmes for school staff.

**Key words:** eating disorders; qualitative study; teachers

## Why do patients with psychosis use cannabis and are they ready to change their use?

Anna Kolliakou

*Psychosis Studies*

**Background:** Many studies have drawn attention to the high levels of cannabis consumption by patients with psychosis. A variety of models have been proposed to explain co-existing substance misuse and psychosis and despite the damaging effects that persistent cannabis use can have on psychotic patients, many fail to gain from substance use treatment due to lack of motivation and drop-out.

**Methods:** MEDLINE (1950 to 2009); PsycINFO (1806 to 2009) and EMBASE (1980 to 2009) were searched. The first systematic review explored the reasons for cannabis use and the search terms used were: ‘psychosis’ and ‘reasons for cannabis, substance and drug use’. The second systematic review focused on how ready psychotic patients are to change their cannabis smoking and if their motivation could be a predictor of outcome. The following search terms were used: ‘psychosis’ and ‘readiness/motivation to change’.

**Results:** Six studies were included in the first systematic review. In the second systematic review, no studies were eligible for inclusion.

**Conclusions:** Patients smoke cannabis mostly because of its ‘enhancing’ effects, and ‘to get high’ or to reduce negative states such as depression and dysphoria. There was little support for the self-medication hypothesis. Although this hypothesis cannot be altogether dismissed due to methodological flaws in the studies, the results point more towards alleviation of dysphoria.

Motivating psychotic patients who use cannabis to commit to a process of behavioural change is difficult. The construct of readiness to change has been extensively investigated in primary substance users but whether it operates similarly in patients with co-morbid psychiatric disorders is still uncertain.

**Key words:** psychosis; cannabis use; reasons for use and readiness to change

## Quantifying Errors in the relationship between alcohol use and mortality

William Lee<sup>1</sup>

Matthew Hotopf<sup>1</sup>, Jens Skogen<sup>2</sup>, Arnstein Mykeltun<sup>2</sup>

<sup>1</sup>*Psychological Medicine*, <sup>2</sup>*Faculty of Psychology, University of Bergen*

**Background:** Since the 1920s studies have found moderate alcohol consumers to have reduced mortality compared to both heavy users and abstainers. There is concern that some or all of this effect may be because of errors: Firstly, the abstaining group has increased mortality because of other factors such as poor physical health or greater age. Secondly, the inclusion of former drinkers in the abstainer group, who may have excess risk.

**Methods:** In a British population-based cohort study carried out in 1984-5 with mortality data up to June 2009 consisting of 9003 participants, we used self-report alcohol consumption in the week before the interview, with a question about former consumption, as the exposure. Covariates were 22 factors associated with heart disease. There was complete data in 96%. The main outcome measures were cardiac and non-cardiac mortality.

**Results:** Former drinkers had greater mortality risk and the occasional drinkers had reduced mortality risk compared to the never drinkers. Adjustment for covariates abolished the excess risk borne by former drinkers. There were numerous differences between these groups. The apparent protective effect of moderate alcohol use was unaffected by correcting for confounding. Cardiac mortality was slightly reduced in all drinkers compared to lifelong abstainers. Non-cardiac mortality increased with alcohol consumption, starting slightly below that of lifelong abstainers.

**Conclusions:** We suggest that the apparent protective effect of alcohol consumption is a result of the problematic comparison with lifelong abstainers; confounders for which we were unable to correct; and/or residual confounding due to misclassification.

**Key words:** alcohol; former use; mortality

## Plasma Inflammatory Markers Correlate with Severity in Alzheimer's Disease

Rufina Leung<sup>1</sup>

Andy Simmons<sup>3</sup>, Petroula Proitsis<sup>3</sup>, Andreas Güntert<sup>1</sup>,

Deborah Kronenberg<sup>2,1</sup>, Simon J. Furney<sup>3</sup>, Megan Pritchard<sup>3</sup>, Magda Tsolaki<sup>5</sup>, Patrizia Mecocci<sup>6</sup>, Iwona Kloszewska<sup>7</sup>, Bruno Vellas<sup>8</sup>, Hilkka Soinen<sup>10</sup>, Christian Spenger<sup>11</sup>, Lars-Olaf Wahlund<sup>9</sup>, Simon Lovestone<sup>1</sup>

<sup>1</sup>*Department of Old Age Psychiatry*; <sup>2</sup>*National Institute for Health Research (NIHR), Biomedical Research Centre Guy's and St. Thomas' NHS Foundation Trust and King's College London, London, UK*; <sup>3</sup>*National Institute for Health Research (NIHR), Biomedical Research Centre for Mental Health, Institute of Psychiatry, King's College London, UK*; <sup>5</sup>*Department of Neurology, Aristotle University, Thessaloniki, Greece*; <sup>6</sup>*Section of Gerontology and Geriatrics, Department of Clinical and Experimental Medicine, University of Perugia, Perugia, Italy*; <sup>7</sup>*Department of Old Age Psychiatry & Psychotic Disorders, Medical University of Lodz, 92-216 Lodz, Poland*; <sup>8</sup>*Department of Internal and Geriatrics Medicine, Hôpitaux de Toulouse, Toulouse, France*; <sup>9</sup>*Department of Neurobiology, Care Sciences and Society, Section of Clinical Geriatrics, Karolinska Institutet, Karolinska University Hospital, Huddinge, Stockholm, Sweden*; <sup>10</sup>*Department of Neurology, Kuopio University and University Hospital, Kuopio, Finland*; <sup>11</sup>*Prodema Medical AG, Industriestrasse 6b, Postfach 51, CH 9552 Bronschhofen, Switzerland*

**Background:** Biomarkers that reflected disease severity would be immensely useful in clinical trials of disease modification therapies. Peripheral markers would be especially welcome as a complement to the imaging and CSF markers currently under investigation. As inflammation plays a critical role in AD, and the inflammatory response might be expected to worsen with disease activity and as an inflammatory signature is readily detectable in plasma and has already been suggested as a marker of AD, we reasoned that an inflammatory signature would be a good marker of disease severity.

**Methods:** A total of 428 subjects including normal elderly, MCI and AD from the AddNeuroMed study from six European countries, were included in this analysis. In all, 311 subjects including three categories were assessed at baseline (visit 1) study. The second follow up samples (AD subject only) were 12 months apart from baseline. Plasma samples were analyzed using Luminex xMAP cytokine and inflammatory protein assays. We used as measured of disease severity, cognition at the point of blood sampling using the CDR, ADAS-cog and MMSE together with volumetric MRI as a measure of brain atrophy.

**Results:** Our study identified nine inflammatory proteins correlated with brain imaging data particularly in entorhinal and left hippocampus measures. In addition, we observed nine analytes which showed significant change in both MMSE and CDR fast decliners compared to slow decliners; four of them (FGF, TNF $\alpha$ , IL-2 and IL-17) were also associated with brain imaging data.

**Conclusions:** IL-2, IL-17, TNF $\alpha$  and FGF were the stronger marker candidates out of the 23, as they overlapped two measurements. IL-1b, IL-5, IL-6, IL-8, IL-9, IL12, IL13, IL-15, GM-CSF and Eotaxin may not be as strong marker candidates as the other four cytokines, but their potential are still worth to consider as they overlapped 2 measurements.

**Key words:** Alzheimer disease; cytokines; brain imaging

## Examining factors associated with Chronic Fatigue Syndrome in adolescence

Kate Lievesley

*Psychological Medicine*

**Background:** Chronic Fatigue Syndrome (CFS/ME) is a condition characterised by physical and mental fatigue, coupled with profound disability. It is associated with a variety of physical complaints such as muscle pain, headache, sore throat and increased somnolence. This fatigue is not alleviated by rest. The aim is to investigate some of the factors hypothesized to be associated with fatigue and disability in CFS/ME in adolescents.

**Methods:** In a sample of 53 adolescents with CFS/ME (mean age 14.89) consecutively referred to a specialist CFS/ME service and 42 healthy controls (mean age 14.49), perfectionism and personality style were assessed by means of questionnaires, as well as parental rearing dimensions. Parents also completed self-report measures, including self-sacrificing behaviours, general health and perceptions of their child's quality of life.

**Results:** Adolescents with CFS/ME were significantly more perfectionist than the healthy controls ( $p = .043$ ) and scored significantly higher on the neuroticism scale ( $p = .029$ ) and lower for extraversion ( $p = .000$ ) on the personality measure. Adolescents with CFS/ME reported significantly more anxious rearing ( $p = .041$ ) and rejection ( $p = .010$ ) from mothers than the healthy controls. Parents of adolescents with CFS/ME were significantly more likely to report self-sacrificing behaviours ( $p = .001$ ), worse general health ( $p = .047$ ) and a worse quality of life for their child ( $p = .000$ ) than the parents of the healthy comparison group.

**Conclusions:** The evidence suggests that a combination of individual characteristics and perceived parenting styles are associated with CFS in adolescents. Parents of adolescents with CFS are more distressed but more self-sacrificing than parents of healthy children.

**Key words:** Chronic Fatigue Syndrome; adolescents; fatigue

## Neuronatin promotes the neural development of mouse embryonic stem cells via regulation of intracellular calcium concentration

Hsuan-Hwai Lin<sup>1</sup>

Yuh-Man Sun<sup>1</sup>, Esther Bell<sup>2</sup>, Dafe Uwanogho<sup>1</sup>, Leo Perfect<sup>1</sup>, Harun Noristani<sup>1</sup>, Thomas Bates<sup>2</sup>, Vladimir Snetkov<sup>3</sup>, Jack Price<sup>1</sup>

<sup>1</sup>Department of Neuroscience, <sup>2</sup>MRC Centre for Developmental Neurobiology, King's College London, <sup>3</sup>Department of Asthma, Allergy and Respiratory Science, King's College London

**Background:** Neural induction is the process that occurs during embryogenesis whereby ectoderm is converted into neural tissue; however the mechanisms underlying this process are not fully understood. For instance, in *Xenopus* calcium signalling is known to play a pivotal role in neural induction but whether a similar mechanism occurs in mammals is unknown. Neuronatin (Nnat), a protein involved in regulating intracellular calcium levels, is highly expressed in mouse embryos during neural induction and neurogenesis, suggesting that Nnat may play a role in these processes. The poster will describe the use of an *in vitro* mouse embryonic stem (ES) cell model to dissect the function of Nnat in neural development.

**Methods:** Nnat expression was knocked down and up-regulated in mouse ES cells and their ability to differentiate along a neural pathway analysed using immunohistochemistry. Chemicals that modulate intracellular calcium levels were used to rescue the knockdown phenotype and show the role of calcium in neural induction.

**Results:** Nnat expression was associated with the generation of neural stem cells (NSCs) from ES cells. ES cells in which Nnat expression had been knocked-down failed to generate NSCs, and subsequently neurons. In contrast, ES cells that over-expressed Nnat generated an excess of NSCs and neurons. Chemicals that inhibited the depletion of cytosolic calcium levels rescued the ability of Nnat knockdown cells to generate neural cell-types.

**Conclusions:** Nnat plays a pivotal role in neural induction and the subsequent neuronal differentiation of mammalian ES cells and this is achieved by Nnat modulating cytosolic calcium levels.

**Key words:** Nnat; embryonic stem cells; neural induction; neurogenesis; calcium concentration

## Environmental stress predicts methylation of CRHR1 but does not predict subsequent antisocial behaviour

Laura Lysenko

Chloe Wong, Sara Jaffee, Jonathon Mill, Alina Rodriguez  
*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** psychosocial stress has been shown to result in changes to future stress responses and may therefore lead to consequential behavioural changes. DNA methylation of genes, subsequently effecting their expression is a potential mechanism via which stressful events may lead to behavioural changes. We therefore aimed to test the effects of both pre-natal and childhood stress exposure on stress pathway gene methylation and on subsequent antisocial behaviour.

**Methods:** methylation patterns were determined across 3 stress pathway genes in a Swedish sample of 91 children. Prenatal-stress, environmental stress, and measures of conduct problems were obtained by maternal reports.

**Results:** environmental stress (measured at age 12) predicted methylation of CRHR1, but methylation did not predict subsequent antisocial behaviour. Pre-natal stress did predict later antisocial behaviour, but did not predict future methylation patterns in any of the 3 stress pathway genes.

**Conclusions:** children who have been exposed to higher levels of environmental stress show a greater level methylation of the CRHR1 gene. However, we found no evidence that exposure to pre-natal stress is associated with differential methylation of CRHR1, GR, or MR.

**Key words:** methylation; stress; antisocial behaviour

## The effectiveness of financial incentives for smoking cessation during pregnancy: Is it from being paid or from the extra aid?

Eleni Mantzari

Florian Vogt, Theresa Marteau

*Health Psychology Section, Department of Health Psychology*

**Background:** Financial incentives appear to be effective in promoting smoking cessation in pregnancy. The mechanisms by which they might operate however are poorly understood. The present study examines how financial incentives for smoking cessation during pregnancy may work, by exploring pregnant women's experiences of trying to stop smoking, within and outside of a financial incentives scheme.

**Methods:** Pregnant smokers (n=36) offered standard NHS Stop-Smoking Services, of whom twenty (n=20) were enrolled in a financial incentives scheme for smoking cessation (n=20) and sixteen (n=16) were not, were interviewed about (i) their motivation to stop smoking, and (ii) the factors they perceived as influencing their quitting efforts. Framework Analysis was used to analyse the data.

**Results:** Women in the two groups reported similar reasons for wanting to stop smoking during pregnancy. However, they described dissimilar experiences of the Stop-Smoking Services, which they perceived to have differentially influenced their quit attempts. Women who were incentivised reported using the services more than women who were not incentivised. In addition, they described the motivating experience of being monitored and receiving feedback on their progress. Non-incentivised women reported problems receiving the appropriate Nicotine Replacement Therapy, which they described as having a detrimental effect on their quitting efforts.

**Conclusions:** Women participating in a financial incentives scheme to stop smoking reported greater engagement with the Stop-Smoking Services, from which they described receiving more help in quitting than women who were not part of the scheme. These results highlight the complexity of financial incentives schemes and the intricacies surrounding the ways in which they operate to affect smoking cessation. These might involve influencing individuals' motivation and self-regulation, changing engagement with and provision of support services, or a combination of these.

**Key words:** financial incentives keyword; smoking cessation; pregnancy

## The validity of the Alcohol Use Disorders Identification Test ("AUDIT") to detect alcohol misuse in populations of women, and the optimum cut-off points for identification of alcohol misuse: A systematic literature review and meta-analysis

Sally Marlow

*Addictions*

**Background:** Since its introduction in 1993, the AUDIT has been used internationally as a validated method of screening for alcohol misuse. In order to take into account gender differences in alcohol problems, items in the AUDIT are sometimes modified, or its cut-off points are adjusted. However, there is little consistency in the literature, and no systematic review of the evidence to guide practice. This study aims therefore to conduct a systematic review and meta-analysis of existing research on i) the validity of the AUDIT to identify alcohol misuse in women; ii) whether the cut-off point of 8 commonly used in England has adequate sensitivity and specificity to detect alcohol misuse in women; and iii) to identify the most appropriate cut-off point.

**Methods:** The review search strategy included: (i) the original AUDIT and subsequent revisions and guidelines; (ii) electronic searches of MEDLINE, psycINFO, EMBASE, Cochrane and PubMed databases; (iii) references and hand-searching from key studies and relevant reviews. Only studies validating AUDIT against validated reference standards were considered.

**Results:** A search revealed 3212 studies, which were systematically reviewed, resulting in 11 studies meeting the criteria for the meta-analysis. AUDIT cut-off points from 2 to 15 were considered, and alcohol dependence, harmful use/abuse and hazardous use were examined individually, along with combined alcohol use disorders. Sensitivity, specificity, prevalence, positive predictive values and positive likelihood ratios were extracted and reported.

**Conclusions:** The AUDIT was found to be valid in women, but the results suggest the cut-off point of 8 for identifying alcohol problems in women may be too high. However, the results showed heterogeneity, which limited interpretation. This is discussed, and recommendations for future research are made.

**Key words:** alcohol use disorders identification test (AUDIT); women and alcohol; alcohol misuse

## Use of lentivirus-mediated gene delivery to investigate the role of the brain specific transcription factor Myt1l in vivo

Lourdes Martinez Medina<sup>1</sup>

P. Muller<sup>2</sup>, Gunter Schumann<sup>1</sup>, Sylvane Desrivieres<sup>1</sup>

<sup>1</sup>*Social, Genetic and Developmental Psychiatry Centre (MRC)*, <sup>2</sup>*Psychiatrische und Psychotherapeutische Klinik, Universitätsklinikum, Erlangen*

**Background:** The development of the brain is a process that goes throughout the life of an organism. The *Myt1l* gene, which encodes a neuron-specific transcription factor, is highly expressed in the developing brain, suggesting a crucial role in neural development. Although expression of this gene lowers after birth, it continues having a good expression through adulthood in localised areas. However, the role of this gene in neural development and associated behaviours has not been firmly established yet.

**Methods:** Different techniques aiming to decrease or increase the expression of a gene have been created to understand gene function. Gene silencing is achieved through the RNA interference (RNAi) pathway. Synthetic small hairpin RNA (shRNA) can follow this pathway and induce silencing of the target gene. Lentivirus vectors provide stable expression of shRNA in the brain because of its ability to infect differentiated cells. A reliable technique to deliver lentiviral constructs is stereotactic surgery; this approach allows manipulation of gene expression in specific brain areas. Once the gene expression is changed, the behavioural phenotype can be studied and the function of the gene can be identified.

**Results:** So far, I have found a shRNA sequence capable of efficient *Myt1l* knockdown *in vitro*. This sequence was cloned into a lentiviral vector. For *Myt1l* overexpression, I have successfully cloned the rat *Myt1l* ORF into a lentiviral expression vector. The corresponding lentiviruses for both constructs were produced and they will be used for in specific regions of the rat brain. The consequences on behaviour will be analyzed.

**Conclusions:** N/A

**Key words:** *Myt1l*; shRNA; lentivirus; rat

## The shared aetiology of ADHD symptoms and Cloninger's temperament dimensions: an adult twin study

Andrew Merwood<sup>1</sup>

Henrik Larsson<sup>2</sup>, Philip Asherson<sup>1</sup>

<sup>1</sup>*Social, Genetic and Developmental Psychiatry Centre (MRC)*, <sup>2</sup>*Department of Epidemiology & Biostatistics, Karolinska Institutet, Sweden*

**Background:** There are few quantitative genetic studies that link ADHD to other co-occurring traits in adults. This study explores the genetic and environmental overlap of ADHD symptoms with temperament dimensions, which may be important in explaining differences in the presentation of ADHD symptoms and associated comorbidities.

**Methods:** 539 adult twin pairs (mean age = 19.62 years) from the Swedish Twin study of Child and Adolescent Development (TCHAD) were included in analyses. Inattentive and hyperactive/impulsive symptoms of ADHD were measured using a DSM-IV-based ADHD rating scale. Temperament dimensions of novelty seeking (NS), harm avoidance (HA), reward dependence (RD) and persistence (PS) were measured using Cloninger's Temperament and Character Inventory. Structural equation modelling was used to estimate genetic and environmental contributions to phenotypic variance/ covariance.

**Results:** All phenotypes were moderately heritable (heritability = 34-47%). Multivariate modelling revealed significant, moderate genetic correlations of inattention with NS, HA and PS, and of hyperactivity/impulsivity with NS. There was also a strong genetic correlation between inattention and hyperactivity/impulsivity. Further examination revealed that genes shared between inattention and hyperactivity/impulsivity were important in explaining the correlation of ADHD symptoms with NS, whereas genes specific to inattention were associated with HA and PS.

**Conclusions:** Results indicate a shared aetiology for ADHD symptoms and the temperament dimensions of NS, HA and PS. Genes common to both inattention and hyperactivity/impulsivity are associated with NS, suggesting that NS may be a core component of ADHD in adults. Temperament profiles may therefore be important in explaining individual differences in ADHD symptoms.

**Key words:** ADHD; genetics; temperament

## POSTER ABSTRACTS – AFTERNOON SESSION

1

### The identification of two designer drugs, 1-benzylpiperazine (BZP) and 1-(3-chlorophenyl)piperazine (mCPP): implications for users

Mario Mifsud<sup>1</sup>

Sue Jickells<sup>2</sup>, Janet Mifsud<sup>3</sup>, Kim Wolff<sup>1</sup>

<sup>1</sup>Addictions, <sup>2</sup>SCI GRAD School, University of East Anglia, Norwich, <sup>3</sup>Clinical Pharmacology and Therapeutics, University of Malta

**Background:** This study reports on the identification of two so called ‘designer drugs’, 1-benzylpiperazine (BZP) and 1-(3-chlorophenyl)piperazine (mCPP) in seizures of illicit tablets. Seizure 1 consisted of two batches of tablets; batch 1 contained 69 diamond shaped white coloured tablets (Sample 1a) and batch 2 contained 100 round shaped white coloured tablets without logo (Sample 1b), and seizure 2 consisted of 50,579 round shaped white coloured tablets (Sample 2) with a crocodile logo.

**Methods:** The analysis involved the use of spot-tests, thin layer chromatography (TLC) and gas chromatography coupled with mass spectrometry (GC-MS) and 1H nuclear magnetic resonance (1H NMR).

**Results:** Tablets in seizure 1, Sample 1a (mean weight of 432 (4.19) mg) and Sample 1b (mean weight 448 (3.40) mg) both contained similar amounts of BZP (sample 1a mean value 206.4 (4.08) mg vs sample 1b mean value 216 (3.31) mg) representing 48.7 ±2.0% and 48.9 ±1.6% of the average content, respectively. In sample 2, GC-MS also identified the presence of CPP and the specific isomer, mCPP, was confirmed using 1H NMR. The tablets had a mean weight of 280 (4.93) mg and contained a mean value of 42.2 (8.27) mg of mCPP per tablet, forming 15.6 ±1.3% of the weight of the tablet.

**Conclusions:** Emergency departments should be aware of the current variability in content of tablets believed to contain ‘ecstasy’ (MDMA). In overdose cases, with an unexplained hyponatremic state, where MDMA is not detected in biological fluids, screening for the presence of BZP or mCPP may be worthwhile.

**Key words:** ecstasy tablets; 1-Benzylpiperazine (BZP); 1-(3-Chlorophenyl)piperazine (mCPP)

2

### Exome capture in Amyotrophic Lateral Sclerosis

Jack Miller

*Clinical Neuroscience*

**Background:** Amyotrophic Lateral Sclerosis (ALS) is inherited in a familial fashion in 10% of cases. To date, around 50% of the genetic causes of this familial form of the disease are known. Variations in two genes, *SOD1* and *c9ORF72* are accountable for 20% and ~25% of cases respectively. Importantly, other than the recently discovered intronic variation in *c9ORF72*, all other known mutations that lead to ALS are within coding regions of the genes. These protein coding regions make up 1.5% of the total genome. Therefore, this project aims to capture this portion of the genome and carry out next generation sequencing on it.

**Methods:** Exome capture is a recently developed technology that allows sequencing of ~80% of the genomic sequence of the exons. I will be using a fluid phase exon-specific oligos to obtain and hybridize only the exonic regions. The advantage of fluid phase is that there is no need for specialist equipment and it also allows a scalable work flow. After subsequent sequencing on next generation platform, the results will be subject to bioinformatic analysis in order to identify any variations in genes of interest.

**Results:** This study is ongoing.

**Conclusions:** Exome capture can be carried out at a fraction of time and cost of whole genome sequencing and has the scope to capture up to 95% of all known SNPs. The success of this technique was illustrated recently by Johnson *et al.* (2011). Any variations in genes of interest will be subject to frequency screening and biological modeling of pathogenicity.

**Key words:** ALS; exome capture; NGS



## Risk Perception, Precautionary Behaviour and Public Health Education for Tick-Borne Disease Risks

Fiona Mowbray<sup>1</sup>

Richard Amlôt<sup>2</sup>, James Rubin<sup>1</sup>

<sup>1</sup>*General Hospital Psychiatry, Psychological Medicine,*

<sup>2</sup>*Behavioural Science Research, Emergency Response Department, Health Protection Agency*

**Background:** Tick-borne disease (including Lyme disease) represents a growing problem in the UK. While some communications materials exist which encourage members of the public to adopt precautionary behaviours when in tick affected areas, these have not been informed by empirical evidence as to what factors promote uptake of protective behaviours and have not had their effectiveness formally tested. Furthermore, despite the existence of tick protective behaviours, relatively few people adopt these behaviours when in areas where ticks are known to be present. One route to encouraging the uptake of protective behaviour may be to exploit a new field of research into 'behavioural immunity'. This theory suggests that instinctive reactions to a hazard such as the emotion of disgust are there to protect us: we seek to avoid those things we find disgusting.

**Methods:** This project will identify knowledge and perceptions of risk concerning tick-borne disease among tick experts and the general public through a series of in depth interviews in order to understand the factors that influence the uptake of health protective behaviour relating to ticks. Using this information, a series of communication materials will be designed to promote the uptake of health protective behaviours. We will test the role which disgust might play in influencing tick protective behaviours by determining whether messages incorporating 'disgusting' components (e.g. images, text emphasis) can be used as an effective behaviour motivator. These materials will be tested among the UK public, first in a pilot study, and then in a randomized controlled trial.

**Results:** We have completed interviews with tick experts and members of the public who live in urban areas but are at risk of ticks through engagement in outdoor activities. The interviews have given an indication of the tick protective behaviours that experts recommend as well as what the public see as the particular drivers of these behaviours, particularly in terms of disgust factors. This allows for a comparison between recommended and practiced behaviours, as well as expert and lay views of disease risk.

**Conclusions:** Upon completion, this project will provide a set of tested messages for use in tick endemic regions across the UK allowing everyone to access the same risk communication messages and interventions. A repository of materials will also be produced to address issues associated with emerging tick-related health threats.

**Key words:** risk communication; ticks; Lyme disease; behavioural immunity

## Trait focused internet-based prevention of common mental health problems in university students

Peter Musiat<sup>1</sup>

Janet Treasure<sup>1</sup>, Andre Tylee<sup>2</sup>, Patricia Conrod<sup>3</sup>, Chris Williams<sup>4</sup>, Ulrike Schmidt<sup>1</sup>

<sup>1</sup>*Section of Eating Disorders, Division of Psychological Medicine and Psychiatry, <sup>2</sup>Health Services and Population Research Department, <sup>3</sup>Section of Addiction Biology, Division of Psychological Medicine and Psychiatry, <sup>4</sup>Mental Health and Wellbeing, Gartnavel Royal Hospital, Glasgow, Scotland, UK*

**Background:** The transition from school to university is associated with an increase in mental health problems. University students often show symptoms of depression, eating disorders, anxiety disorders or alcohol and substance abuse. Research suggests that shared personality risk factors such as high levels of perfectionism, low self-esteem, anxiety, or negative affect play an important role in the development of such problems.

**Methods:** A study in undergraduate university students investigated the association between personality risk factors and mental health problems. Students (N=240) completed personality, psychological and behavioural questionnaires. Personality questionnaires included the NEO-five factor personality inventory, the Substance User Risk Profile and the Frost Multidimensional Perfectionism Scale. Psychological and behavioural questionnaires included the Three Factor Eating Questionnaire, the IAPT phobia scales, the General Anxiety Scale, the Patient Health Questionnaire, Drinking and Eating Motives Questionnaire, the Rosenberg Self-Esteem Scale and others.

**Results:** A cluster analysis on psychological and behavioural measures revealed that students can be categorised into two clusters. Students in the first cluster (23%) showed low self-esteem, high general anxiety and depression, higher levels of drinking, uncontrolled eating and lower quality of life. The remaining students (77%) showed no symptoms for mental health problems. In terms of personality variables, students in the first cluster showed higher levels of perfectionism, neuroticism, introversion, anxiety sensitivity and hopelessness.

**Conclusions:** Students can be grouped into distinct clusters at different risk for developing mental health problems. A prevention programme, which targets the identified personality risk factors and symptoms, is now being developed.

**Key words:** prevention; internet; e-health

## Resting state functional connectivity in an executive control network in young adults who were born very preterm

Kie Woo Nam<sup>1</sup>

Matthew Allin<sup>1</sup>, Muriel Walshe<sup>1</sup>, Robin Murray<sup>1</sup>, Jonathan O'Muircheartaigh<sup>2</sup>, Chiara Nosarti<sup>1</sup>

<sup>1</sup>*Psychosis studies, <sup>2</sup>Clinical Neuroscience*

**Background:** To date, resting state functional connectivity (RSFC) following very preterm birth has been studied in infants. However, alterations in RSFC have been found in developmental disorders such as autism and attention deficit hyperactivity disorder. The present study investigated RSFC within an executive control network (ECN) in preterm born adults, prompted by the observed deficits in executive functions following preterm birth. We hypothesised that RSFC within the ECN would be altered in preterm born adults compared to age-matched controls.

**Methods:** RSFC was assessed in 10 preterm born adults and 13 controls (age range 26-28). Several networks were identified via independent component analysis, as implemented in FMRIB's Software Library MELODIC. Dual regression analysis was performed within an ECN in order to compare differences in RSFC between preterm born adults and controls.

**Results:** Within the ECN, preterm born adults showed decreased RSFC compared to controls predominantly between frontal pole, superior and inferior frontal gyri, and middle and inferior temporal gyri. Preterm born adults also displayed increased RSFC between prefrontal regions, basal ganglia and cerebellum.

**Conclusions:** RSFC in ECN in preterm born adults shows several alterations compared to controls. These alterations may partly explain the deficits in executive processing often observed in very preterm born samples. The observed decreases and increases between key nodes of an ECN in preterm born adults further reflect underlying processes of neural plasticity, which have a significant role in recovery after neuronal insult.

**Key words:** preterm; executive control network; independent component analysis

## The Impact of Migration and Stressful Life Events on Women's Mental Health and Quality of Life

Laura Nellums<sup>1</sup>

Stephani Hatch<sup>2</sup>, Louise M Howard<sup>1</sup>

<sup>1</sup>Section for Women's Mental Health, Health Services and Population Research Department, <sup>2</sup>Department of Psychological Medicine

**Background:** Stressful life events are risk factors for common mental disorders. Women experience higher rates of common mental disorders than men, and there is inconsistent evidence on whether migrants experience a higher prevalence than non-migrants. This mixed-methods study aims to investigate the impact of migration and stressful life events on mental health outcomes in first generation immigrant women in London compared with women born in the UK.

**Methods:** Study 1: Analysis of data from a cross-sectional survey, the National Institute for Health Research-funded Specialist Biomedical Research Centre for Mental Health South East London Community Health Study (SELCoH Study), comparing mental health outcomes in migrant and non-migrant women.

Study 2: Thematic analysis of data from interviews with migrant and non-migrant women recruited from community organizations and the SELCoH Study, exploring what events affect mental health and quality of life.

**Results:** Study 1: The SELCOH Study included 391 migrant and 553 non-migrant women. Preliminary analysis found common mental disorders in 29.5% (95% CI 24.8 – 34.6) of migrants and 28.6% (95% CI 24.9 – 32.6) of non-migrants (OR 1.05; 95% CI 0.78 – 1.41). Study 2: 27 qualitative interviews have been conducted. Preliminary analysis indicates migrant women find separation from family and lack of agency worsen their mental health and quality of life. Variables promoting resilience are being explored.

**Conclusions:** There is no evidence of a difference in the prevalence of common mental disorders in migrant compared with non-migrant women in South East London. Reasons for this are being explored.

**Key words:** mental health; life event; migration

## The Molecular Relationship Between TDP-43 and Tau Pathology

Michael Niblock

Jean-Marc Gallo

*MRC Centre for Neurodegeneration, Clinical Neuroscience*

**Background:** At present there are very limited treatment options for sufferers of dementia and with an aging population in the developed world, the cost burden for dementia patient care is projected to become a serious problem for the future. The biological correlate of the cognitive deficits seen in many dementias including Alzheimer's disease (AD) is the accumulation of abnormal intracellular filaments formed by the microtubule associated protein tau (MAPT) into tangles. Tau positive neuropathological cases are collectively called tauopathies. In addition to tau pathology, TAR DNA-binding protein (TDP-43) inclusions have been found in 20-50% of AD cases as well as other tauopathies. TDP-43 is a predominately nuclear protein that binds to both DNA and RNA and has a major role in regulating gene expression by modulating transcription, RNA stability and micro-RNA biogenesis via its role in the Drosha complex. It also forms a complex with other splicing factors including CUGBP1, FUS and hnRNP proteins and plays a role in regulating splicing of RNA targets. The cytoplasmic TDP-43 inclusions in post-mortem human brain result in a reduction of nuclear TDP-43 suggesting that the presence of cytoplasmic TDP-43 inclusions will result in a loss of its nuclear function, impairing TDP-43 role in gene expression and pre-mRNA splicing. One of the major questions we are investigating in this project is the contribution of TDP-43 misregulation in triggering or exacerbating tau pathology.

**Methods:** RT-PCR

**Results:** The aim of the project is to correlate TDP-43 pathology with altered RNA splicing and transcription levels in AD post-mortem brain tissue. We have found that exon 10 inclusion of the MAPT gene is increased in AD cases compared to controls and we are correlating the data to assess the role of TDP-43 misregulation in these cases. We are currently quantifying expression ratios of other alternative splicing isoforms of MAPT (exons 2 and 3) as well as measuring tau expression levels by qRT-PCR.

**Conclusions:** N/A

**Key words:** TDP-43; Tau; alternative splicing

## Validating exogenous labels for cell transplantation

Francesca Nicholls<sup>1</sup>

Ellen Bible<sup>1</sup>, Lara Stevanato<sup>2</sup>, Dafe Uwanogho<sup>1</sup>, Caroline Hicks<sup>2</sup>, Christos Tolia<sup>3</sup>, Brenda Williams<sup>1</sup> and Mike Modo<sup>4</sup>

<sup>1</sup>Department of Neuroscience, <sup>2</sup>ReNeuron Ltd, Guildford, UK, <sup>3</sup>King's College Hospital, Department of Neurosurgery, London, UK, <sup>4</sup>University of Pittsburgh, Department of Radiology & McGowan Institute for Regenerative Medicine, Pittsburgh, PA

**Background:** Post-mortem evaluation relies on the ability to identify transplanted cells within the brain weeks and potentially years after transplantation. Exogenous labels are often used for histological detection of cells using fluorescence, but their reliability to identify transplanted cells is potentially compromised due to label transfer from grafted to host cells. Additionally, characteristics of labeled cells may be altered, potentially affecting their therapeutic efficacy.

**Methods:** Human neural stem cells (hNSC) were labeled with Hoechst, BrdU, PKH26 or eGFP, and assessed *in vitro* to analyze label efficiency, and effects on cell viability and phenotype. To establish temporal evolution of the reliability of these labels *in vivo*, hNSC were grafted into rat striatum and histological analyses were conducted after 1, 7, 28 and 64 days. The label was assessed on the extent to which it co-localized with specific endogenous markers of human cells, such as human nuclear antigen (HNA).

**Results:** Hoechst, eGFP and PKH26 efficiently labeled cells, with BrdU being lowest, at ~90%. All four labels affected cell proliferation. BrdU labeling was generally co-localized with HNA, although at day 7, there were also many HNA-/BrdU+ cells, suggesting label transfer to host cells, and thereby a potential overestimation of transplanted cells. However, at 64 days, the presence of HNA+/BrdU- cells suggests an underestimation of transplanted cell number.

**Conclusions:** All labels tested had some effect on cells *in vitro*, showing the importance of conducting such tests prior to using any label for *in vivo* experiments. BrdU's reliability *in vivo* was shown to be dependent on the time point.

**Key words:** transplantation; cell labeling

## Life events in Conversion Disorder: timing and nature of psychological precipitants

Tim Nicholson

Selma Aybek, Tom Craig, Anthony David, Richard Kanaan  
*Section of Cognitive Neuropsychiatry, Department of Psychosis studies*

**Background:** Current models of conversion disorder propose psychological stressors ("life events") are present around the time of symptom onset are "converted" into physical symptoms. Freudian models further hypothesise that the resulting disability will allow "escape" from the stressor (reducing its severity) and that it can be "repressed" from consciousness (i.e. its significance or severity is not acknowledged by the patient).

**Methods:** 25 patients with motor conversion disorder within 2 years were assessed for the presence of preceding psychological stressors using the Life Events and Difficulties Schedule and compared to 13 age and sex matched healthy controls. Stressors were rated by a consensus panel, blind to clinical status, rating for; 1. Temporal relationship of the event to symptom onset; 2. Potential for avoiding unwanted circumstances ("escape") and 3. Relative under-reporting of the severity of the event by the patient compared to contextual ratings ("repression").

**Results:** Conversion disorder patients had significantly more severe events in the 3 months, particularly the last month, before symptom onset compared to controls. An "escape" event was found more frequently in patients than controls. There was no increase in repressed events in patients compared to controls.

**Conclusions:** This study provides evidence for a causal association between stressful life events and Conversion disorder and that the time frame (within 3 months) and the nature ("escape") of events may play an important role in Conversion disorder onset. There is therefore evidence to support the psychological model of Conversion disorder and for Freud's theory of "escape" (but not for his theory of repression).

**Key words:** conversion disorder; psychology; aetiology

## Extracting the high frequencies from the EEG

Judith Nottage<sup>1</sup>

Dominic ffytche<sup>3</sup>, Elvira Bramon-Bosch<sup>2</sup>, Paul Morrison<sup>4</sup>

<sup>1</sup>*Neuroimaging*, <sup>2</sup>*Psychosis Studies*, <sup>3</sup>*Old Age Psychiatry*,

<sup>4</sup>*Psychological Medicine*

**Background:** There has been considerable interest in the gamma band (30-100 Hz) of brain oscillations, since it has been shown to be associated with attention and active brain processing. However there are problems in extracting gamma from the scalp electroencephalograph (EEG) due to interference from electrical activity generated by muscles.

**Methods:** Methods have been developed to reduce the effects of power-line noise, extra-ocular muscle activity and scalp muscle tension.

**Results:** Neuronal gamma was detectable in both motor and visual tasks.

**Conclusions:** Neuronal gamma is detectable in the scalp EEG provided the artifacts are dealt with. This makes it possible to investigate the high frequencies of the EEG in psychiatric and pharmacological research.

**Key words:** EEG; gamma

## MAOA genotype protects against hyperactivity through the inhibition of caudate activity during reward anticipation

Charlotte Nymberg

Eva Loth, Gunter Schumann

*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** MAOA genotype is frequently implicated in the development of Attention Deficit Hyperactivity Disorder (ADHD). However, few studies have investigated the neurobiological mechanisms which mediate this effect. Firstly, this study aimed to identify whether MAOA genotype has a neurobiological effect on the processing of reward anticipation. Secondly, we aimed to identify whether these brain structures mediated hyperactivity.

**Methods:** To test the hypothesis that brain regions modulated by MAOA genotype mediate hyperactivity we used a gene-neuroimaging approach in 366 13-14-year old adolescents (206 girls). We examined whether a common MAOA polymorphism, rs12843268 (G/A) affected brain activation during reward anticipation as measured during the monetary incentive delay task (MID). Brain regions identified to modulate reward anticipation – in this case the caudate – were linked with hyperactivity-scores.

**Results:** We found robust genotype effects of rs12843268 on brain function and behaviour. Minor allele carriers showed significantly lower caudate activation during reward anticipation than major allele homozygotes and had significantly fewer hyperactivity symptoms compared to major allele homozygotes. Furthermore, in boys carrying the rs12843268 minor allele we found a negative association between caudate activation and hyperactivity symptoms, suggesting that the potentially protective effect of the rs12843268A allele for hyperactivity may be mediated by caudate activation.

**Conclusions:** Together, our findings describe a neurobiological mechanism by which MAOA protects against hyperactivity symptoms in boys.

**Key words:** hyperactivity; monoamine Oxidase A (MAOA); caudate

## Anorexia nervosa and the motivation to restrict food intake: the effects of acute dopamine precursor depletion

Caitlin O'Hara

*Eating Disorders, Department of Psychological Medicine*

**Background:** Several behaviours associated with anorexia nervosa (AN) (e.g., food restriction, exercise, and weight loss) have been hypothesised to be highly salient and rewarding for these people. Central to understanding the aetiology and maintenance of AN is the identification of mechanisms that underpin its pathology. Recent evidence suggests that alterations in brain dopamine (DA) function are important in the development of AN and may be involved in the association of illness-specific features with increased motivational value. Aberrant reward processing in AN may therefore represent an important maintaining factor to be targeted by future treatments.

**Methods:** This study will test the hypothesis that DA is involved in maintaining the perceived salience of AN-specific cues (e.g. thinness, low-calorie foods) and in the willingness to sustain effort in AN-specific behaviours (e.g., exercise, food restriction). A series of behavioural experiments will be conducted to investigate the role of DA in the perceived salience of AN-specific cues and behaviours. Specifically, the effects of DA depletion on the attention attributed to these stimuli will be measured using a startle eye-blink modulation task, a progressive ratio breakpoint task, and a food challenge task. Dopamine synthesis will be transiently decreased using the acute phenylalanine/tyrosine depletion method. Participants include individuals who are either ill with AN, recovered from AN, or healthy controls.

**Results:** Ethical approval has been sought (REC reference: 11/LO/1082). Recruitment will start in October 2011.

**Conclusions:** Findings will advance understanding of the role of motivational processes in the development of AN and extend current concepts related to mechanisms that maintain its symptoms.

**Key words:** anorexia nervosa; dopamine; reward

## Major depressive disorder in pregnancy and the hypothalamic-pituitary-adrenal axis.

Sarah Osborne

S.J. Pawlby, S. Conroy, P. Zunszain, C.M. Pariante

*Perinatal Psychiatry and Stress, Psychiatry and Immunology, Psychological Medicine*

**Background:** Antenatal depression is common and is associated with increased risk of preterm birth. The hypothalamic-pituitary-adrenal (HPA) axis, the hormonal stress system, both plays a critical role in timing of delivery and has consistently been shown to be overactive in major depressive disorder (MDD) outside of pregnancy. We hypothesized that antenatal depression would be associated with HPA axis overactivity and shortened gestational length. We compared cortisol levels and length of gestation in depressed and non-depressed pregnant women.

**Methods:** A prospective study of pregnant women aged 20-40. Cases with MDD (n=11) and controls without history of psychiatric disorder (n=32). Exclusion criteria were obstetric complications, chronic medical conditions or taking medication. Assessment of maternal mood was performed at 25 weeks gestation, and saliva cortisol measured at awakening and in the evening on two consecutive days at 32 weeks gestation. Gestational length was recorded. Groups were compared for average morning and evening cortisol and gestational length.

**Results:** Compared with healthy women, the MDD group had statistically significant higher average evening salivary cortisol levels at 32 weeks gestation (control (n=30) mean rank, 17.47; depressed (n=8) mean rank, 27.13;  $p = 0.029$ ). There was no group difference in gestational length.

**Conclusions:** Our findings mirror the pattern of cortisol secretion frequently found in MDD outside of pregnancy and replicate recently published data. Although there was no difference in gestational length between the two groups in our study, the sample size was small. These results demonstrate a link between depression and altered pregnancy biology which may connect depression and shortened gestational length.

**Key words:** depression; pregnancy; HPA axis

## Imagery Rescripting For Obsessive Compulsive Disorder: A Pilot Study

Nicholas Page

David Veale, Paul Salkovskis

*Psychology*

**Background:** As part of a wider study into treatment adjuncts for Cognitive Behavioural Therapy for Obsessive Compulsive Disorder (OCD), Imagery Rescripting as an experimental treatment adjunct was investigated for its efficacy in addressing Obsessive Compulsive symptomology. The presentation will include an overview of the pilot study before presenting some clinical detail from the cases involved.

**Methods:** The study aimed to establish whether Imagery Rescripting could be an effective intervention for OCD. 3 participants were involved in a randomised case series. All participants were first involved in a semi-structured interview to establish imagery phenomenology and then randomized to 7, 14, 21 or 28 days where they received the imagery intervention session. All participants had a placebo session 7 days prior to the imagery intervention. Outcomes were measured by idiosyncratic daily measures, weekly self-report measures and a weekly Y-BOCS clinician administered questionnaire. The subjects presented here in more detail received an Imagery Rescripting session similar to that outlined in Arntz's Treatment of Childhood Memories (1999).

**Results:** The cases detailed in the presentation showed significant improvements on many of the measures following the Imagery Rescripting.

**Conclusions:** Imagery interventions show promise as treatment adjuncts to Cognitive Behavioural Therapy as usual for OCD and could be particularly useful in treatment resistant OCD. They are entirely consistent and therefore compatible with the Salkovskis (1999) model for OCD.

**Key words:** obsessive compulsive disorder (OCD); Cognitive Behavioural Therapy; imagery

## The Genetics of Metabolic Syndrome in Schizophrenia

Evangelos Papanastasiou<sup>1</sup>

Shubulade Smith<sup>1</sup>, Evangelos Vassos<sup>2</sup>, Fiona Gaughran<sup>3</sup>

<sup>1</sup>*Department of Forensic and Neurodevelopmental Sciences,*

<sup>2</sup>*Social, Genetic and Developmental Psychiatry Centre (MRC),*

<sup>3</sup>*Department of Psychosis Studies*

**Background:** Schizophrenia is associated with a variety of physical manifestations (i.e. metabolic, neurological) and although psychotropic medication is blamed for some of these (in particular obesity and diabetes), there is evidence that schizophrenia itself confers an increased risk of physical disease and early death. Metabolic syndrome (MetS), is excessively presented among patients with schizophrenia and has been associated with a variety of intrinsic and extrinsic factors. Genetic analysis has revealed a number of genetic loci (single nucleotide polymorphisms, SNPs) associated with each of the major components of metabolic syndrome, namely obesity, dyslipidaemia, hypertension and diabetes. We will perform a prospective observational study in a group of first onset schizophrenia patients, and a cross sectional observation study in a second group of chronic schizophrenia patients. We will ascertain whether their genetic profile, based on SNPs associated with various components of the MetS, can predict the development of the syndrome during a year in the initial phase of their illness or the existence of the syndrome at an advanced stage of the course of the illness. Metabolic syndrome (MetS), a constellation of hypertension, dyslipidaemia, glucose intolerance and central obesity (International Diabetes Federation, IDF, 2006), is excessively presented among patients with schizophrenia and has been associated with a variety of intrinsic and extrinsic factors. Numerous Genome Wide Association Studies (GWAS) have identified various Single Nucleotide Polymorphisms (SNPs) associated with all the components of metabolic syndrome

**Methods:** Study 1, Prospective case-control study: a cohort of 200 patients with first episode schizophrenia (onset of psychotic illness within one year of entry to the study) will be compared with 200 people of similar age, sex and ethnicity who do not have schizophrenia. Data will be collected retrospectively (before the onset of antipsychotic medication, at baseline and at 12 month follow up). *In this study we aim to examine whether genes can predict that patients with a first episode of schizophrenia will develop MetS.* Study 2, Observational cross-sectional study: a study of 200 patients with chronic schizophrenia (>10 years of illness), measured at one time-point at an advanced stage

of their illness. Those with metabolic syndrome will be compared with those without metabolic syndrome to see if genetic markers for MetS can help to distinguish between the groups. *In this study we aim to examine whether genes can establish that patients with chronic schizophrenia have developed MetS.*

**Results:** not available yet

**Conclusions:** N/A

**Key words:** schizophrenia; metabolic syndrome; genetics

## Prenatal Tobacco Exposure and Intrauterine Growth: A Gene-Environment-Wide Interaction Study of Foetal Genetic Modifiers

Jennifer T. Pararajasingham

Thomas S. Price, Robert Plomin

*Statistical Genetics, Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** In developed countries, the effect of smoking during pregnancy (SDP) has been identified as the single strongest preventative risk factor for restricted foetal growth. In this study, an agnostic gene-environment-wide interaction (GEWI) analysis was carried out, aiming to test the hypothesis that foetal genotype modifies the effect of intrauterine tobacco smoke exposure to restrict foetal growth.

**Methods:** *Data:* The Twins Early Development Study (TEDS) is a large-scale longitudinal study of twins from early childhood through adolescence. The twins were identified from birth records of twins in the UK in 1994-96. In this study, 2800 individuals (1 twin per family) were analysed. *Measures:* The outcome of primary interest was birth weight ratio, defined as birthweight standardised for gestational age, sex and zygosity. The primary environmental exposure was SDP. *Analysis:* Gene-Smoking interactions were tested using linear models that included terms for: SDP; foetal genotype; foetal genotype-SDP interaction, and various covariates.

**Results:** No foetal genotype-SDP interactions obtained p-values of less than  $1e-6$ , indicating the results were consistent with random chance; no foetal genotypes were identified as having an interactive effect with genome-wide significance.

**Conclusions:** As expected, larger datasets are required in order to identify foetal genotype\*SDP interactions in such GEWI studies. With this in mind, the next step in this study is to perform a meta-analysis that integrates the TEDS results with results from other studies.

**Key words:** GWAS keyword; gene-environment interactions



## Measures of global DNA methylation in post-mortem Alzheimer's disease brain

Yogen Patel<sup>1</sup>

Jon Mill<sup>2</sup>, John Powell<sup>1</sup>

<sup>1</sup>MRC Centre for Neurodegeneration Research, <sup>2</sup>Social, Genetic and Developmental Psychiatry Centre (MRC)

**Background:** A role for epigenetics in the complex aetiology of the neurodegenerative disease Alzheimer's disease (AD) has been proposed. The most studied epigenetic mark is DNA methylation (the addition of methyl groups to cytosine located in CpG dinucleotides) and is known to change over time with aging and may also reflect more subtle changes in gene expression.

**Methods:** Global DNA methylation by ELISA (Enzyme-Linked ImmunoSorbent Assay) based assays and global methylation status of DNA repetitive elements (Alu and LINE1) by Pyrosequencing at CpG dinucleotides in post-mortem brains of AD cases and controls (20 AD cases and 20 controls).

**Results:** Preliminary results from comparing affected (Superior Temporal Gyrus) and unaffected (Visual Cortex) areas of AD brain and age-matched cognitively normal controls show a trend for a decline in global methylation and a significant decline at LINE1 CpGs in both affected and unaffected tissue.

**Conclusions:** These changes in global methylation may reflect changes in tissue composition as a consequence of the neurodegenerative process and/or an affect of the oxidative and the inflammatory processes active in the degenerating Alzheimer's brain.

**Key words:** Alzheimer's; DNA methylation; post-mortem brain

## Working memory in postpartum psychosis (PP)

Astrid Pauls<sup>1</sup>

Mitul A Mehta<sup>2</sup>, Owen G O'Daly<sup>2</sup>, Susan Pawlby<sup>3</sup>, Costanza Vecchio<sup>3</sup>, Sridevi Singh<sup>1</sup>, Gertrude Seneviratne<sup>4</sup>, Michael Marsh<sup>5</sup>, Carmine M Pariante<sup>3</sup>, Steven CR Williams<sup>2</sup>, Paola Dazzan<sup>1</sup>

<sup>1</sup>Psychosis Studies, <sup>2</sup>Department of Neuroimaging, <sup>3</sup>Department of Psychological Medicine, <sup>4</sup>Bethlem Royal Hospital London, <sup>5</sup>King's College Hospital London

**Background:** Working memory is impaired in those at risk of or suffering from psychosis unrelated to childbirth (Bora, 2008) which is accompanied by functional brain changes (Fusar-Poli, 2011). In contrast, there is paucity of knowledge about working memory function in women at risk of PP (i.e. women diagnosed with bipolar or schizoaffective disorder, a previous episode of or family history of PP).

**Methods:** 17 women at risk, of which 6 had a recent episode of PP and 9 healthy women were scanned on average 15 weeks postpartum, SD 10 (range 4-43 weeks) while performing an n-back working memory task. Images were acquired on a 3T GE HDx System (TR/TE=2000/30). Data were analysed in SPM8. The n-back task, lasting 6:20 minutes with 180 stimuli and an inter-stimulus interval of 2 seconds, required responses to a series of letter stimuli when they matched a target (control) or the stimulus presented 1-, 2- or 3-back.

**Results:** Patients were able to perform the task with the expected linear effect of task difficulty across all three groups on accuracy  $F_{1,22} = 19.16$   $p < .0001$  and reaction time  $F_{1,22} = 5.5$ ,  $p = .007$ . No significant group differences for task performance, reaction times or brain activation were found.

**Conclusions:** Women at risk of or with a recent PP do not show impairment in working memory compared to healthy controls. These preliminary results differ from those found in other psychoses, suggesting that women at risk of postpartum psychosis do not carry a psychosis-vulnerability indicator such as working memory impairments.

**Key words:** postpartum psychosis; working memory; FMRI

## Monoallelic gene expression in human neural stem cells

Leo Perfect

Jack Price, Aaron Jeffries

*Neuroscience*

**Background:** Monoallelic (MA) expression is well described in phenomena such as imprinting and X-inactivation. Recently, it has been demonstrated that the less well characterised autosomal stochastic MA expression occurs on a large scale in human B-lymphoblastoid cells (Gimelbrant et al., 2007). We sought to determine the extent to which this process happens in clonal human neural stem cells, and by extension the developing human brain.

**Methods:** A microarray based approach was used for genome-wide detection of MA expression. In vitro tissue culture techniques and single nucleotide primer extension were used for differentiation studies and validation. Quantitative PCR was utilised to assess transcript levels.

**Results:** We first demonstrate that widespread MA expression occurs on the autosome in human clonal neural stem cells. A large proportion of this was apparently stochastic, but we also discovered evidence for novel imprinted genes. In the genes investigated, MA status was maintained after differentiation into mature neurons and glia. There appears to be no global relationship between allele imbalance and transcript levels, although several known haploinsufficient genes were found to be subject to stochastic MA expression. The predicted imprinted genes are currently being followed up.

**Conclusions:** The adult CNS may be a mosaic of clones of cells, each with a different pattern of MA expressed genes. Surprisingly, there appears to be no global correlation between allele imbalance and mRNA levels. However, widespread MA expression could still have a functional impact by exposing functionally different protein variants or by unmasking recessive deleterious mutations.

**Key words:** Monoallelic; imprinting

## Systematic review of screening tools and procedures to identify hazardous drinking and alcohol use disorders in adult attendees in emergency departments (ED)

Thomas Phillips<sup>1</sup>

Simon Coulton<sup>2</sup>, Colin Drummond<sup>1</sup>

<sup>1</sup>*Section of Alcohol Research, Addictions Department, <sup>2</sup>Centre for Health Service Studies, University of Kent, Canterbury, UK*

**Background:** This systematic review aims to compare the diagnostic accuracy of screening tools and procedures in identifying hazardous drinking and alcohol use disorders amongst adult attendees of ED.

**Methods:** The search strategy identified studies that recruited adults from English speaking countries receiving  $\geq 1$  screening procedure compared to a validated reference standard. OVIDSP was searched along with hand-searching key journals and checking reference lists from key citations. Data was extracted to examine sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV). RevMan (v5.1) was used to calculate confidence intervals, and plot forest and summary receiver operator characteristic (SROC).

**Results:** 3,264 citations were identified, with 96% (3,168) being excluded following review of titles/abstracts. 96 papers were reviewed and 8 were included in the review. Multiple reference standards were employed: hazardous drinking, harmful drinking/alcohol abuse, alcohol dependence, and combined categories. Of the eight tests examined to identify harmful drinking/alcohol abuse AUDIT, RAPS and TWEAK show acceptable sensitivity and specificity, with AUDIT having higher PPV scores. Nine tests were assessed to identify alcohol dependence with acceptable sensitivity and specificity being found in AUDIT, CAGE, RAPS, RAPS-4 & TWEAK, with AUDIT, CAGE & RAPS-4 having higher and similar PPV scores. When procedures were compared to harmful drinking/alcohol abuse or alcohol dependence AUDIT performed better than other measures. When short-form tools CAGE, FAST, PAT and SASQ were examined compared to a standard of AUDIT  $\geq 8$ , FAST outperformed all other tests on sensitivity, specificity and PPV.

**Conclusions:** Caution needs to be applied to these results due to the limited number of studies and different reference standards used. These results differ from previous reviews in identifying AUDIT as consistently performing well across diagnostic categories and amongst the short-form tools FAST outperformed other tests.

**Key words:** alcohol misuse; screening; emergency departments

## Dissociation in individuals diagnosed with Dissociative Seizures (DS): a study of psychological and somatoform symptoms relative to a healthy control group.

Susannah Pick<sup>1</sup>

Dr John Mellers<sup>2</sup>, Prof Laura Goldstein<sup>1</sup>

<sup>1</sup>*Department of Psychology, <sup>2</sup>Neuropsychiatry Department, Maudsley Hospital, South London and Maudsley NHS Foundation Trust*

**Background:** Dissociative Seizures (DS) are episodic alterations in behaviour and awareness, resembling epilepsy, but lacking concomitant electrophysiological discharges. This study will further characterise the types of dissociative symptoms reported by DS patients, using a multidimensional measure of psychological dissociation (Multiscale Dissociation Inventory, MDI; Briere, 2002) and a standardised somatisation scale (Somatoform Dissociation Questionnaire-20, SDQ-20; Nijenhuis et al., 1996). It tests the prediction that DS patients will have higher total MDI and SDQ scores than healthy controls.

**Methods:** This cross-sectional study will compare 40 DS patients and 40 healthy controls. Data collection is ongoing (DS, n = 24; Controls, n = 28). The MDI yields six subscale scores (Depersonalisation, Derealisation, Disengagement, Emotional Constriction, Memory Disturbance, Identity Dissociation). The SDQ-20 provides a single score indicating current somatisation. The Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) assesses current mood. Statistical analyses using SPSS v18 included an ANCOVA for the SDQ-20, and a MANCOVA for the MDI.

**Results:** The two groups are currently well matched for age, gender, and IQ. After controlling for the effects of anxiety and depression, the DS group had higher subscale scores on the MDI ( $p < .01$ ) except for Identity Dissociation. The DS group also showed significantly elevated SDQ scores ( $p < .001$ ). These data are preliminary only.

**Conclusions:** The initial analyses indicate that DS patients report higher levels of both psychological and somatoform dissociation than controls, independently of depression and anxiety scores. However, this group appear to retain basic integrity to their sense of self and identity.

**Key words:** seizures; dissociation; somatisation

## The separation of ADHD inattention and hyperactivity-impulsivity symptoms: specific pathways from genes to cognitive impairments and symptoms

Rebecca Pinto<sup>1</sup>

Jonna Kuntsi<sup>1</sup>, Nick Illot, Thomas S. Price<sup>1</sup>, Jaap van der Meere<sup>2</sup>, Alexis C. Wood<sup>1,3</sup>, Philip Asherson<sup>1</sup>

<sup>1</sup>*Social, Genetic and Developmental Psychiatry Centre (MRC), <sup>2</sup>University of Groningen, Department of Clinical and Developmental Neuropsychology, the Netherlands, <sup>3</sup>University of Alabama at Birmingham, Department of Epidemiology and Section on Statistical Genetics, USA*

**Background:** Both shared and unique genetic risk factors underlie the two ADHD symptom domains of inattention and hyperactivity-impulsivity. We aimed to determine, using multivariate genetic model fitting and molecular genetics approaches, whether separable pathways from genetic risk factors to cognitive impairments underlie inattention and hyperactivity-impulsivity symptoms.

**Methods:** A population twin sample of 1314 children was assessed on a 4-choice reaction time task and a go/no-go inhibition task.

**Results:** Inattention showed substantial genetic overlap with reaction time variability (RTV), compared to hyperactivity-impulsivity. Both inattention and RTV were associated with the 5HT2A gene (rs7322347), with significant evidence for mediation. Hyperactivity-impulsivity and inattention showed low, but equal sized genetic correlations with commission errors (CE). Hyperactivity-impulsivity, inattention and CE were associated with rs3785157 in the SLC6A2 gene, with evidence for mediation.

**Conclusions:** We obtained evidence for separable pathways from genetic risk factors to specific cognitive impairments and behavioural symptom domains. Overall, the findings extend a previous model of two familial cognitive impairment factors in combined subtype ADHD to separate pathways underlying inattention and hyperactivity-impulsivity symptoms and to specific genetic risk variants.

**Key words:** ADHD; genetic mediation; cognitive impairments

## Maternal Childhood Trauma Predicts Maternal Psychopathology In Pregnancy And Offspring Outcome At 11 Years

Dominic T. Plant

Carmine M. Pariante, Susan Pawlby

*Sections of Perinatal Psychiatry and Stress, Psychiatry and Immunology*

**Background:** Experience of childhood abuse and neglect elevates risk for mood disorders in later life. Maternal psychopathology during pregnancy has been identified as a key risk factor for childhood maltreatment and adolescent depression. The purpose of this study was to investigate maternal history of childhood trauma as a risk factor for offspring maltreatment and psychopathology.

**Methods:** Information on maternal history of childhood trauma, maternal antepartum depression, offspring maltreatment and offspring childhood emotional problems was collected from a South London community-sample of 207 mother-infant dyads, who were followed prospectively from gestation to 11 years.

**Results:** Maternal history of childhood trauma significantly predicted offspring childhood maltreatment ( $p = .0003$ ), childhood emotional problems ( $p = 0.001$ ) and maternal antepartum depression ( $p < 0.001$ ). Antepartum depression moderated the effects of maternal childhood trauma on offspring maltreatment and offspring psychopathology, whereby children whose mothers had a history of childhood trauma *and* who experienced antepartum depression, had significantly more reports of childhood maltreatment ( $p = 0.001$ ) and significantly more emotional problems ( $p = 0.001$ ), compared to children whose mothers did not have a history of childhood trauma *and* did not have antepartum depression

**Conclusions:** Children exposed to both maternal risk factors are at the greatest risk. Clinicians should endeavour to screen for a history of childhood trauma in early pregnancy in order to identify and support those women who may be at an elevated risk for mood disorders in the perinatal period.

**Key words:** antepartum depression; maltreatment; longitudinal study

## The effects of early stressful life events on gene expression in the brain

Timothy R. Powell

Cathy Fernandes, Rachel Kember, Jonathan Mill,

Leonard C. Schalkwyk

*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** Gene-environment interaction (GxE) studies have shown that the existence of susceptibility genes (G) in the presence of early life stress (E) increases the chances of developing psychiatric illness in adulthood. The current study aimed to investigate the effects of early life stress on genome-wide expression in two key areas of the brain involved in stress and depression, the hypothalamus and hippocampus.

**Methods:** A maternal separation paradigm in two inbred strains of mice, C57BL/6J and DBA/2J, was used to model early life stress in humans. Our aim was to determine whether different genetic backgrounds (G) in the presence of the same early life stress (E) showed differential gene expression (GxE) in the two key brain regions. Mice were assigned to either a control ( $n=10$  C57BL/6J,  $n=13$  DBA/2J) or separated group ( $n=9$  C57BL/6J,  $n=10$  DBA/2J). Separated groups underwent maternal separation at postnatal day 9 for 24 hours, and separated and controls underwent culling at week 15. The hippocampus and hypothalamus were dissected and RNA was extracted. cDNA was synthesized *in vitro* for use on Affymetrix Mouse Gene Chip microarrays.

**Results:** Results failed to reveal any GxEs. However, across both of the strains there were six gene expression changes considered to be true discoveries under the False Discovery Rate method of multiple correction. Three gene expression changes were found in the hippocampus (*Wnt4*, *Rasgrf1*, *Atp6v0b*), one expression change in the hypothalamus (*Tmem208*), and two expression changes across both tissues (*Insig1*, *Rbm3*).

**Conclusions:** Gene expression hits have functional relevance to smaller hippocampal volumes found amongst depressed patients.

**Key words:** gene expression; stress; depression

## Mental capacity assessment for terminally ill patients requesting assisted suicide in England and Wales: how concepts of knowing the patient impact upon process and outcome

Annabel Price

*Department of Psychological Medicine*

**Background:** This project aims to explore senior doctors' perspectives of mental capacity assessment for patients requesting physician assisted suicide (PAS) in England and Wales. The outcome will inform ongoing debate about PAS and the safeguards needed to protect adults requesting it.

**Methods:** A qualitative study using grounded theory methodology. A purposive sampling strategy has identified two groups of participants 1) Doctors who are likely to make the initial assessment of a patient requesting PAS; 2) Psychiatrists: the clinicians who would be asked to further assess mental capacity if in doubt. In depth, one to one interviews using topic guides are transcribed then coded and constant comparison is used to generate theory and derive conclusions. Data collection and analysis run concurrently in order to further develop emerging themes. NVivo software has been used to aid data storage and management.

**Results:** From analysis of the 19 interviews conducted so far, a core theme of 'knowing the patient' has been identified. A sense of 'knowing' can come from a number of sources and comprises a number of factors, both patient and doctor related. The way a doctor 'knows' the patient impacts upon the way capacity assessment is undertaken and may influence the outcome of assessment. Both 'knowing' and 'not knowing' may have both positive and negative implications for those involved in the process.

**Conclusions:** 'Knowing' the patient has been identified as an important factor in the process and outcome of mental capacity assessment. Further planned interviews will explore this theme further and theoretical sampling will be used to provide further data on which to build theory.

**Key words:** mental capacity; physician assisted; qualitative

## Effects of the COMT x 5-HTTLPR genetic interaction on brain grey matter volume

Joaquim Radua<sup>1</sup>

Wissam El-Hage<sup>2</sup>, Gemma C. Monté<sup>3</sup>, Mary L. Phillips<sup>4</sup>, Simon Surguladze<sup>5</sup>

<sup>1</sup>*Psychosis Studies*, <sup>2</sup>*INSERM U930 ERL CNRS 3106, Université François Rabelais, Tours*, <sup>3</sup>*FIDMAG and CIBERSAM, Sant Boi de Llobregat, Spain*, <sup>4</sup>*Western Psychiatric Institute and Clinic, Pittsburgh*, <sup>5</sup>*Cygnnet Health Care, London*

**Background:** Genetic polymorphisms of the catechol-O-methyltransferase gene (COMT *Val<sup>158</sup>Met*) and the serotonin transporter linked promoter region (5-HTTLPR) have been reported to influence the grey matter volumes of amygdala and hippocampus, but some studies have been inconsistent.

**Methods:** We conducted a voxel-based morphometry (VBM) study of the effects of COMT and 5-HTTLPR and their interaction on the grey matter volumes of 91 healthy controls.

**Results:** A small increase of grey matter volume in right angular gyrus was detected in carriers of the Met allele of COMT, and no main effects of 5-HTTLPR on grey matter volume were detected. Conversely, the effects of the interaction between COMT and 5-HTTLPR on grey matter volume were large and mainly involved bilateral amygdala and hippocampus.

**Conclusions:** The effects of the genetic interaction found in this study might explain the relative inconsistency in the results from previous studies, and suggest further research into genetic interactions.

**Key words:** catechol-O-methyltransferase; serotonin transporter linked promoter region; voxel-based morphometry

## Psychological and physiological consequences of caring for patients with treatment resistant depression

Lena Rane

Abebaw Fekadu, Andrew S. Papadopoulos,  
Sarah Wooderson, Lucia Poon, Kalypso Markopoulou,  
Anthony J. Cleare

*Affective Disorders Research Group, Psychological Medicine*

**Background:** Carers of patients with psychiatric disorders show high levels of anxiety and depression, possibly mediated through disruption of the hypothalamo-pituitary-adrenal (HPA) axis. Amongst carers of patients with treatment-resistant depression (TRD), we set out to determine the psychological and physiological (HPA-axis) consequences of caring, and the association of these consequences with long-term outcome in patients.

**Methods:** 35 informal carers of patients with severe TRD requiring inpatient treatment were recruited and compared with 23 controls. HPA-axis activity was assessed by measuring post-awaking salivary cortisol. The Involvement Evaluation Questionnaire and General Health Questionnaire were administered to measure carer burden and psychiatric caseness respectively. Independent t-tests were used to compare differences between carers and controls and a linear regression model was used to determine the association of post-awakening cortisol with carer status whilst controlling for confounding variables. Data on long-term patient outcome (12 to 83 months) measured using the Hamilton Depression Rating Scale, were also obtained and linear regression was used to determine the association between cortisol output in carers and remission status in patients.

**Results:** Carers experienced high carer burden and high psychiatric caseness. Carers showed reduced cortisol output after awakening, calculated as the area under the curve with respect to ground (AUCg), which remained significant after controlling for potential confounders. In a linear regression model, non-remission in patients was associated with reduced cortisol output in carers.

**Conclusions:** Caring for patients with TRD is associated with adverse psychological and physiological changes suggesting hypocortisolism post-awakening. These changes are associated with poor patient outcome.

**Key words:** carer; depression; cortisol

## Effects of social (mis)understanding on IQ in Autism Spectrum Disorder

Antonia San José Cáceres<sup>1</sup>

Francesca Happé<sup>1</sup>, Rhonda Booth<sup>1</sup>, Mike Anderson<sup>2</sup>

<sup>1</sup>*Social, Genetic and Developmental Psychiatry Centre,*

<sup>2</sup>*Neurocognitive Development Unit, School of Psychology, University of Western Australia*

**Background:** Inspection Time (IT) tasks in relation with traditional IQ tools correlates around -0.5. Scheuffgen et al. (2000) showed that, despite low measure IQ, children with ASD performed as good or better than age-matched controls in the IT task. The authors suggested that IQ tests may be tapping Theory of Mind (ToM) ability (or the ability to understand other people's minds), known to be impaired in ASD individuals. Wallace et al. (2009) corroborated the lack of relation between IT and IQ but not the superiority of IT in ASD, concluding that this difference may be more pronounced in ASD individuals of low IQ. The present study aimed to examine the relationship between IT and IQ in ASD with low IQ in relation to ToM. In particular, it was hypothesized that participants with ASD and low IQ would show faster IT than participants with low IQ but not ASD, and that discrepancy of scores would be determined by the deficit on ToM.

**Methods:** 47 intellectually disabled and 33 low-IQ ASD participants completed an IT task, and a battery of social measures, tapping ToM, adaptive behaviour and social ability.

**Results:** ASD individuals outperformed ID individuals in the IT task. IT-IQ discrepancy was highly related to social measures in the ASD group, but not in the ID group.

**Conclusions:** These findings support the hypothesis of an untapped intelligence where low IQ results from a failure in ToM, impeding ASD individuals to access information through social means, which implies a future difference in the way that autistic intelligence is conceptualized.

**Key words:** ASD; intelligence; Theory of Mind

## Neural Correlates of insight in psychosis investigated with fMRI of working memory

Adegboyega Sapara<sup>1</sup>

Dominic H Ffytche<sup>2</sup>, Emmanuelle Peters<sup>1</sup>, Michael Cooke<sup>1</sup>, Max Birchwood<sup>3</sup>, Elizabeth Kuipers<sup>1</sup>, Veena Kumari<sup>1</sup>

<sup>1</sup>Department of Psychology, <sup>2</sup>Section of Old Age Psychiatry and Department of Neuroimaging Sciences, <sup>3</sup>School of Psychology, University of Birmingham, Edgbaston, Birmingham

**Background:** According to a recently proposed theory of neurobiology of insight (Shad et al., 2007, *Int. Rev. Psychiatry*), poor working memory and associated neural deficits may underlie poor insight in psychosis. This study investigated whether the groups of patients with schizophrenia with low and high insight differ in brain activity, as detected with fMRI, elicited by a parametric working memory (N-Back) task.

**Methods:** This study included 40 stable outpatients with schizophrenia, 20 with score 2 or below (low insight) and 20 with score 8 or higher (high insight) on the Birchwood Insight Scale (Birchwood et al., 1994; *Acta Psychiat. Scan.*) Of these, 32 patients (14 with low, 18 with high insight) provided usable data. Twenty healthy participants were also examined for comparison purposes. All participants underwent fMRI during a parametric 'N-back' task.

**Results:** The low and high insight patient groups were comparable in age, education, premorbid IQ, age at illness onset and symptoms. The low insight group showed lower performance accuracy, compared to the high insight ( $F = 3.23$ ,  $df = 1,30$ ,  $p = 0.08$ ) and healthy participant ( $F = 6.70$ ,  $df = 1,32$ ,  $p = 0.01$ ) groups; the high insight group did not differ from healthy participants. fMRI data revealed lower activation of the inferior-middle frontal, superior parietal and cerebellum areas in low insight group, relative to the high insight group.

**Conclusions:** Our data confirm poor working memory and frontal-parietal-cerebellar dysfunction with poor insight in stable schizophrenia patients.

**Key words:** insight; fMRI; psychosis

## Growing up with body confidence: A qualitative study of young people's views on appearances and dieting

Helen Sharpe

Janet Treasure, Ulrike Schmidt

*Section of Eating Disorders*

**Background:** Body dissatisfaction and dieting are common during adolescence, and are associated with a risk of later eating disorders. Few studies use qualitative methods to explore young people's views on factors underlying body dissatisfaction and dieting, and what can be done to promote body confidence.

**Methods:** Four one-hour focus groups were conducted with 22 female secondary school students aged between 13 and 15 years. Transcripts were explored using a thematic analysis.

**Results:** Body dissatisfaction and dieting in school was explained by four themes: peer acceptance; social comparison online; pressure from family; and pressure from the media and fashion industries. There were seven main areas of recommendation for preventing problems with body dissatisfaction and dieting: building sources of support; educating about signs and symptoms of eating disorders; working with people who have suffered from eating disorders; learning to be more critical of the media; monitoring the school gym; help from professionals; and working with parents.

**Conclusions:** For young people, peer pressures, and to a lesser extent family and media pressures, were at the heart of body dissatisfaction and dieting. Students had many recommendations for preventing these difficulties, including changes to be made within the school setting and further afield. Implications of these recommendations for the development of prevention programmes are discussed.

**Key words:** body dissatisfaction; dieting; adolescence

## Mood instability in adults with Attention Deficit Hyperactivity Disorder (ADHD): characterization, relationship to ADHD symptoms, and response to treatment

Caroline Skirrow

Philip Asherson

*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** Mood instability (MI) is commonly noted in ADHD. Using self-report data we investigated the relationship of MI with ADHD, and its response to treatment.

**Methods:** We compared 48 control and 40 ADHD subjects, all adult males. 21 ADHD subjects were reassessed once stabilized on psycho-stimulant medication. Measures included the Barkleys Adult ADHD Rating Scale (BAARS) and the Affective Lability Scale (ALS).

**Results:** ALS scores were elevated in ADHD subjects ( $p < .001$ ), and correlated well with BAARS hyperactivity-impulsivity and inattention ( $\rho = .44-.67$ ,  $p < .001$ ). ROC analysis with an ALS cut-off of 2.2 showed reasonable sensitivity (81%) and specificity (80%) for predicting ADHD diagnosis (area under the curve = .908;  $SE = .033$ ). ALS scores decreased with psycho-stimulant medication ( $p < .001$ ), and this covaried with change in BAARS scores during treatment response ( $\rho = .5$   $p < .02$ ).

**Conclusions:** MI was elevated in ADHD subjects and highly correlated with ADHD symptom domains. Furthermore, MI responded to psycho-stimulant medication, in conjunction with ADHD symptoms. MI shows a similar profile and treatment response as 'core' ADHD symptomatology and may be best considered as a feature of ADHD rather than a co-occurring condition.

**Key words:** mood; ADHD; treatment

## Care-giving processes in Adulthood

Lindsay Smith

*Psychology*

**Background:** Informal carers play a critical role in promoting the well-being and recovery of individuals with psychosis. This is recognised within national policy and clinical guidelines and the National Institute of Clinical Excellence recommends the provision of evidence-based family interventions for all individuals with psychosis. A robust collection of findings highlights that carers can be negatively affected by their care-giving role and that service-user outcomes are closely linked to care-giving processes.

**Methods:** The present study will examine variation in responses to care-giving across ethnic groups. It will focus on white British and black or black British communities in South London. 40 service users who self-identify with each of the selected groups, along with their carers ( $n = 80$  dyads), will be recruited through Early Intervention services to take part. A series of cross-sectional studies will investigate Expressed Emotion in the care-giving relationship, carer and patient appraisals, illness beliefs, styles of coping and their relationships to carer and service-user health and wellbeing. Carers will complete a series of questionnaires and a structured interview (Camberwell Family Interview) investigating appraisals of the care-giving relationship. All patients will complete a similar series of questionnaires investigating mood and functioning and a clinical symptom interview. The research is influenced by reports of elevated incidence of psychosis within black or black British groups in the UK; as well as reduced satisfaction with clinical support services amongst ethnic minority groups. Results are intended to inform the development of culturally sensitive family interventions in psychosis.

**Results:**  $n = 9$  at present.

**Conclusions:** N/A

**Key words:** care-giving; psychosis; expressed emotion



## Views and Experiences of physical health in First Onset Psychosis: a qualitative study

Poonam Sood<sup>1</sup>

Khalida Ismail<sup>2</sup>, Anthony David<sup>1,3</sup>, Craig Morgan<sup>1,4</sup>

<sup>1</sup>*Psychosis Studies*, <sup>2</sup>*Psychological Medicine & General Hospital Psychiatry*, <sup>3</sup>*Cognitive Neuropsychiatry*, <sup>4</sup>*Health Service and Population Research*

**Background:** There is growing interest in the relationship between poor physical, unhealthy lifestyle and the increased risk of preventable disease among people with psychosis. The aim of this study was to explore the views of individuals experiencing their first episode of psychosis regarding their physical health needs and perceptions of what contributes to risk of developing adverse health outcomes.

**Methods:** Semi-structured interviews were conducted with 15 first-episode psychosis participants. Data were analysed using thematic analysis.

**Results:** Five key themes were identified: disempowerment from poor professional-patient communication; experiences and management of medication; meaning and value of health; health risk perceptions and ability to change; available support. Notably, patients variously: experienced disempowerment in the early phase of their mental health journey, because of a lack of autonomy regarding their mental health care; reported considerable goals on hospital discharge that competed with physical health goals; felt confident in their ability to avoid future illnesses; and expressed the need for greater social support as a potential mechanism to assist physical wellbeing.

**Conclusions:** Health care professionals might utilise their close contact with first episode psychosis patients to provide education about the potential consequences of leading a poor lifestyle.

**Key words:** first episode psychosis; physical health; risk perceptions

## Cumulative Impact of Social Disadvantage in a Sample of First Episode Psychosis Patients

Simona A Stilo<sup>1</sup>

Robin M Murray<sup>2</sup>, Craig Morgan<sup>1</sup>

<sup>1</sup>*Health Service and Population Research*, <sup>2</sup>*Psychoses Studies*

**Background:** The robust evidence that the incidence of schizophrenia and other psychoses is elevated in many migrant and minority ethnic population, especially black population in the United Kingdom, has led to a resurgence of interest in the potential role of socio-environmental factors. Three main questions will be addressed: (i) does social disadvantage in childhood and in adulthood increase the risk of psychosis? (ii) does it contribute to the higher rates of psychosis among African-Caribbeans and other migrant groups in the UK? (iii) is gene environment-interaction a possible aetiological explanation for psychosis?

**Methods:** In order to address these points we have been collecting information regarding social disadvantage in childhood and adulthood from cases presenting with a first episode of psychosis to the South London & Maudsley National Health Service (NHS) Foundation Trust and from a control sample representative of the local population. Associations will be expressed as odds ratios from logistic regression models. All analyses will be adjusted for age, gender, ethnicity and other possible confounders.

**Results:** Experiences of adversity in childhood and in adulthood may increase risk of psychosis, particularly in the presence of other known risk factors (e.g. genetic risk).

**Conclusions:** Social disadvantage, especially in the case of cumulative exposure, may increase the risk of psychosis and may be one contributory explanation for the higher rates of psychosis among African-Caribbeans and other migrant groups in the United Kingdom.

**Key words:** social disadvantage; psychosis; ethnicity

## Amyotrophic Lateral Sclerosis-associated proteins TDP-43 and FUS disrupt the ER-mitochondria interaction

Radu Stoica

Kurt De Vos, Chris Miller

*Departments of Neuroscience and Clinical Neurosciences*

**Background:** Vesicle-associated membrane protein associated protein-B (VAPB) is an integral ER protein that interacts with the mitochondrial outer membrane protein, protein-tyrosine phosphatase interacting protein-51 (PTPIP51). Up to approximately 20% of the mitochondrial surface is closely associated with ER in regions termed mitochondria-associated ER membranes (MAM). MAM facilitate the exchange of Ca<sup>2+</sup> and phospholipids between these organelles. A mutation in VAPB causes amyotrophic lateral sclerosis (ALS) type-8 and disrupts the VAPB-PTPIP51 interaction. To determine whether other ALS-associated insults influence the VAPB-PTPIP51 interaction, the effects of wild-type and ALS-associated mutants of SOD1 (ALS type-1), TDP-43 (ALS type-10) and FUS (ALS type-6) on the VAPB-PTPIP51 interaction were studied.

**Methods:** CV1 cells were plated on coverslips 48h before the experiment, fixed and permeabilized. After 1 h incubation with PTPIP51 and VAPB primary antibodies, the proximity ligation assay (Duolink® *in situ* PLA) was performed, according to the manufacturer's instructions. In brief, PLA probes were diluted in the buffer provided and incubated in a pre-heated humidity chamber, followed by hybridization, ligation and amplification. Coverslips were mounted and images captured using a fluorescence microscope. Particles were analyzed using the ImageJ software, each particle corresponding to one VAPB-PTPIP51 interaction.

**Results:** Expression of wild-type or mutant SOD1 did not influence the VAPB-PTPIP51 interaction. However, expression of wild-type and mutants of both TDP-43 and FUS decreased the VAPB-PTPIP51 interaction.

**Conclusions:** These results implicate TDP-43 and FUS in defective MAM function in ALS. Further experiments are needed to elucidate the molecular mechanism and the consequences of decreased ER-mitochondria contacts.

**Key words:** ER; Amyotrophic Lateral Sclerosis; mitochondria

## The development of a new paradigm to clarify the role of childhood trauma in emotional processing of depressed individuals

<sup>1</sup>Akiko Suzuki

Prof. Veena Kumari<sup>2</sup>, Prof. Anthony Cleare<sup>1</sup>

<sup>1</sup>*Section of Neurobiology of Mood disorders, Department of Psychological Medicine,* <sup>2</sup>*Psychology*

**Background:** Dysfunctional stress reactivity confers vulnerability to depression, with some evidence that enduring HPA (Hypothalamic-Pituitary-Adrenal) axis dysregulation can be acquired through excessively stressful experiences in childhood. However, how this hormonal dysregulation explains behavioural expression of the symptoms of depression has not yet fully been clarified in the previous studies of the effect of childhood trauma. The current project aims to examine emotional reactivity by using a novel affect-modulated startle reflex paradigm designed to assess both subjective and objective responses to the images depicting childhood trauma in addition to the standard stimuli taken from the international affective picture system.

**Methods:** Patients with depression and healthy controls, both with and without history of childhood maltreatments will be recruited. Their reactivity to acoustic startle probes during the viewing of pictures with a variety of emotional valence (positive, neutral, negative, trauma-relevant) will be assessed. The first step in this project requires validation and development of the images specific to the types of childhood trauma by recruiting raters on the severities of and the category of trauma portrayed in the images chosen from a public photo archive.

**Results:** 24 images specific to the trauma (6 images each for physical abuse, sexual abuse, emotional abuse and emotional neglect) have been selected for the startle reflex paradigm.

**Conclusions:** The newly developed set of images allows progression to the main experimental phase of the PhD project to determine whether the effect of childhood trauma would enhance the responses to the self-referencing images of trauma relative to non-self-referencing negative images.

**Key words:** childhood trauma; depression; emotional reactivity

## Stable genetic influence on anxiety ratings across middle childhood

Maciej Trzaskowski

Helena Zavos, Claire M.A. Haworth, Robert Plomin,

Thalia C. Eley

*TEDS/Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** We examined the aetiology of anxiety symptoms in an unselected population at ages 7 and 9, a period during which anxiety disorders first begin to develop (mean age at onset is 11 years). Specifically, the aim of the study was to investigate genetic and environmental continuity and change in components of anxiety in middle childhood.

**Methods:** Parents of over 3500 twin pairs completed the Anxiety-Related Behaviours Questionnaire (ARBQ) when twins were 7 and 9 years old. Multivariate-longitudinal analyses were conducted to examine genetic and environmental influences on stability and change in four anxiety scales: Negative Cognition, Negative Affect, Fear and Social Anxiety.

**Results:** We found moderate temporal stability in all 4 scales from 7 to 9 years (correlations ranging from .45 to .54) and moderate heritability (average 54%). Both shared and non-shared environmental influences were modest (average 18% to 28% respectively). Genetic factors (68%) explained most of the homotypic continuity in anxiety.

**Conclusions:** We show that homotypic continuity of Anxiety-Related Behaviours (i.e. the continuation of one specific type of anxiety over time) was largely driven by genetic factors. In contrast, though more varied, heterotypic continuity between some traits (i.e. the change from one type of anxiety-related behaviour into another over time) was mainly due to shared-environmental factors.

**Key words:** anxiety; twins; genetics; genetic continuity; developmental anxiety; longitudinal-multivariate study; anxiety-related behaviours; middle childhood

## A study of Audiovisual Emotional Integration

Huai-Hsuan Tseng

Paul Allen

*Department of Psychosis Studies*

**Background:** Facial expression and prosodic emotion recognition is consistently reported to be defective in schizophrenia and in individuals with an At Risk Mental State (ARMS), in an attenuated form. Furthermore, researches also suggested that patients with schizophrenia have difficulties in the multisensory integration (MSI). The aims of the main study are to examine the ability of MSI in ARMS subjects, subjects with first episode of psychosis, and healthy volunteers; and also explore possible abnormalities in the emotional-related neural substrate using functional Magnetic Resonance Imaging. A pilot study has been conducted so far to examine the facilitative and interfering pattern of emotional integrative process in normal subjects.

**Methods:** 10 Healthy subjects were recruited and 15 pairs of morphing faces were displayed concurrently with 15 voice clips; both congruent and incongruent pair trials were included. Participants were asked to pay attention on both the morphing facial expression and voice clips, but to base their judgments on the prosody of the voices clips. Accuracy and reaction times were recorded as a measure of facilitation and interference effects.

**Results:** The mean accuracy for congruent pairs showed a trend towards facilitation effect in comparison with the overall accuracy over emotional prosody only. Furthermore, there was a trend for longer reaction times during incongruent trials relative to both congruent trials and single modality voice clips.

**Conclusions:** Congruency has a trend of effect on emotional integration in terms of both accuracy and reaction time. The difference of the effect between normal subjects, ARMS subjects and subjects with first episode psychosis will be the main focus of the future study.

**Key words:** emotion recognition; multi-sensory integration; at-risk mental status

## Shared and distinct Neurophysiological markers of Attention and Inhibition in Children with ASD and ADHD

Charlotte Tye

Philip Asherson, Karen Ashwood, Bahare Azadi, Patrick Bolton, Gráinne McLoughlin

*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** There is substantial overlap between attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD), two common neurodevelopmental disorders that until recently have been treated as separate research fields. In particular both disorders demonstrate attentional and inhibitory deficits, but these have not been directly compared with concurrent electrophysiological recording that is able to capture these fast occurring cognitive events.

**Methods:** 18 children with ADHD, 19 children with ASD, 26 children with ASD+ADHD and 25 typically developing (TD) children, were compared on performance and underlying brain responses during a cued continuous performance task (CPT- OX), with the aim of discovering shared and distinct markers of attentional processing and better understand the basis of comorbidity.

**Results:** Children with ADHD symptoms had increased omission errors and response variability during the task. Event-related potential (ERP) indices of response preparation and inhibition were altered specifically in children with ADHD symptoms.

**Conclusions:** ASD and ADHD do not share attentional dysfunction, suggesting they can be dissociated at the neural level using ERPs. ASD+ADHD are not a qualitatively distinct subtype and appear to more closely resemble ADHD in this domain, highlighting potential diagnostic and treatment implications.

**Key words:** ADHD; ASD; ERP

## Smell identification test as a progression marker in Alzheimer's disease

Latha Velayudhan

Megan Pritchard, Simon Lovestone

*Old Age Psychiatry*

**Background:** Factors influencing or predicting progression in Alzheimer's disease (AD) is not well understood. Olfactory dysfunction, particularly impaired smell identification, is known to occur in AD. Mesial temporal lobe, important for memory function is also critical for the processing of olfactory information. In view of a common anatomical substrate, we hypothesized that olfaction dysfunction worsens faster in people with AD with rapid cognitive decline compared to those with slower cognitive decline. The aim was to test whether smell identification test can be used as a predictor for illness progression in AD patients.

**Methods:** 41 participants with late onset mild to moderate AD were recruited from mental health services for older adults (SLaM). Subjects were classified as 'Rapid Progressors' defined on 'a-priori' with a loss of  $\geq 2$  points in Mini-Mental State Examination (MMSE) within six months. Assessments included MMSE, Neuropsychiatric Inventory, Bristol Activities of Daily Living, and the University of Pennsylvania Smell Identification Test (UPSIT), at baseline and after 3 months.

**Results:** Twenty subjects were 'Rapid Progressors', and had lower UPSIT scores compared to 'Non-Rapid Progressors' both at the baseline ( $p=0.02$ ) and at follow up after 3 months ( $p=0.05$ ). Baseline UPSIT correlated with follow up UPSIT ( $r = 0.5, p < 0.01$ ) and MMSE ( $r=0.4, p = 0.04$ ). Also it was the baseline UPSIT score that best predicted ( $p < 0.05$ ) the follow up smell and cognitive function on linear regression analysis.

**Conclusions:** Smell identification function could be useful as a clinical measure to assess and predict progression in AD

**Key words:** olfaction; Alzheimer's disease; disease progression

## Improving the Quality of Brain Images for Functional Magnetic Resonance Imaging Applications

Stephen Wastling  
David Lythgoe, Gareth Barker  
*Centre for Neuroimaging Sciences*

**Background:** Functional magnetic resonance imaging (fMRI) data, used to explore brain function, are acquired using gradient-echo echo-planar imaging (GE-EPI). Because of the differing magnetic properties of tissues in the head, images are seriously degraded by regions of missing data, especially in the orbitofrontal and inferior temporal lobes, which hinders the efficacy of techniques used to determine how different regions of the brain are interconnected. It has been shown that, by the addition of magnetic field gradients (z-shims), this missing data may be partially recovered, at a cost of reduced data quality in other brain regions. In this work we seek to recover missing data whilst attempting to maintain data from functionally active grey matter in all other areas of the brain.

**Methods:** A GE-EPI sequence, with additional of z-shim gradients, was used to image a single healthy subject on a General Electric scanner (3T GE Signa HDx). An algorithm was produced to determine the two z-shim gradients that lead to maximum signal across all voxels containing grey. The optimisation was constrained to grey matter using a map acquired with a Dual Inversion Recovery EPI sequence.

**Results:** The missing data was partially recovered; comparing the images acquired using z-shims optimised for grey matter in each slice and those optimised for the whole brain as in previous work, we find that 57% of grey matter voxels showed increased signal.

**Conclusions:** By constraining the algorithm used to select z-shims to grey matter improves signal recovery over a whole-brain optimisation therefore we believe this methodology will prove useful in any fMRI studies using z-shimming.

## Emotional Processing and Social Cognition in Amyotrophic Lateral Sclerosis / Motor Neurone Disease

Tamlyn Watermeyer  
Richard Brown, Laura Goldstein  
*Psychology*

**Background:** Although historically characterized as purely a disease of the motor system, Amyotrophic Lateral Sclerosis (ALS) is now recognised as a multisystem disorder. Evidence of impairments in social and emotional cognition, reflective of dysfunction of the orbital and frontal pathways, in people with ALS (pwALS) is growing (e.g. Meier *et al.*, 2010). Deficits in the recognition of facial emotion (Zimmerman *et al.*, 2007) and Theory of Mind (Gibbons *et al.*, 2007; Giradi *et al.*, 2010), the ability to infer other peoples' mental and emotional states, have been reported. Previous tests used static facial images, inanimate cartoons and written vignettes, requiring the attribution of intentions, feelings and beliefs. Since emotions and intentions are substantially altered through facial movement, vocal tone, gesture and social context, the ecological validity of inanimate stimuli is restricted. The current study will adopt videoed vignettes depicting realistic scenarios of emotional expression and social discourse, alongside traditional measures. This will explore if reported impairments persist in realistic paradigms. The study will also use measures of executive function, mood, personality and empathy, to examine if these variables contribute to the possible impairments. The findings may potentially inform existing knowledge of the phenotypic variation in ALS and its underlying neuropathology.

**Methods:** The study will recruit 55 pwALS, 55 carers and 55 controls. Controls and pwALS will be matched for gender, age, IQ and education. We have so far recruited 15 controls and 6 patients. Testing comprises neuropsychological tests (memory, executive function); emotion tasks (animated and static vignettes); and questionnaire-based interviews (personality, mood and empathy).

**Results:** N/A

**Conclusions:** N/A

**Key words:** emotional processing; social cognition; amyotrophic lateral sclerosis

## Imagery re-scripting for body dysmorphic disorder

Rob Willson<sup>1</sup>

David Veale<sup>1</sup>, Mark Freeston<sup>2</sup>

<sup>1</sup>Centre for Anxiety Disorders and Trauma, <sup>2</sup>University of Newcastle

**Background:** Individuals with Body Dysmorphic Disorder (BDD) are preoccupied with the idea that they are ugly and defective. The problem results in significant levels of distress and impairment in social, occupational or some other important area of functioning. BDD affects around one percent of the population, yet research in understanding and treating this problem is still very much in its infancy (Veale 2004). Given that BDD is inherently a body image problem it seems logical that imagery related interventions would be worthy of investigation. Furthermore, there is evidence that imagery re-scripting may benefit individuals with social phobia (Wild et al 2008), which shares a number of features with BDD.

**Methods:** Single case series

**Results:** Data on a single case series design of using imagery re-scripting with individuals who have BDD will be presented. The data will be analysed using visual graphs and randomisation tests. To illustrate the process in more depth the treatment of a participant will be presented in detail.

**Conclusions:** Initial data supports that imagery rescripting may be a helpful procedure for individuals suffering from BDD.

**Key words:** BDD; imagery; single case design

## Profiling DNA methylation in human Period 1 and negative life events in adolescents

C. Peng Wong

Cattrell, A., Carvalho, F.M., Jia, T., Loth, E., Lourdasamy, A., Mill, J., Desrivieres, S., Schumann, G.

*Social, Genetic and Developmental Psychiatry Centre (MRC)*

**Background:** The propensity of developing alcohol drinking can be modified by experience and various environmental factors. Stress is one major factor that increases the risk of alcohol drinking and disrupts the circadian rhythm in mammals. A major circadian gene Period 1 (*PER1*) has been associated with heavy alcohol drinking and high level of psychosocial adversity among the adolescents (Dong et al., 2011). In this study we investigate the relationship of the DNA methylation in *PER1*, negative life events and alcohol drinking.

**Methods:** We took a sub-sample of n=700 14-year old adolescents from the IMAGEN project, for which the genetic, neuroimaging and behavioural data are available. Whole blood DNA samples of these individuals were used to analyse the DNA methylation patterns in the *PER1* promoter region using Sequenom<sup>®</sup> MALDI-TOF technology. Life-Events Questionnaire (Newcomb, Huber & Bentler, 1981) will be used to examine the negative life events experienced by the individuals.

**Results:** We analysed the DNA methylation status of 19 CpG units on the *PER1* promoter region. Differential DNA methylation ranging 0.02 – 0.77 was found across the CpG units and the individuals. Regression analyses will be performed to associate the DNA methylation with negative life events.

**Conclusions:** We found inter-individual variations in DNA methylation patterns within the promoter of *PER1*. We are currently investigating the significance of the variations in DNA methylation in stress-related alcohol drinking. The comparison of methylation levels at the *PER1* promoter region will provide insight on the importance of epigenetic modification on *PER1* function and its impact on human behaviour.

**Key words:** Period 1; stress; DNA methylation







