1. Burghölzli Psychiatry Meeting
October 22, 2014 / 2 – 8pm

venue und organisation
Hörsaal, Gebäude Z, Psychiatrische Universitätsklinik Zürich, Lenggstrasse 31

contact:
Anja Seidl (Forschungssekretariat KPPP, Tel. 044 384 24 04)
Monique Meier (Direktionssekretariat KPPP, Tel. 044 384 23 32)

organizing committee:
Dominik Bach (Klinik für Psychiatrie, Psychotherapie, Psychosomatik)
Elmar Habermeyer (Klinik für Forensische Psychiatrie)
Lawrence Rajendran (Klinik für Alterspsychiatrie und Departement Psychiatrische Forschung)

program – english-speaking part
12.00 – 13.15:  German language talks for staff and patients
13.15 – 14.00:  Lunch
14.00 – 20.00:  Scientific Meeting
   14.15:  R. Derungs (DPR/KAP):
   „Reversal of cognitive impairment by p66Shc deletion in an AD mouse model“
   14.30:  F. Wirth (DPR/KAP):
   „Therapeutic efficacy of a conformation-specific human-derived anti-SOD1 antibody to fight familial and sporadic amyotrophic lateral sclerosis (ALS)“
   14.45:  N. Tesler (Children’s Hospital/KiSpi):
   „Reduced Sleep Spindle Activity in Early Onset Schizophrenia“
   15.00:  Q. JM Huys (DPPP/KPPP – TNU):
   „Alcohol addiction: dopamine, goals, habits and relapse“
   15.30:  M. Kirschner (DPPP/KPPP):
   „Apathy but not diminished expression in schizophrenia is associated with ventral striatal activation during reward anticipation“
   15.45:  M. Staib (DPPP/KPPP):
   „Human primary auditory cortex encodes threat-predicting information of complex but not simple sounds during fear conditioning“
   16.00:  M. Aebi (Child Psychiatry/KJPD):
   „Testing the “sexually-abused abuser hypothesis” in adolescents: a population-based study“
   16.15:  A. Mokros (Forensic Psychiatry/KFP):
   „The Emotion paradox in psychopathy: Experimental findings on Emotion recognition and expression“
   16.30:  Poster presentations
   17.30:  Keynote lecture: Dr. Bogdan Draganski, Director LREN, University of Lausanne
   „What can we learn about mood disorders by studying brain anatomy with magnetic resonance imaging?“
   18.30:  Apero riche and posters
ORT UND ORGANISATION
Hörsaal, Gebäude Z, Psychiatrische Universitätsklinik Zürich, Lenggstrasse 31

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PROGRAMM – DEUTSCHSPRACHIGER TEIL
12.00 Uhr Dr. Jasmin Bartl (KJPD):
„Auswirkungen von Methylphenidat auf die Entwicklung des Gehirns: Risiko oder Nutzen?“

12.15 Uhr: PD Dr. Stefan Kaiser (KPPP):
„Negativsymptome der Schizophrenie – von der Psychopathologie zur Neurophysiologie“

12.30 Uhr: PD Dr. Andreas Mokros (KFP):
„Das Emotionsparadoxon bei Psychopathy: Experimentelle Befunde zur Emotionserkennung und –ausdruck“

12.45 Uhr: Nadine Saxer (DPTS):
„Wie unterstützt die Ergotherapie depressiv Erkrankte in ihrer Alltagsbewältigung? Evaluation der ergotherapeutischen Behandlung in der Tagesklinik für Affektkranke der Psychiatrischen Universitätsklinik Zürich“

13.00 Uhr: Dr. Gabriele Siegel (KAP):
„Lifestyle-Risikofaktoren der Alzheimer Erkrankung“

13.15 Uhr: Stehlunch
A) Cellular and Molecular Psychiatry, Systems Biology of Neurodegeneration
**Title**

*Effects of functional lymphocyte ablation in a mouse model of Alzheimer's disease*

**Authors**

Späni, C., Suter, T., Ferretti, M.T., Derungs, R., Wirth, F., Welt, T., Hock, C., Nitsch, R.M. & Kulic, L.

**Affiliations**

*Division of Psychiatry Research, University of Zurich, Wagistrasse 12, 8952 Schlieren, Switzerland*

**Introduction**

According to the “amyloid cascade hypothesis” accumulation of amyloid beta-peptide (Aβ) plays a central role in the development of Alzheimer’s disease (AD), leading to inflammatory responses mainly arising from the local innate immunity of the central nervous system (CNS) including activation of resident microglia and astrocytes and the release of a wide range of inflammation-related proteins such as complement factors, pro-inflammatory cytokines and chemokines. If these local innate immune responses are beneficial or detrimental (or both) is still highly debated. Furthermore, the role of the adaptive immune system, both humoral and cellular, and the interplay with the innate immune system in AD remains largely unknown. In this study we aimed to elucidate the role of the adaptive immune system in Aβ-related pathology and cognitive dysfunction in AD mouse models.

**Methods**

Transgenic APPdE9 mice were lethally irradiated and reconstituted with bone marrow cells from mice lacking functional T and B cells (Rag2 knockout mice) or from wildtype mice. To control for possible confounding factors due to the irradiation procedure a second experiment was performed, in which APPdE9 mice were crossed with Rag2 knockout mice.

**Results**

Mice lacking functional adaptive immune cells showed a reduced Aβ load in the brain along with an increase in phagocytic Iba1-positive cells. Interestingly, peripheral plasma Aβ levels were also increased, suggesting a shift of Aβ from the brain to the periphery. Astrocytic GFAP-positive cells were not altered by the absence of functional adaptive immune cells.

**Discussion**

The results of our experiments demonstrate an impact of functional adaptive immune cells on Aβ-related neuroinflammation and amyloid plaque burden *in vivo.*
Reversal of cognitive impairment by p66Shc deletion in an AD mouse model

Rebecca Derungs, Claudia Späni, Fabian Wirth, Tobias Welt, Roger M. Nitsch, Luka Kulic

Division of Psychiatry Research, University of Zurich

Introduction
According to the “vascular hypothesis of AD”, age- and cerebrovascular-related risk factors play a critical role in AD pathogenesis, leading to early vascular dysregulation, which is considered to precede significant Aβ plaque deposition, cognitive decline and onset of neurodegenerative changes. The mitochondrial adaptor protein p66Shc is involved in ageing/longevity and vascular disease. p66Shc knockout mice are characterized by a 30% prolonged life span, lower levels of ROS and they are protected against age-associated endothelial dysfunction. Moreover, p66Shc activation has been shown to be involved in Aβ-induced neurotoxicity in vitro.

Methods
To study the role of p66Shc deletion on AD-related pathology in vivo, we generated a novel APP transgenic mouse line lacking p66Shc. The four genotypes (wildtype, PSAPP, p66 ko, p66 ko/PSAPP) of this novel p66 ko/PSAPP mouse line were extensively tested, including cognitive behavioural, histopathological, and biochemical analyses. Cognitive behaviour was analysed using three different hippocampus-dependent tasks at three different ages (3, 6, and 15 months).

Results
Behavioural testing revealed cognitive deficits in the PSAPP group at 15 months in the Y maze and Novel object recognition task (NORT) and already at 3 months in the Barnes maze. Strikingly, all observed impairments could be rescued by p66Shc ablation. This rescue effect was independent of Aβ pathology as we did not observe significant differences in Aβ-plaque burden. Interestingly, we found a “hypervascularity phenotype” in the APP transgenic animals, which was reversed by p66Shc ablation. Furthermore, the PSAPP mice showed a trend towards increased blood brain barrier leakages.

Discussion
The results of this study suggest that the protective effects of p66Shc ablation on Aβ-related cognitive dysfunction are most likely downstream of Aβ generation and deposition and may be mediated via beneficial effects on vessel architecture and subsequent vascular dysfunction. Further functional analyses and mechanistic studies are ongoing.
Title

Mutations in the serotonin transporter and tryptophan hydroxylase genes modulate working memory impairment of cocaine users

Authors

Havranek M\textsuperscript{a}, Vonmoos M\textsuperscript{b}, Büetiger J\textsuperscript{b}, Tasiudi E\textsuperscript{c}, Hulka LM\textsuperscript{b}, Preller KH\textsuperscript{b}, Mössner R\textsuperscript{d}, Seifritz E\textsuperscript{a,e}, Grünblatt E\textsuperscript{e}, Quednow BB\textsuperscript{b,e}

Affiliations

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Background

Cocaine users consistently display working memory impairments but the mediating mechanism is unknown so far. The serotonin (5-HT) system is involved in working memory processes and recent evidence suggests that 5-HT neurotransmission is altered in cocaine users. Thus, the effect of three 5-HT-impacting polymorphisms on working memory performance and peripheral expression of serotonin transporter (5-HTT) mRNA was investigated in cocaine users and stimulant-naïve controls.

Methods

220 participants (126 cocaine users, 94 controls) underwent neuropsychological testing of working memory (visuospatial and verbal) and genotyping for the length polymorphism in the promoter region of the 5-HTT (5-HTTLPR), the variable number of tandem repeats in the second intron of the 5-HTT (VNTR In2), and a single nucleotide polymorphism (rs1386497) in the tryptophan hydroxylase 2 (TPH2) gene. Additionally, 5-HTT mRNA was quantified in full blood samples.

Results

Several significant interactions between cocaine use and genotype were found: In controls, the short/short genotype of 5-HTTLPR, 12/12 genotype in 5-HTT VNTR In2, and A/A genotype in TPH2 rs1386497 were associated with lower working memory performance, whereas carriers of the respective long/long, 9+10/9+10, and the C/C genotype showed higher performance. However, in cocaine users, this pattern was completely inversed and this gene\textasciitildeenvironment interaction was consistently found across all working memory subdomains. Furthermore, similar interaction effects on working memory were found between 5-HTT mRNA expression and VNTR In2 as well as TPH2 genotype.

Conclusions

These findings suggest that the 5-HT system plays an important role in the development of working memory deficits under chronic cocaine use. Finally, pharmacologically compounds targeting 5-HT neurotransmission might be promising for the treatment of cognitive deficits in cocaine dependence.
Title

Therapeutic efficacy of a conformation-specific human-derived anti-SOD1 antibody to fight familial and sporadic amyotrophic lateral sclerosis (ALS)

Authors

F. Wirth¹,², M. Maier³, F. Montrasio³, D. Preisig¹, S. Imobersteg¹, M. Krueger¹, A. Jeske¹, B. Ries¹, R. Derungs¹,², C. Spaeni¹,², L. Kulic¹,⁴, M. Weber⁵, J. Grimm³, R.M. Nitsch¹,² and T. Welt¹

Affiliations

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Introduction

ALS is a progressive neurodegenerative disease selectively affecting lower and upper motor neurons leading to paralysis and ultimately death. Strong evidence suggests that modifications in Cu/Zn Superoxide Dismutase 1 (SOD1) are directly linked to ALS. While mutations in SOD1 account for 1-2% of familial ALS cases, the generation and use of SOD1-antibodies recognizing non-native conformations supports a toxic role of misfolded wildtype SOD1 in sporadic ALS (sALS) as well. Our goal was to assess the presence of misfolded SOD1 in sALS and validate misfolded SOD1 as a potential therapeutic target in all forms of ALS.

Methods

Using the Reverse Translational Medicine (RTM) technology we screened for human-derived antibodies against pathological SOD1 conformations. Specificity of SOD1 antibodies to toxic conformations was assessed biochemically and immunohistologically. Therapeutic efficacy of the most promising candidate was validated by direct and continuous intracerebroventricular antibody delivery or intraperitoneal drug application in two different SOD1 transgenic animal models.

Results

We identified a human-derived monoclonal SOD1 antibody (α-miSOD1) that recognized misfolded SOD1 in spinal cord motor neurons in the majority of sALS patients. α-miSOD1 displayed high affinity and selectivity for different in vitro preparations of misfolded SOD1, and showed therapeutic efficacy by prolonged survival in both animal models examined. Gait analysis showed improved motoric functions in the fast-progressing model upon i.c.v treatment. In the slow-progressing mouse line α-miSOD1 delayed disease onset and rescued motor neuron degeneration in the anterior horn.

Discussion

Our experiments support the relevance of misfolded SOD1 as a common pathological hallmark not only in familial but also sporadic ALS, and beneficial motoric effects and prolongation of survival in two different animal models of ALS highlight the therapeutic potential of α-miSOD1. Furthermore, the fully human origin designates α-miSOD1 a promising drug candidate for a fast and safe translation into clinical ALS trials.
Case-Control and sibling association study of CNTNAP2 and high functioning autism and a meta-analysis evaluation

Authors
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Introduction
Autism spectrum disorder (ASD) is a highly heritable neurodevelopmental disorder but its aetiology is still elusive. The Contactin Associated Protein-like 2 (CNTNAP2) gene has been discussed to be associated in ASD and other neurodevelopmental disorders such as intellectual disability (ID), dyslexia and language impairment. Therefore, we aimed to elucidate the genetic association of CNTNAP2 gene within high functioning ASD (HFA) to eliminate intelligence related factors and combine all published results to-date in a meta-analysis for ASD and HFA.

Method
We performed case-control association study for HFA in two independent populations (Swiss, n=174 & German, n=64) and a family based association (DFAM) analysis with siblings (n=57 sibs, n=45 cases). Individuals were genotyped for two SNPs on the CNTNAP2 gene (rs2710102, rs7794745). Furthermore, a meta-analysis was conducted with previously published results using the MIX2 software.

Results
The rs2710102 deviated in both populations for Hardy-Weinberg equilibrium (p-value<0.001), while rs7794745 did not deviate. A significant association for the carriers of the T-allele of the rs7794745 with HFA was found only in the case-control sample from Zurich (OR=1.757 95% CI 1.12-2.77; p=0.02). No association could be proved by DFAM with any of the CNTNAP2 SNPs with HFA. The meta-analysis of both SNPs (rs2710102, rs7794745) did not result in significant association with either ASD (OR=1.01 p=0.34 n=5; OR=0.99 p=0.53 n=7, respectively) nor with HFA (OR=1.009 p=0.515 n=3, OR=0.95 p=0.37 n=3, respectively).

Discussion
Since our study focused on a special population of ASD, the HFA, we could eliminate any affects due to ID or language disabilities, which resulted in no significant association. Therefore, we might conclude that if CNTNAP2 plays a role in neurodevelopmental disorders, than rather in individuals displaying ID or developmental delays, as recently discussed.
Title
Region-specific regulation of the serotonin 2A receptor expression in development and aging in postmortem human brain.

Authors
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Introduction
The serotonin 2A receptor (HTR2A) is widely expressed in the brain and involved in the modulation of fear, mood, anxiety and other symptoms. HTR2A and HTR2A gene variations are implicated in depression, schizophrenia, anxiety and obsessive-compulsive disorder. To understand HTR2A signalling changes in psychiatric or neurodegenerative disorders, its normal pattern of brain expression and region specificity during development and aging needs to be clarified. The aim of the present study was to assess HTR2A expression through developmental and aging stages in six brain regions in postmortem human brain samples from individuals with no clinical or neuropathological evidence of neuropsychiatric disorders and to investigate the interaction with the rs6311 HTR2A promoter polymorphism.

Methods
DNA, RNA and protein were isolated from postmortem brain samples including six regions (frontal cortex, striatum, amygdala, thalamus, brain stem and cerebellum) from 55 individuals. HTR2A mRNA levels were assessed using quantitative real time RT-PCR, and HTR2A protein levels - with western blot. The rs6311 HTR2A polymorphism was analyzed with genotyping.

Results
We found that HTR2A mRNA and protein levels are differentially regulated with age in different brain regions studied, but are not affected by gender. Significant changes in HTR2A expression with age were found in frontal cortex, amygdala, thalamus, brain stem, and cerebellum.

Discussion
Our results show plasticity and region specificity of HTR2A expression regulation in human brain with age, which may be important for the interaction with other neurotransmitter systems and for the occurrence of developmental periods with increased vulnerability to neuropsychiatric or neurodegenerative disorders.
Title

Molecular Genetic Aspects of Psychopathy: A Study Outline

Authors
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Introduction
There is a considerable amount of evidence that psychopathic individuals show deficits in emotion perception, especially concerning negative emotions such as fear or sadness. Since emotion perception is positively related to the ability to express emotions in the face, it is also assumed that psychopaths show deficits in emotion expression. Furthermore, recent meta-analyses revealed that genetic variations, especially in the serotonergic system, contribute to the development of psychopathic traits. In the present study we aim to examine whether and how deficits in emotion perception and expression are related to candidate polymorphisms in psychopaths.

Methods
By the end of the data collection, a total of more than 300 psychopathic and non-psychopathic patients and controls will be tested using multiple measures of interpersonal abilities, other cognitive abilities, and psychopathy. Data collection includes computerized assessment of emotion perception and recognition performance, explicit emotion expression (through videotaping of facial expressions), and implicit emotion expression (i.e., facial mimicry assessed via facial electromyography). Psychopathy is assessed both through clinical observer rating and self-report on behalf of the participants. Saliva samples are collected and analyzed for candidate polymorphisms.

Results and Discussion
Since the data collection is still in progress, no final results can be presented. The poster presentation will give an account of the empirical background, hypotheses, and methodology. Apart from increasing our understanding of the basic processes involved in altered emotion processing in psychopathy, we expect that the results will have implications for assessment and treatment. In particular, the results are expected to shed light onto the distinction between psychopathic and antisocial personalities.
Title

Establishing the roles of TNF and the kynurenine pathway in inflammation-induced emotional and cognitive dysfunction

Authors

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Affiliations

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Introduction

A high comorbidity of MDD (major depressive disorder) and autoimmune disorders (e.g. multiple sclerosis) supports the growing evidence that inflammatory processes might play an important role in the aetio-pathophysiology of mood disorders. Several candidate mediators of these effects are proposed, including increased brain pro-inflammatory cytokine levels per se or altered metabolism of tryptophan.

Methods

In the present study, different approaches were applied to activate the immune system in mice: (1) single, intra peritoneal injection of a CD40 agonist antibody (CD40 AB), (2) region-specific TNF (Tumor necrosis factor) overexpression in the central nervous system and (3) peripheral TNF increase by repeated daily injections. The behavioural readouts consisted of a home-cage saccharin preference test and fear conditioning experiments. Using neuro-biochemical methods (e.g. flow cytometry), we further examined changes in TNF-levels and substrates of the tryptophan metabolism.

Results

Acute peripheral CD40 AB induced an increase in plasma TNF, sustained activation of the kynurenine pathway, and depression-relevant behaviour (decreased saccharin consumption and decreased fear conditioning). These behavioural effects were prevented by the co-administration of the TNF blocker etanercept. Chronic TNF over-expression in CNS did not result in behavioural effects. Repeated peripheral TNF induced depression-relevant behaviour, either similar (i.e. decreased saccharin consumption) or opposite (i.e. increased CS fear expression) to those of acute CD40 AB, but without activating the kynurenine pathway.

Discussion

We could show that peripheral TNF was sufficient to induce emotional dysfunction via a non-kynurenine pathway and was necessary but not sufficient to induce emotional and cognitive dysfunctions via a kynurenine pathway. Building on this evidence, on-going studies will elucidate the specific role of TNF, additional pro-inflammatory cytokines and the kynurenine pathway, in periphery and CNS, in the aetio-pathophysiology of depression and its co-morbidity with autoimmune disorders.
Title

Methylphenidate and Neuronal Maturation

Authors

Jasmin Bartl, Katharina Schmidt, Stefania Niedecker, Susanne Walitza, Edna Grünblatt

Affiliations

University Clinics of Child and Adolescent Psychiatry, Neurobiochemistry Laboratory, University Zurich

Introduction

The psychostimulant methylphenidate (MPH; often known as Ritalin®) is one of the most controversy discussed medication for children with attention-deficit/hyperactivity disorder. Almost no other drug based therapy leads to so highly emotional discussions between public, politicians, parents and researcher. Since therapy often begins at a time when the brain still maturate and still too less is known about the influence of MPH on the brain development and the long-time consequences, parents can be worried and ask the question: Is the treatment with MPH a benefit or a risk for my affected child? We tried to learn more about the therapeutic effect of MPH on neuronal level and examined the influences of acute treatment with MPH on the maturation and proliferation rate of different dopaminergic neural cell types, including neural stem cells.

Methods

Different cell types (murine stem cells; rat pheochromatocyte; human neuroblastoma) were treated with a range of MPH (1-100nM; 1-100µM). Cell proliferation was monitored noninvasively, in real-time using impedance measurement and maturation rate was investigated via cytochemistry staining. Determination of the first significant time point of treated cells in comparison to untreated cells were analysed using MATLAB® followed by verification of proliferation results using in-vitro labelling with the thymidine analogue 5-bromo-2-desoxyuridine.

Results

After already the very low dose of 1nM MPH treatment, the cell proliferation was significantly inhibited in all used cell types, while in contrast the neuronal maturation was significantly enhanced. This effect was detectable up to 100nM MPH.

Discussion

The effects of MPH on neuronal maturation are highly specific and dependent on numerous factors, but our first results lead to hypothesis that MPH enhances brain maturation in a positive way. Future studies on structural and functional neuronal changes will be necessary to enlighten more details about this possible neurotrophic effect of MPH.
B)  
*Theoretical Psychiatry: Computational approaches, behavioral models, humanities*
Maintaining homeostasis by decision-making

Authors
Christoph W. Korn1 and Dominik R. Bach1, 2

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Introduction
Living organisms need to maintain energetic homeostasis, which often implies making complex long-term decisions. For example, humans may have to decide between foraging for attractive but hard-to-get, and unattractive but easy-to-get food, under threat of starvation. In contrast to standard economic decision-making models, homeostatic principles predict that such decisions should minimize the probability of starvation. Here, we aim to validate a model of homeostasis in healthy participants that can be extended to test for the assumed dysfunctional homeostatic set points entertained by psychiatric populations.

Methods
In a first study, we tested whether models based on homeostatic considerations explain human decisions better than standard economic models. We devised a virtual foraging task. Participants (n=22) chose repeatedly between two foraging environments, in which they gained and lost energy probabilistically according to the statistics of the chosen environment. Reaching zero energy was framed as starvation. We used the mathematics of random walks to derive outcome distributions of the environments. This also furnished equivalent lotteries, presented in a purely economic, casino-like frame, in which starvation corresponded to winning nothing. In a second study, we tested whether human decisions optimally minimize threats to homeostasis. An independent group of participants (n=28) performed an adapted version of the virtual foraging task, in which optimal choices were analytically derived.

Results
The model comparison of the first study showed that—in both the foraging and the casino frames—participants’ choices minimized starvation probability and maximized expected value. In both frames models based on homeostatic considerations outperformed economic models. The second study showed that participants were almost optimal in minimizing long-term starvation probability.

Discussion
Homeostatic principles may be better suited to explain human decision-making than standard economic models—even for virtual threats to homeostasis. Our results promise an empirical test of the assumed links between altered homeostatic mechanisms and decision-making deficits in psychiatric patients.
Modelling approach-withdrawal oscillations in a human anxiety test bed

Authors
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Introduction
Defensive behaviours in rodent conflict tests are often regarded as a model for understanding human anxiety. The mouse defence test battery (MDTB) is a test bed to quantitatively measure defensive reactions of mice facing a predator. A version of it consists of a natural predator placed at one end of a closed straight alley, in which approach-withdrawal oscillations of the position of the mouse are observed.

Methods
A computerised human translation of the MDTB has recently been proposed, in which a volunteer controls a virtual agent through a joystick. The agent moves between two moving virtual predators, and gets punished if any of the predators reaches the player. In this task, oscillations of the player's position are observed and interpreted as risk assessment behaviour, in analogy with the animal test. Here, we sought to model the behaviour of the agent under plausible assumptions on biological constraints and costs involved in the task.

Results
Our model argues that the policy of the agent relies on a trade-off between estimated future position and action uncertainty: keeping the current speed might lead toward an undesirable position but allows for a more precise estimation of it, while modifying the speed also involves motor uncertainty, making the future position more distributed. Simulations reveal approach-withdrawal oscillations in the player's position, in line with experimental data.

Discussion
This provides an explanation of observed behaviour in the framework of sensorimotor control theory. Future work will test the predictions of the model in light of the effect of anxiolytic drugs on approach-withdrawal oscillations.
Title

Schizophrenia*: use and function of a contested term

Authors

Anke Maatz MA MD, Speciality trainee and postdoctoral researcher

Affiliations

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Introduction

Whilst one of psychiatry’s most prominent diagnoses, term and concept ‘schizophrenia’ remain contested. Criticisms of ‘schizophrenia’, brought forward by ‘experts by training’ and ‘experts by experience’ alike, take issue with the purported lack of a scientific basis as well as with ‘schizophrenia’s being harmful and stigmatising. In response to such criticisms, some countries have already embarked on re-naming ‘schizophrenia’. Yet a systematic analysis of the term’s usage is lacking.

Method

By offering tools to analyse large quantities of text – so-called corpora – in which in this case the term ‘schizophrenia’ is used, a corpuslinguistic approach can yield insights into the (linguistic) functioning as well as the conceptual understanding of the term. For this purpose, all articles published in the Schizophrenia Bulletin since 1979 were made available as a corpus searchable for lexical and grammatical parameters employing CQPweb software. Subcorpora were built such that language use by ‘experts by training’ could be compared to that of ‘experts by experience’.

Results

The analysis shows significant variations in the use of ‘schizophrenia’ and its derivatives between ‘experts by experience’ and ‘experts by training’ and thereby recasts questions of stigmatisation. It also makes visible the close connectedness of conceptual understanding and linguistic expression pointing to discrepancies as well as to attempts to express complexity and fluidity.

Discussion

Language usage mirroring discourses and ways of thinking, a corpuslinguistic analysis of psychiatric literature can thus not only help answer the question whether our conceptual understanding is adequately expressed in the way we speak and write, but also tell us something about the very conceptual understanding we hold.
Reduced Sleep Spindle Activity in Early Onset Schizophrenia

Tesler, N.\textsuperscript{1,2,4}, Gerstenberg, M.\textsuperscript{2}, Franscini, M.\textsuperscript{2}, Jenni, O.G.\textsuperscript{1}, Walitza S.\textsuperscript{2}, Huber, R.\textsuperscript{1,2,3,4}

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\end{enumerate}

Introduction
Schizophrenia is a complex neuropsychiatric disorder affecting 1% of the worldwide population. Its typical onset is during late adolescence. Abnormal brain connectivity, specifically, thalamocortical deficits have been reported in adult schizophrenia. The sleep spindle, a thalamocortically generated phasic oscillation between 12-15 Hz during non-rapid eye movement (NREM) sleep, reflects the integrity of the thalamocortical system. Adult patients with schizophrenia show a decrease in sleep spindles. Furthermore, spindle deficits were associated with a greater severity of positive symptoms. The focus of our study was on investigating sleep spindles in adolescents at an early stage of the disease by means of high density electroencephalogram (EEG) and relating alterations in sleep spindles to symptom severity.

Methods
All-night high-density EEG was recorded in 9 patients (16.1±0.5y) and 9 controls (16.2±0.5y). Study inclusion for the patients required a diagnosis of a schizophrenia, schizophreniform disorder or a brief psychotic disorder according to DSM-IV. Actual symptom severity was assessed using the Positive and Negative Syndrome Scale (PANSS). Sleep stages were visually scored. Automatic sleep spindle detection was performed, to assess spindle characteristics. As we found major differences in spindle density, subsequent analysis was focussed on sleep spindle density, in the first hour of NREM sleep.

Results
Early onset patients showed significantly reduced spindle density over a large area of centro-temporal brain areas. A correlation of the electrodes showing a significant group difference with the PANSS positive score showed a significant negative correlation (r=-0.75, p=0.02).

Discussion
Our findings indicate that sleep spindle deficits can already be detected in early onset schizophrenia, are associated with positive symptoms and may therefore be an electrophysiological marker for the disorder.
Title

Alcohol addiction: dopamine, goals, habits and relapse

Authors

Dr. med. Quentin Jan Marie Huys

in collaboration with the DFG-FOE ‘LEaD’ Group (including Lorenz Deserno, Maria Garsusow, Andreas Heinz, Stephan Nebe, Michael Rapp, Daniel Schad, Florian Schlegenhaus, Miriam Sebold, Michael Smolka, Christian Sommer, Ulrich Zimmermann) and Dirk Geurts

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Introduction

Addictive drugs often prove too much of a temptation to resist, possibly because they undermine neural learning signals. Learning in Alcohol Dependence (LeAD) is a longitudinal study examining the contribution of model-based and model-free learning mechanisms in alcohol addiction.

Methods

Longitudinal two-centre study of detoxified patients with alcohol use disorder. Participants and matched controls underwent fMRI with two tasks assessing the relative impact of model-based and model-free learning: a two-step task, and a Pavlovian-instrumental transfer (PIT) task. A subset of controls also underwent F-DOPA PET. Patients were followed up for three months.

Results

Alcohol addiction was behaviourally accompanied by a shift towards away from model-based behaviour. After losses, there is difficulty in re-establishing goal-directed control. Intriguingly, measures of presynaptic dopamine synthesis in the nucleus accumbens reduced model-free signals and promote model-based learning. During PIT, patients show a slightly enhanced influence of Pavlovian stimuli on instrumental behaviour. In those patients who go on to relapse, this PIT behaviour appears to be driven by the nucleus accumbens.

Conclusion

A shift towards model-free neural systems is a relapse risk for alcohol use disorders. The PET-fMRI findings raise important questions about the distinct contributions phasic and tonic dopamine may have in addiction.
Title
Affective State and Voice

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Background
Human speech is greatly influenced by the speakers’ affective state, such as sadness, happiness, grief, guilt, fear, anger, aggression, faintheartedness, shame, sexual arousal, love, amongst others. Attentive listeners discover a lot about the affective state of their dialog partners with no great effort, and without having to talk about it explicitly during a conversation or on the phone. On the other hand, speech dysfunctions, such as slow, delayed or monotonous speech, are prominent features of affective disorders.

Methods and Materials
This project was comprised of 4 studies with healthy volunteers from Bristol (English: n=117), Lausanne (French: n=128), Zurich (German: n=208), and Valencia (Spanish: n=124). All samples were stratified according to gender, age, and education. The specific study design with different types of spoken text along with repeated assessments at 14-day intervals allowed us to estimate the “natural” variation of speech parameters over time, and to analyze the sensitivity of speech parameters with respect to form and content of spoken text. Additionally, our project included a longitudinal self-assessment study with university students from Zurich (n=18) and unemployed adults from Valencia (n=18) in order to test the feasibility of the speech analysis method in home environments.

Results
The normative data showed that speaking behavior and voice sound characteristics can be quantified in a reproducible and language-independent way. The high resolution of the method was verified by a computerized assignment of speech parameter patterns to languages at a success rate of 90%, while the correct assignment to texts was 70%. In the longitudinal self-assessment study we calculated individual “baselines” for each test person along with deviations thereof. The significance of such deviations was assessed through the normative reference data.

Conclusions
Our data provided gender-, age-, and language-specific thresholds that allow one to reliably distinguish between “natural fluctuations” and “significant changes”. The longitudinal self-assessment study with repeated assessments at 1-day intervals over 14 days demonstrated the feasibility and efficiency of the speech analysis method in home environments, thus clearing the way to a broader range of applications in psychiatry.
References

Acknowledgements
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Memory reactivation during sleep supports qualitative changes in memories

Introduction
Memory reactivations during sleep have been demonstrated to immediately stabilize newly acquired memory contents during sleep. However, it still remains unclear whether reactivation also supports qualitative changes of these memories (e.g. the extraction of a gist). The emotional valence being defined as the level of pleasantness that is generated when a stimulus is processed (varies from positive to negative) is one of the most pervasive and fundamental gist representation of a stimuli. Because children were found to outperform adults in their ability for qualitative changes of memory representations during sleep, we chose this age-group to scrutinize the impact of memory reactivation during sleep on qualitative and quantitative changes in memories.

Methods
In the evening, subjects learnt to associate ambiguous pictures of every-day life situations with either positive or negative semantically related words which thereby induce a corresponding valence of the presented pictures. During post-learning deep sleep half of the picture-word associations were reactivated by acoustically presenting the words.

Results
Picture-word associations that were reactivated during the post-learning night were better remembered the next morning but worse one week later when compared to non-reactivated stimuli. Valence rating of pictures the next morning was not affected by reactivation during the post-learning night. However, this was the case one week later as indicated by greater knowledge about the acquired emotional tone of reactivated picture-word associations.

Conclusion
These findings suggests that memory reactivation during sleep supports the long-term extraction of a gist of memories (i.e. the valence of an acquired memory) at the expense of context information.
Influence of aripiprazole, risperidone, and amisulpride on sensory and sensorimotor gating in healthy “low and high gating” humans and relation to clinically associated psychometry

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It has been suggested that the assessment of gating in humans and rodents with naturally low gating levels might be a useful model to screen for novel compounds with antipsychotic properties. In order to validate and extend this translational approach of neurochemical manipulation in healthy human volunteers exhibiting low levels of gating, several atypical antipsychotics (APPs) (aripiprazole, risperidone, amisulpride) have been tested. Furthermore, neuropsychopharmacological compounds (lorazepam, modafinil, valproate) without antipsychotic properties serving as negative control treatments were investigated. Moreover, gating measures were related to clinically associated psychometric indices.

In a placebo-controlled within-subjects design, healthy males received either a single dose of aripiprazole (15mg risperidone (n=28), amisulpride and lorazepam (n=30), or modafinil and valproate (n=30), and placebo. Prepulse Inhibition (PPI) and P50-suppression were assessed and subjects were stratified into low and high gaters. Furthermore, clinically associated symptoms were assessed using the SCL-90-R.

Aripiprazole, risperidone, and amisulpride increased P50-suppression in subjects with low P50 gating. In contrast, lorazepam, modafinil, and valproate did not influence P50-suppression in low gating volunteers. Furthermore, P50 gaters reported more clinically associated symptoms than high P50 gaters. Aripiprazole led to a PPI increase in the low subgroup. In contrast, modafinil and lorazepam attenuated PPI, whereas risperidone, amisulpride, and valproate did not influence PPI in either subgroup.

P50 suppression in low gating volunteers was enhanced by AAPs and seems to be an antipsychotic-sensitive neurophysiologic marker. This is supported by the association of low P50 suppression levels and higher clinically associated scores. P50 suppression in low gating healthy subjects might reflect a different surrogate maker than low PPI gating. The translational model investigating differential effects of AAPs on gating in healthy subjects with naturally low gating might be beneficial for phase I/II development-plans by providing additional information for critical decision-making (i.e., dose-finding).
Neuroimaging: MRI, PET, NIRS, Spectroscopy, EEG, MEG
Serotonergic modulation of emotion processing by the mixed 5-HT1A/2A receptor agonist psilocybin reduces amygdala activation to negative stimuli – a pharmacological fMRI study

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Purpose:
There is growing evidence supporting the notion that the serotonin (5-HT) agonist psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine), the main psychoactive principle of “magic mushrooms”, may reduce neural responses to negative stimuli and induce long-lasting positive mood and attitudes [1]. Such a profound effect on emotion and mood processes might underlie the putative antidepressant properties of psilocybin, as it has repeatedly been shown that a critical mechanism for antidepressant efficacy may be an effect which counteracts negative mood states and limbic hyperactivity in response to negative stimuli in patients with major depression. A recent clinical study [2] in patients with depression and anxiety related to advanced-stage cancer supports this notion: a single dose of psilocybin significantly decreased anxiety and increased positive mood for up to 6 months. However, the neurobiological mechanisms by which psilocybin influences emotion processing remain poorly understood. In particular, it is still unclear whether psilocybin modulates the activity of the amygdala, a region that plays a crucial role in the neural effects of antidepressants, during emotion processing, and whether any psilocybin-induced effect on amygdala activity during emotion processing is related to changes in mood state.

Methods:
In this study, the acute effects of low-dose psilocybin (0.16 mg/kg) on amygdala activation were measured using blood oxygenation level-dependent (BOLD) functional magnetic resonance imaging (fMRI) during an emotion processing task and in combination with assessment of mood changes. 25 healthy subjects (16 males, mean age 24.2 ± 3.42 years) were included in the study. The study followed a randomized, double-blind, placebo-controlled, cross-over design. Subjects received either placebo or 0.16 mg/kg oral psilocybin at two separate imaging sessions 2 weeks apart. During scanning, subjects performed an established amygdala reactivity task, using picture stimuli from the International Affective Picture System (IAPS). Mood changes were assessed using the Positive and Negative Affect Schedule (PANAS) and the state portion of the State-Trait Anxiety Inventory (STAI).

Results:
Both whole-brain voxel-wise and region of interest (ROI)-based analyses showed that right-amygdala activation in response to negative stimuli was significantly lower after psilocybin administration than after placebo administration (psilocybin mean ± SD: 0.36 ± 0.28; placebo: 0.58 ± 0.36; p < 0.001). Further, psilocybin significantly increased positive mood (p = 0.001), but not anxiety (p = 0.37), and this effect was correlated to psilocybin-induced decrease of amygdala reactivity (r = -0.46, p < 0.05).

Conclusions:
Results show that acute administration of low-dose psilocybin decrease amygdala reactivity to negative pictures. Notably, this effect was correlated with psilocybin-induced increase in positive mood. These findings confirm and extend previous evidence that 5-HT1A/2A receptor stimulation
may induce positive mood states and decrease neural responses to negative stimuli. In addition, this study demonstrates that the amygdala, a key component within limbic structures implicated in emotion processing, may be an important neural target underlying the hypothesized antidepressant properties of psilocybin.

References:


Title

State-dependent functional connectivity disturbance within and between brain networks in children with ADHD

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Background

Attention deficit hyperactivity disorder (ADHD) is one of the most common childhood neuropsychiatric disorders. Recent approaches examined brain connectivity for dysfunction in functional network organization. We hypothesize that connectivity within the default mode network (DMN), and the anticorrelation between the DMN and the cognitive control network (CCN) is reduced in ADHD, especially when switching from rest to task states. We thus examined altered state-dependent functional connectivity (FC) within and between two brain networks (DMN, CCN) in children with ADHD.

Methods

We recorded fMRI data to compare functional brain network differences between resting and task states in children with ADHD and a control group. ICA was used for functional segmentation of both tasks and groups before calculating FC within and between different networks, and compare them among tasks and groups. We only report on differences between the Stop task and the resting state.

Results

Preliminary results suggest that within the DMN, children with ADHD showed less negative FC in the long-range connections between anterior and posterior cingulate cortex (ACC–PCC) and between ACC and precuneus. The FC group comparison between states and networks (DMN – CCN) indicated that the ADHD group had less negative correlations between CCN and DMN particularly in PCC.

Conclusions

These findings suggest that children with ADHD may display disturbed FC differences between task and resting states. Children with ADHD show generally less negative FC differences within the DMN. The inverse correlation of the DMN and CCN is less pronounced in children with ADHD. Especially the long-range connections within the DMN and between the DMN and the CCN may be particularly impaired. These results suggest that children with ADHD may have specific difficulties while switching between rest and task states. These findings improve the understanding of ADHD as a disorder characterized by a dysfunctional network organization.
Title

Specific Connectivity Profiles for Deep and Superficial Amygdala Nuclei in Humans

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Amygdalo-cortical (AC) pathways have been studied thoroughly in animals using qualitative and semi-quantitative tracing techniques. Probabilistic tractography supplies a quantitative method for analyzing connectivity in humans. Systematic analyses of AC networks in humans are still missing. Here we provide detailed connectivity profiles for deep and superficial amygdala nuclei.

Probabilistic tractography was performed in 8 individuals, using DW-MRI. We relied on a previously established amygdala parcellation into 2 clusters (deep/sup). Using these as seed areas, we determined connections to the cortex, segmented into 2x35 areas based on T1w images.

Parahippocampal, entorhinal, fusiform, insula and lateral occipital cortex, in descending order, showed highest connectivity to the amygdala. Differences in deep and superficial profiles were found. We observed stronger connections for deep clusters to the entorhinal and the pericalcarine or for superficial clusters to the inferior parietal and the lateral occipital cortex.

Several AC pathways are proposed to be implicated in various neurological and neuropsychiatric disorders, e.g. autism (fusiform) or schizophrenia (visual cortex). Thus a sound understanding of AC connectivity in humans is needed.

We propose that connectivity profiles may be used as a guide for functional and pathophysiological neuroimaging studies.
Title

Improving amygdala regulation during emotional stimulation using real-time fMRI neurofeedback training

Authors

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Introduction

The amygdala is a key structure in the processing of emotional information and the main target of emotion regulation strategies (cognitive reappraisal, mindfulness). In anxiety and affective disorders, the amygdala is overactive, but resolves with successful therapy. Training to regulate amygdala activity by means of real-time fMRI neurofeedback could therefore represent an additional therapeutic approach in emotion regulation disorders.

Methods

All subjects underwent 4 training sessions. The first study included 6 subjects, the second study 16 subjects. In every session, the amygdala was stimulated using negative emotional faces (study 1) and negative emotional IAPS pictures (study 2). The feedback of the intensity of amygdala activity was presented to the participants by changing colour blocks on both sides of the stimuli. The training effect of the real-time fMRI neurofeedback was measured comparing the difference between a regulation condition (instruction: use of cognitive reappraisal) and a passive viewing condition over time in the amygdala.

Results

In both studies, amygdala down-regulation increased over the sessions, with a maximum in the last session. Conclusions: We could show in two studies with different stimuli that it is possible to use real-time fMRI neurofeedback for training of amygdala regulation. The neural circuit involved in this training as well as methodological questions (optimal number of sessions) will be further investigated.
Apathy but not diminished expression in schizophrenia is associated with ventral striatal activation during reward anticipation

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Introduction
The negative symptoms of schizophrenia strongly contribute to impairments in social and occupational functioning. In neuroimaging research, increasing evidence suggests that negative symptoms are associated with altered hemodynamic activation of subcortical regions in the mesolimbic reward system. However, the neurobiological basis of the distinct symptom dimension in negative symptoms is poorly understood. This study examines the neural correlates of negative symptom total and factor scores during a reward processing task.

Methods
We included 27 patients with schizophrenia and 25 healthy controls. Negative symptoms were assessed with the Brief Negative Symptom Scale (BNSS) and the Scale for the Assessment of Negative Symptoms (SANS). Both groups performed a modified version of the Cued Reinforcement Reaction Time Task emphasizing task performance for obtaining rewards. Functional Imaging Data were acquired on a Philips Achieva 3.0T magnetic resonance (MR) scanner.

Results
We focused our fmri analysis on the contrast “anticipation of a high reward versus anticipation of no reward” in the nucleus accumbens as predefined ROI. There were no significant differences between groups during anticipation of a reward. Correlation analysis for patients with schizophrenia yielded a significant negative correlation between the “Apathy” dimension and activation in the nucleus accumbens during reward anticipation (r=-0.62, p=0.001). Concerning the “Diminished Expression” dimension no correlation with activation in the nucleus accumbens was observed (r=-0.23, p=0.24).

Discussion
Reduced activation in the nucleus accumbens during Anticipation of reward is more specifically related to the negative symptom dimension of Apathy than to the “Diminished Expression” dimension. This aberrant neural response in the subcortical reward system emerged dimensionally in all severity stages. We suggest that dysfunction in reward anticipation leads to the clinical expression of apathy.
Title

Effects of Posture and Stimulus Bandwidth on Peripheral Physiological Responses to Loud

Authors

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Background

The “loud-tone” procedure consists of presenting a series of brief, loud, pure-tone stimuli in a task-free situation and is an established paradigm for measuring autonomic sensitization in posttraumatic stress disorder (PTSD). Successful use of this procedure during fMRI requires elicitation of brain responses that have sufficient signal-noise ratios when recorded in a supine, rather than sitting, position. We investigated the effect of posture and stimulus bandwidth on peripheral psychophysiological responses to loud sounds.

Methods

Healthy subjects (N=24) weekly engaged in a loud-tone-like procedure that presented 500 msec, 95 dB pure-tone or white-noise stimuli, either while sitting or supine and while peripheral physiological responses were recorded.

Results

Heart rate, skin conductance, and eye blink electromyographic responses were larger to white-noise than pure-tone stimuli (p’s < 0.001, generalized eta’s squared between 0.073 and 0.076). Psychophysiological responses to the stimuli were similar in the sitting and supine position (p’s ≥ 0.082).

Discussion

Presenting white noise, rather than pure-tone, stimuli may improve the detection sensitivity of the neural concomitants of heightened autonomic responses by generating larger responses. Recording in the supine position appears to have little or no impact on psychophysiological response magnitudes to the auditory stimuli. The supine position seems to have only a limited impact on psychophysiological, primarily skin conductance, responses to the sounds.
**Title**

*Amyloid-beta correlates with 7 Tesla fluid-attenuated inversion recovery (FLAIR) in hippocampus and brainstem of cognitively healthy elderly subjects*

**Authors**

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**Keywords:** MRI, 7 Tesla, Alzheimer’s disease, PiB PET, FLAIR

**Introduction**

The deposition of cerebral amyloid-beta (Aβ) is a pathological hallmark of Alzheimer’s disease (AD), and can be assessed in vivo using Pittsburgh compound-B positron emission tomography (PiB PET). Since Aβ accumulation begins years before the clinical onset of AD, the significance of Aβ deposits in healthy elderly subjects is a research topic of particular relevance. The current study investigates potential regional effects of Aβ on brain tissue integrity as indicated by fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI) in healthy elderly subjects.

**Methods**

Fourteen healthy elderly subjects (age=69±8; female/male=6/8) underwent neuropsychological assessment to guarantee normal cognition, and PiB PET for quantification of regional Aβ. Additionally, structural T1-MPRAGE and FLAIR MRI were obtained at high field strength of 7 Tesla. Whole brain segmentation was applied to T1-MPRAGE, FLAIR and PiB PET volumes, and volume-normalized intensities were calculated for anatomical subregions. Regional relationships between PiB and FLAIR signal intensities were assessed based on spearman’s rank correlation coefficient rho, followed by Holm-Bonferroni correction for multiple testing.

**Results**

Neuropsychological assessment showed normal cognitive performance in all participants. Mean regional PiB PET and FLAIR intensities were normally distributed and independent. Significant statistical dependence between volume-normalized PiB PET signals and FLAIR intensities resulted for the following brain regions: hippocampus (right: rho=0.86; left: rho=0.84), brain-stem (rho=0.85), left basal ganglia vessels (rho=0.82).

**Conclusions**

This finding of significant relationships between PiB PET and FLAIR MRI signals mainly observable in the hippocampus and brainstem, suggests regional Aβ-associated brain tissue abnormalities such as edema in cognitively healthy elderly subjects. Further studies are necessary to clarify the relevance of this finding regarding risk for neurodegenerative diseases such as AD.
Frontal brain activation during emotional Stroop task in individuals at risk for schizophrenia and bipolar disorder using fNIRS.

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The study was conducted within the framework of The Zurich Program for Sustainable Development of Mental Health Services (ZInEP).

Introduction
Emotional interference is a well-known phenomenon described in healthy individuals and in different groups of psychiatric patients. A recent imaging study has linked decreased activation in the dorsolateral and medial prefrontal cortex (PFC) during the emotional Stroop task with increased anxiety sensitivity. Our goal was to investigate frontal brain activity in individuals at risk for schizophrenia and bipolar disorder during the emotional Stroop task.

Methods
The analysis included the following four groups: at-risk for bipolar disorder (BIP; n=16), at-high risk for schizophrenia (HR; n=41), at-ultra-high risk for schizophrenia (UHR; n=48), and healthy controls (HC; n=46). A 52-channel fNIRS was used to measure brain activity during the emotional Stroop task, which was composed of positive, negative and neutral words in four colors (red, yellow, blue and green). Activity in medial and bilateral dorsolateral PFC was compared between all the groups.

Results
The analysis of the PFC revealed significantly lower levels of oxygenated hemoglobin in HR and UHR compared to HC in the right dorsolateral PFC but only for the negative words (t_{85}=2.42 and t_{92}=2.74, p<0.05 respectively). There were no differences in the medial PFC activity between the groups.

Discussion
This is the first study investigating frontal brain activity during the emotional Stroop task in individuals at risk for schizophrenia and bipolar disorder. Significantly lower activity in the right dorsolateral PFC for the negative words in the HR and UHR groups was in line with previous studies. These findings could indicate that individuals at high risk for schizophrenia show higher fear sensitivity compared to the healthy controls.
Title

Frontal and temporal brain activity during a verbal fluency task in individuals at risk for psychosis – a functional near-infrared spectroscopy study.

Authors

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The study was conducted within the framework of The Zurich Program for Sustainable Development of Mental Health Services (ZInEP).

Introduction

Lower frontal brain activity during the verbal fluency task (VFT) has been observed in individuals suffering from schizophrenia and bipolar disorder by means of the functional near-infrared spectroscopy (fNIRS). Our goal was to investigate if the abnormalities in the frontal brain activity can also be observed in the at-risk individuals for schizophrenia or bipolar disorder.

Methods

Four groups of individuals were examined in the study: at-risk for bipolar disorder (BIP; n=13), at-risk for schizophrenia (HR; n=39), at-ultra-high risk for schizophrenia (UHR; n=41), and healthy controls (HC; n=35). We used a 52-channel fNIRS to measure the changes in concentration of the oxygenated hemoglobin, which reflects the brain activity. During the measurement all participants performed semantic and phonemic VFT. The analysis focused on the bilateral prefrontal and frontotemporal cortex (PFC, FTC).

Results

Individuals in the HR and UHR groups produced significantly less words in phonemic and semantic VFT compared to the HC. The region of interest analysis of the brain activity revealed significant differences between the groups in the left PFC during the phonetic VFT \((F_{(3,122)}=3.059, p < 0.05)\). Furthermore, post-hoc tests revealed a lower left prefrontal activation in the UHR group compared to the HC \((p < 0.05, 95\% \text{ CI } [0.007-0.055])\).

Discussion

These preliminary findings indicate that the behavioral deficits observed in the UHR group are partially reflected in the lower PFC activation. These results are in line with previous studies investigating patients with manifest schizophrenia and allow an interpretation that the functional deficits in the PFC appear already in individuals at ultra-high risk for psychosis.
Title

Neurobiological underpinnings of auditory intensity processing: a MEG study

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Introduction
The loudness dependence of auditory evoked potentials (LDAEP) is a proposed biomarker for central serotonergic activity. The validity of this biomarker is unsatisfactory for practicable application thus far. Particularly, the different source localization approaches applied in LDAEP research are not comparable. Thus, underlying generators in loudness perception that contribute to the scalp potentials are of interest. Although a wide research have proposed the involvement of higher-order networks, its precise location is still debated.

Methods
Magnetoencephalography (MEG, whole-head 248 channels) was applied in order to localise the sources of the N1m (75-125 ms) component elicited by tones of different intensities with high temporal resolution. We investigated 19 healthy male right-handed subjects (mean age 26.5 ± 4.0 years). Tones of six different intensities (10-60 dB SL, 1000 Hz, 40 ms duration, SOA randomized between 2-3 s) were presented binaurally in a pseudo-randomized order through earphones with plastic tubes. Magnetic field tomography was used in order to localise the primary current density in each voxel and at each time point. Voxel-wise root mean squared values were entered in a generalized linear model, corrected for multiple comparisons. Within the anatomical regions of interest we performed a time-course analysis for each intensity to elucidate the cortical activation sequence across time.

Results
We found significant activations in the primary auditory cortex, the posterior cingulate cortex (PCC), the premotor cortex and the primary somatosensory cortex by comparing the tones with highest and lowest sensation levels. The time course analysis revealed that the primary sensory areas were activated earlier (90 ms) than the PCC (100 ms) and the premotor cortex (120 ms).

Conclusion
The results show the activation of a widespread network in loudness perception. The PCC, which plays an essential role as a hub in intrinsic connectivity networks by activating networks appropriate for the current behavioural state, might be involved in the top-down processing during perception. In line with other findings, the activation in the premotor cortex might be related to an orienting response linked to a novel stimulus or to a startle response to a harmful stimuli both aiming at an action preparation to protect the body from harmful events. These findings have strong implications on analysis approaches used in LDAEP research.
Acknowledgements
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Symptom dimensions are differentially associated with reward processing in unmedicated persons at risk for psychosis

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Introduction
There is growing evidence that reward processing is disturbed in schizophrenia. However, it is uncertain whether this dysfunction predates or is secondary to the onset of psychosis. Thus, the aim of this study was to examine the neural response to reward expectation and reward outcomes in unmedicated participants at-risk for psychosis compared to healthy adults.

Methods
A modified version of the monetary incentive delay task was presented to 21 unmedicated individuals at-risk for psychosis and 24 healthy controls during fMRI scanning. Data analysis focused on neural responses to expectation and receipt of reward. Individual parameter estimates were then extracted in a priori defined region-of-interest (i.e. left and right ventral striatum (VS), anterior Insula (Alns) and medio orbitofrontal Cortex (mOFC)) and were used to determine how these were correlated with clinical symptom scores.

Results
While anticipating rewards, the high-risk sample exhibited additional activation in the posterior cingulate cortex, and the medio- and superior frontal gyrus, whereas no significant group differences were found after rewards were administered. Importantly, symptom dimensions were differentially associated with anticipation and outcome of the reward. Positive symptoms were correlated with the anticipation signal in the ventral striatum VS and the rAl. Negative symptoms were inversely linked to outcome-related signal within the VS, and depressive symptoms to outcome-related signal within the mOFC.

Discussion
Our findings provide evidence for a reward-associated dysregulation that can be compensated by recruitment of additional prefrontal areas.
We propose that stronger activations within VS and rAI when anticipating a reward reflect abnormal processing of potential future rewards. Moreover, this may predispose a person to positive symptoms. Additionally, we report evidence that negative and depressive symptoms are differentially associated with the receipt of a reward, which might demonstrate a broader vulnerability to motivational and affective symptoms in persons at-risk for psychosis.
**Title**

*Human primary auditory cortex encodes threat-predicting information of complex but not simple sounds during fear conditioning*

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**Introduction**

Learning to predict an aversive event from neutral stimuli is experimentally modelled in fear conditioning. In delay conditioning paradigms, a neutral stimulus (conditioned stimulus, CS+) contingently co-terminates with an aversive stimulus (unconditioned stimulus, US) which after a few trials induces a conditioned response (CR) during anticipation of the US. In animal studies the amygdala has been identified as brain structure required for this type of learning when simple sine tones are used as CS. On the other hand, rodents with lesioned primary auditory cortex (PAC) still show a CR, suggesting the PAC may not be required for fear learning. Recently this view has been challenged by studies using complex sounds as CS, comprised of multiple frequencies and temporal patterns. In these studies, fear learning was impaired after PAC inhibition. This suggests that PAC is necessary for fear learning from complex sounds, either in order to extract information from the individual sounds and forward them to the amygdala where CS/US association is learned, or to directly form a CS/US association.

**Methods**

In the present study, we investigate the role of PAC for fear learning in humans. Twenty healthy subjects underwent a differential delay fear learning paradigm in a reinforcement context where the CS+ is probabilistically paired with an unpleasant electrical stimulation while the CS− is always presented alone. In a non-reinforcement context, different sets of complex and simple sounds were always presented alone (neutral sounds, NS). High-resolution functional MRI (fMRI) was recorded to measure blood-oxygen-level dependent (BOLD) signal associated with the presentation of sounds. Skin conductance response (SCR) was recorded simultaneously to estimate the conditioned sympathetic response.

**Results**

We employed multivariate pattern analysis (MVPA) to discriminate BOLD patterns elicited by CS+/CS−, or two different NS, in the superior temporal sulcus including PAC. Classification performance in the STS was higher for complex CS than for simple CS or NS, as shown by an interaction complexity x reinforcement context.

**Discussion**

Our results indicate that PAC encodes differences between complex (but not simple) CS+ and CS− over and above physical differences between the two sounds. This suggests that the role of the PAC extends beyond sound processing and is in keeping with a model of a distributed fear learning network in the human brain, involving both PAC and amygdala for establishing fear memory.
Title

Towards metabolic profiling of the reward circuitry in addiction: Small-voxel, non-water-suppressed 1H-MRS in the nucleus accumbens at 3T

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Introduction

Data from animal studies show that chronic administration of cocaine leads to decreased levels of glutamate (Glu) in the nucleus accumbens (NAcc); whereas drug-seeking reinstatement is associated with enhanced glutamatergic transmission. However, little is known about neurometabolic changes in humans, mainly due to previous methodological restrictions. We thus aim to investigate the changes associated with chronic cocaine use on Glu homeostasis in NAcc of human subjects using a proton magnetic resonance spectroscopy (1H-MRS) protocol that we have recently developed. 1H-MRS allows for the quantification of brain metabolites such as Glu even within small subcortical volumes that have been difficult to assess in humans yet. The aim of this pilot study was to verify the intra-individual consistency of metabolic concentrations in NAcc over time by sequential 1H-MRS measurements.

Methods

To detect potential individual fluctuation, five non-water suppressed PRESS localization combined with inner-volume saturation was performed in one healthy volunteer at five different time points. MRS spectra were obtained from the left NAcc as the region of interest (voxel size=9.4x18.8x8.4mm). Metabolite concentrations ratios to creatine (Cr) based on fitting results (LCModel) with Cramer-Rao lower bounds lower than 20% were considered as reliable.

Results

Average spectra (n=5), LCmodel fit, and the fit-residual of the five measurement time points indicate good spectral quality. The metabolic concentration ratios over all measurement points as shown in Cr, N-acetyl-aspartate (NAA), glutamate (Glu) and the combination of Glu and glutamine (Glx), and choline (Cho) could be quantified reliably and were stable over time.
Discussion
Despite small voxel size, the proposed method allows the detection of metabolite markers in NAcc with high data quality. Furthermore, intra-individual metabolic concentrations remain relatively constant and thus, providing a feasible measure for differences between healthy controls and cocaine users especially in regard to glutamatergic alterations observed in preclinical models.
**Title**

*Neural basis of visual processing in prereaders*

**Authors**

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**Introduction**

Specialized processing of print in the brain develops during reading acquisition and is considered to be a crucial factor for fluent reading. Processing of letters, digits or falsefonts differs in adults in the event-related potential (ERP) N1 after around 150-200ms and the corresponding activation of the left ventral visual stream.

**Methods**

In our ongoing study, we examine the differences in the activation patterns to letters, digits, learned and unfamiliar falsefont characters by using simultaneous EEG-fMRI recordings in kindergarteners with a risk for developmental dyslexia. Children learn the association between falsefont characters and speech sounds shortly before the neuroimaging session. As a control conditions, a second set of falsefont characters for which no phonological associations are taught, as well as letters and digits are presented.

**Results**

In our preliminary analysis, we focus on visual processing of the four different conditions in prereaders. We expect a higher N1 and a greater activation in the left ventral visual stream when processing a set of learned falsefonts as compared to a set of unfamiliar falsefonts and more right lateralized activation for digits.

**Discussion**

Our findings will be discussed in the frame of cortical reorganization processes when learning to read and fine-tuning of the ventral visual stream.
Title

Audiovisual integration in the prereading brain

Authors

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Introduction

Reading acquisition includes the process of learning to link orthographic (letters) with phonological (speech sound) information. So far, fMRI studies have shown that the disruption of integrating auditory and visual information represents a core deficit in developmental dyslexia (DYS) and is characterized by reduced BOLD signal changes in superior temporal regions of the brain.

Methods

In an ongoing study using simultaneous EEG/fMRI recordings and neuropsychological assessments, we investigate the impact of learning grapheme-phoneme integration on the development of the language and reading network in the brain prior to reading acquisition. Prereading children with a familial risk for DYS passively perceive four types of congruent and incongruent audiovisual pairs: letters and speech sounds, trained false fonts and speech sounds, unfamiliar false fonts and speech sounds, and numerals and number names.

Results

We will present data of a preliminary analysis comparing the integration of these four audiovisual pairs in the brain. We expect pronounced integration effects for numbers and trained false fonts as compared to letters and unknown false fonts.

Discussion

We will discuss our results in the context of the development of audiovisual integration.
Quantifying in vivo iron levels in prodromal Huntington’s Disease using MRI

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Introduction:
Postmortem neuropathology studies and in vivo MRI studies have demonstrated altered iron levels in the basal ganglia of prodromal (non-symptomatic) and advanced Huntington’s disease (HD) patients. Quantitative Susceptibility Mapping (QSM) allows quantitative in vivo mapping of iron levels in the brain using MRI phase data and is more specific than other, e.g. relaxation based, iron measures. In this pilot study the use of QSM in prodromal HD was explored as a potential biomarker of disease progress by correlating QSM results with established biomarkers and comparing prodromal-HD patients and controls.

Methods
QSM maps of 15 prodromal-HD patients and 16 age-matched healthy controls were reconstructed using the phase images of a 3D multi-echo GRE sequence, acquired on a 7T MR scanner. Automated atlas based image segmentation was performed to select the regions of interest. CAG-Age Product (CAP) score, indicating the HD genetic burden at the time of the scan, was determined in the prodromal-HD patients to compare the QSM results with this established biomarker.

Results
Prodromal-HD patients showed significantly higher average susceptibility values (p<0.01) in the caudate nucleus (CN) and the putamen (PT), indicating higher iron levels. Significant decrease in average susceptibility (p<0.05) in both the substantia nigra and hippocampus indicated a significantly lower iron level in these structures. Decreased susceptibility was also measured in the amygdala and red nucleus and increased susceptibility in the globus pallidus. The average susceptibility of the CN and PT correlated (p<0.05) with the CAP scores of the prodromal-HD patients.

Conclusions
Prodromal-HD patients show altered iron levels in the basal ganglia structures even before disease onset. The correlation with the CAP score in the CN and PT indicates that detection of iron levels using QSM should be further investigated as a biomarker of disease progress in prodromal-HD.
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**Title**

*Neural oscillations in human approach-avoidance conflict*

**Authors**

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**Introduction**

Common non-human animal models of anxiety build on conflict between approach and avoidance motivation, as in elevated plus maze and open-field test. A body of rodent studies have demonstrated the role of ventral hippocampus in arbitrating approach-avoidance conflict, and recent work has extended this to its human homologue, the anterior hippocampus. In these tasks, rodent hippocampus shows increase in power and frequency of theta band oscillations. Here, we probe the functional homology of electrophysiological responses in human hippocampus during approach-avoidance behavior, using magnetoencephalography (MEG).

**Methods**

Emulating rodent paradigms drawing on operant conflict tests, we developed a human approach-avoidance task, embedded in a computer game. In each trial, participants could make a response to collect a monetary token that served as approach incentive. To provide avoidance motivation, a sleeping "predator" present in each trial could catch the human player, leading to loss of tokens. The predator had three different levels of threat, corresponding to wake up probability. We report a behavioral study with 20 participants and a MEG study with 25 participants, playing the same game with 648 and 540 trials, respectively.

**Results**

In the behavioral task, participants collected more tokens and had faster reaction times in low threat and low loss situations, while they showed avoidance (no response) and behavioral inhibition (longer RTs) when threat or potential losses were higher. In MEG signal, we observed increased induced theta (4-6 Hz) responses across all threat levels in medial temporal lobe within 1s of the token appearance. Evoked responses in parieto/temporal areas distinguished between threat levels.

**Discussion**

To summarize, our results suggest that human hippocampal theta activity increases during approach/avoidance conflict. This establishes homology to previous rodent work and paves the way towards probing the underlying functional role of this oscillatory activity.
AD risk factors seem to interact on regional cerebral blood flow estimated by dynamic 11-C-PiB-PET

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Introduction
Alterations in rCBF play an important role in AD-pathogenesis with some studies identifying increased rCBF in subjects at risk of AD whereas others demonstrating reductions. [11C]-PiB provides an estimate of cerebral amyloid-beta deposition. Due to its kinetics the early frames (ePiB) of a dynamic PiB-scan can also be used to estimate rCBF, thus it allows to study cerebral amyloid deposition and cerebral blood flow simultaneously.

Methods
We studied 11-C-PiB-PET in a cohort of 93 healthy elderly subjects and 25 subjects with mild cognitive impairment in six bilateral volumes of interest (bilateral superior parietal gyrus, bilateral temporoparietal region, right inferior frontal gyrus, right posterior cingulate and left parahippocampal gyrus). Early uptake 0-6 minutes of 11-C-PiB was used to estimate regional cerebral blood flow, late frame data (50-70 minutes) was used to estimate cerebral amyloid-deposition (cortical PiB-retention). All subjects were characterized by clinical and neuropsychological examination as well as ApoE-genotyping.

Results
The frequency of healthy elderly subjects with strong amyloid-deposition was 14 % (Clopper-Pearson CI: 95% 0.08 to 0.23). Inheritance of at least one Apo E4- allele (OR 10; 95% CI: 3.6 to 27.7) and mild cognitive impairment (OR 5.7; 95% CI: 2.1 to 15.1) was associated with elevated amyloid-deposition. Age was correlated with cortical PiB-retention (Spearman’s rho (rho): 0.33, p<0.001) but not with rCBF. An interaction with amyloid-deposition was identified with a negative correlation of rCBF and age in subjects with elevated amyloid deposition. Greatest reductions in rCBF were found in subjects with mild cognitive impairment above the age of 75 that also displayed strong amyloid-deposition.
Discussion
Our results further underscore the importance of rCBF alterations in AD pathogenesis. Two major important risk factors of AD (age and amyloid-deposition) seem to interact on rCBF. The assessment of the potential causality of that interaction would require longitudinal studies.
D)

Clinical Research: Pharmacotherapy, Psychotherapy, Neuropsychology, Healthcareresearch, Epidemiology
Neural correlates and predictive value of auditory discrimination in early coma and hypothermia

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Introduction
Auditory discrimination, assessed by mismatch negativity (MMN) paradigms has been recently studied in acute post-anoxic comatose patients treated with therapeutic hypothermia (TH). Previous work has shown that the progression of auditory discrimination over the first two days of coma is informative of the patient’s chances of awakening. Here, we expanded this previous work on 30 patients to a cohort of 73 patients in total, in order to evaluate the suitability of this approach for use in a clinical routine and to systematically study the neural correlates of auditory discrimination under hypothermia and early coma.

Methods
We recorded 19-channel electroencephalography (EEG) responses during a MMN paradigm under TH and after re-warming to normal temperature (NT). Auditory discrimination was quantified by decoding EEG responses to standard vs. deviant sounds for each patient and recording separately. Prediction of awakening was based on the progression of decoding performance from TH to NT recording.

Results
Average decoding performance for the 45 patients who later awoke (survivors) was 0.63±0.01 in TH and 0.63±0.01 in NT, and for the 28 non-survivors it was 0.66±0.01 and 0.62±0.01 (TH/NT). Decoding performance improved from TH to NT for 23 patients; out of them 21 awoke beyond a vegetative state within three months (0.91 predictive power for awakening; 95% Confidence Interval: [0.72-0.99]). Auditory discrimination decreased for 50 patients, among which 26 were non-survivors. The overall accuracy of this method was 0.64.

Discussion
The progression of auditory discrimination has a high predictive value for awakening and can be measured already during the first two days after coma onset. This quantitative measure could complement currently available clinical tests which are mainly informative of poor outcome.
Testing the “sexually-abused abuser hypothesis” in adolescents: a population-based study

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Funding
The data presented in this paper were assessed in the context of the Optimus Study. The Optimus Study was initiated and funded by the UBS OPTIMUS FOUNDATION (http://www.optimusstudy.org).

Introduction
A long-standing belief in the literature on sex offenders is that sexually-victimized youths are at increased risk of becoming sex offenders themselves. The present study tested the link between past sexual abuse, either with or without contact, and sexually-offending behavior in a representative sample of male and female adolescents while controlling for other types of abuse, mental health problems, substance use, and non-sexual violent behaviors.

Methods
Self-reported data were collected from a nationally-representative sample of 6’628 students attending 9th grade public school in Switzerland (3’434 males, 3’194 females, mean age = 15.50 years, SD = 0.66 years). Exposure to contact and non-contact types of sexual abuse was assessed using the Child Sexual Abuse Questionnaire (CSAQ) and sexually-offending behavior by the presence of any of three behaviors indicating sexual coercion.

Results
Two-hundred-forty-five males (7.1%) and 40 females (1.2%) reported having sexually coerced another person. After controlling for non-sexual abuse, low parent education, urban vs. rural living, mental health problems, substance use, and non-sexual violent behavior, male adolescents who were victims of contact sexual abuse and non-contact sexual abuse were significantly more likely to report coercive sexual behaviors. Females who experienced contact or non-contact sexual abuse were also found at increased risk of committing sexual coercion after controlling for covariates.
Discussion
The present findings highlight the extreme importance of CSA prevention in children and adolescents, given that victims themselves may become perpetrators, maintaining an endless cycle. Consequently, a comprehensive assessment of several risk factors in children and adolescents seems necessary to estimate the potential for future or ongoing sexual coercion. Reducing exposure to non-contact sexual abuse (like Internet-based sexual exploitation) should become a new area of sexual violence prevention in youths.
Title
Comparing subjective and objective neurocognitive functioning in AT-RISK States in PSYCHOSIS: Schizophrenia proneness instrument (SPI-A/SPI-CY) and ITS neuropsychological correlates

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Keywords: early detection, psychosis, risk factors, neuropsychological performance, neuropsychological correlates

Affiliations
All authors declare that there are no conflicts of interest in relation to the subject of this study. All data was drawn from the ZInEP-Study. The ZInEP-Study is supported by a foundation. The foundation had no further role in the experimental design, the collection, analysis and interpretation of data, the writing of this report, or the decision to submit this paper for publication.

Introduction
The at-risk state for developing psychosis is well established and there is lots of evidence for deficits in neuropsychological functioning already during the prepsychotic period. The purpose of this study was to compare the subjective perception of cognitive disturbances and objective variables according to neurocognitive measures in individuals at risk for psychosis.

Methods
Subjects were recruited from the ZInEP-Study, a prospective longitudinal multidimensional study of individuals at risk for psychosis, from the area of Zurich, Switzerland. For the current study, N=207 individuals were targeted meeting criteria for a risk-state for psychosis (high-risk according to the Schizophrenia Proneness Instrument, SPI-A, or ultra high-risk criteria according to the Structured Interview for Psychosis-Risk Syndromes, SIPS). The relationship of the “cognitive-attentional impediments” (ATTENT) and “cognitive disturbances” (COGNIT) items from the SPI-A / SPI-CY with performance on cognitive tests from the neuropsychological battery was examined.

Results
Using a latent class approach an empirical derivation was conducted into homogeneous subgroups that showed unique patterns of ATTENT and COGNIT. Based on a five-class solution, a “little subjective cognitive impairment” (LSCI) class, a “subjective drifting of thoughts” (SDT) class, a “subjective concentration and memory impediments” (SCMI) class, a “subjective cognitive-attentional impediments” (SCAI) class and a “severe subjective cognitive impairment (SSCI)” class were found.
In subsequent regression models SDT was found linked to worse performance in processing speed, verbal fluency, 5-Point-Tast and perseveration-errors in the Wisconsin Card Sorting Test (WCST). The SCAI class performed worse in the 5-Point-Task and the perseveration errors of the WCST.

Discussion
Our findings suggest differential subjective perceptions of neuropsychological functioning that can be subdivided into impaired thought initiative and disturbances of receptive speech. Specific associations with neurocognitive variables support this view. This raises the question of whether there are distinctive impairment subtypes as indicated by specific psychopathological and functional outcomes.
Title

Distinctive diagnoses of agoraphobia and panic disorder – risk factors and comorbidities

Authors

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Introduction

Many studies have provided heterogeneous results regarding epidemiology, risk factors and comorbidities of agoraphobia and panic disorder. Therefore, a separate diagnosis for agoraphobia, independent from the panic disorder has been a subject of a controversial debate. The goal of this study was to investigate and compare common risk factors and comorbid disorders for the individuals suffering only from agoraphobia, only from panic disorder as well as from agoraphobia and panic together.

Methods

The data used in this study were derived from the baseline interview of the PsyCoLaus survey (N=3720). A French version of the semi-structured Diagnostic Interview for Genetic Studies was applied to assess the psychiatric symptoms and assign potential diagnoses. Individuals with agoraphobia and panic diagnoses were assigned to one of the following distinct classes: pure agoraphobia (AG, n=67), pure panic (PA, n=103) and agoraphobia-panic (AG-PA, n=65). Contingency tables were computed to analyze the associations with common risk factors and comorbid disorders.

Results

Apart from similarities in common risk factors, AG, PA and AG-PA showed several distinctions regarding their comorbidity patterns. The pure AG subtype showed fewer associations with other mental disorders than the pure PA and AG-PA subtypes. Furthermore, several comorbid disorders, such as OCD and MDD, seem to be specific either for AG or PA.

Discussion

These findings support the status of agoraphobia as an independent diagnostic category, as it is described in the DSM-V. Contrary to most previous results, AG differs from PA as well as from AP-AG regarding the comorbidities. Furthermore, the identification of comorbidities specific for pure AG and PA increases our knowledge, which has been obscured by the previous, fuzzy (overlapping) classification. These findings support the notion that overlapping classes or subtypes should be routinely challenged by the distinctive (pure) ones.
5-HT1A receptor agonist buspirone modulates visual hallucinations induced by the mixed 5-HT2A/1A agonist psilocybin in healthy volunteers

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Introduction
Recent pharmacological studies indicate that non-hallucinogenic serotonin (5-HT)²A/₁A receptor or 5-HT₁A receptor agonists reduce the head shake response induced by the hallucinogenic 5-HT₂A/₁A receptor agonist psilocybin in rats.

Method
To investigate the impact of these findings in humans, we tested whether pre-treatment with the non-hallucinogenic 5-HT₂A/₁A agonist ergotamine (3mg) or the 5-HT₁A agonist buspirone (20mg) may block the hallucinogenic effects of psilocybin (170µg/kg) in healthy subjects. Using a within-subject design, 14 subjects received either ergotamine, placebo, psilocybin or psilocybin + ergotamine, a second group of 16 subject received buspirone instead of ergotamine. Psychological alterations were assessed using the 5D-ASC (Altered State of Consciousness) Rating Scale.

Results
At the dose tested, psilocybin produced as expected only moderate depersonalisation phenomena but robust emotional and perceptual alterations. While pre-treatment with ergotamine did not affect any of the psilocybin-induced psychological or behavioral effects, buspirone significantly reduced the 5-ASC dimension visionary restructuralization including elementary and complex hallucinations.

Discussion
The apparent discrepancy of the effect of ergotamine in rats and humans needs further exploration while the present finding with buspirone is in line with single cell recordings indicating that 5-HT₁A receptors exert opposite effects on 5-HT₂A receptor activation in cortical neurons which are thought to mediate the visual effects of psilocybin.
Title

The Emotion paradox in psychopathy: Experimental findings on Emotion recognition and expression

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Keywords: psychopathy, interpersonal ability, emotion recognition, emotion expression

Introduction

The research literature indicates a small-to-moderate performance deficit in psychopaths for decoding emotional states of others from facial cues, particularly for emotions with negative valence (Wilson et al., 2011; Crim Just Behav 38: 659-668). As psychopaths are considered experts at manipulation and deceit, the question arises how individuals with less-than-optimal emotion processing become proficient at conning others.

Method

In a sample of 171 men (57 psychopathic inmates, 66 non-psychopathic inmates, and 48 community controls) interpersonal abilities were assessed using computerized tasks. Participants carried out tasks on general cognitive ability, face perception, emotion recognition, and facial mimicry. Psychopathy was assessed using both clinical observer ratings and self-report questionnaires.

Results

Psychopathy was moderately related to a deficit in emotion perception, more specifically to decoding affective states from photographs of faces showing the six basic emotions. This inverse relationship between psychopathy and performance was not moderated by fluid intelligence but attenuated by face perception ability. The strength of the psychopathy/emotion recognition link was similar for five of the six basic emotions with the exception of disgust. Further deficits were noted with regard to self-reported empathy functioning and incidental facial mimicry (implicit emotion expression) as measured via electromyography.

Discussion

The emotion recognition deficit in psychopaths is most likely due to a deficit in general face perception abilities. The results help to integrate the previously scattered findings from the area of emotion processing in psychopathy by using a comprehensive research paradigm that combines different modes of functioning with potential covariates. The finding of deficient emotion recognition due to limited face perception abilities is in accord with a prominent etiological theory that posits a dysfunctional violence inhibition mechanism (Blair, 1995; Cognition 57: 1-29). Since the data collection is ongoing, the current results are, however, preliminary. Data on the explicit production of emotional expressions are currently being analyzed.
Measuring heroin craving: The German version of the Heroin Craving Questionnaire (HCQ)

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Introduction
Craving is newly introduced as a core symptom of substance dependence/addiction in DSM-V. The 45-item Heroin Craving Questionnaire (HCQ) was designed to measure four domains of a broader concept of craving (in opioid dependence). The validation of the German version of this widely used craving questionnaire is still missing.

Methods
A total of 219 German-speaking opioid-dependent patients from six different clinical subsamples maintained either on methadone or diacetylmorphine (pharmaceutical heroin) filled in the HCQ and, in most cases, a visual analog craving scale (VAS) right before administering their prescribed maintenance medication. Data were analyzed using confirmatory factor analysis (CFA), exploratory factor analysis (EFA), and reliability analysis.

Results
An initial CFA failed to replicate the 4-factor structure of the English version. Furthermore, none of the exploratory 2-, 3- and 4-factor models reached sufficient goodness-of-fit indices, indicating that multi-dimensionality of craving cannot be confirmed by the German HCQ version. We only found, in addition to a single craving factor as identified for the whole sample, a factor with loadings of mostly negatively keyed items within a subsample of diacetylmorphine-maintained patients (n=87), which, however, showed no significant correlation to the VAS-craving measure. Finally, a short 8-item scale measuring craving is being proposed showing very good internal consistency and high correlation with the VAS-craving measure.

Discussion
Craving is an important construct for clinical and research contexts which can be easily measured by an 8-item HCQ version showing very good reliability and construct validity across patients in different treatment settings. Especially, the negatively keyed items of the 45-item HCQ seem to be problematic, most likely because of participants’ possible inattention to item content. Predictive validity of the proposed short scale needs to be demonstrated.
Modelling suicide and unemployment: A longitudinal analysis covering 63 countries, 2000-2011

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Introduction
As in earlier economic crises, there has been recent debate about an association between the economy and suicide. Unemployment rises during economic crises and directly affects individuals’ health. Unsurprisingly, studies have proposed an association between unemployment and suicide. However, a consistent analysis examining the relationship between unemployment and suicide over wider world regions is still lacking.

Methods
We retrospectively analysed public data on suicide, population and economy from 2000 to 2011. We selected 63 countries and extracted the information on four age groups and gender. Statistical analyses were conducted by random coefficient models, dealing with missing data appropriately. To check the stability of findings we examined both region-specific models and an overall model.

Results
The overall model, adjusted for the unemployment rate, showed that the annual suicide rate decreased by 1.1% (95% CI 0.8-1.4). In all four world regions, we found a similar effect of unemployment rate on suicide risk. The best model fit indicated that a higher suicide risk preceded a rise in unemployment (lagged by six months) and that the effect was non-linear (higher effects for world regions with lower baseline unemployment rates). We found no interaction effects between age, gender, and unemployment. The suicide risk associated with unemployment was elevated by 20-30% in all world regions. Overall, there were N=41 148 (39 552-42 744) suicides associated with unemployment in 2007 and N=46 131 (44 292-47 970) in 2009, indicating 5000 excess suicides since the economic crisis in 2008.

Discussion
Suicides associated with unemployment totalled a nine-fold higher number of deaths than excess suicides attributed to the most recent economic crisis. Prevention strategies focusing on the unemployed as well as on employment and its conditions are necessary not only in difficult times but also in times of stable economy.
Title

Self-reported impulsivity and decision-making but not delay discounting varies with changing cocaine use: Evidence from a longitudinal study

Authors

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Introduction

Cocaine addiction is characterized by disrupted behavioral self-control and compulsive drug-seeking. Accordingly, it was consistently shown that cocaine users display elevated impulsivity and worse decision-making. Nonetheless, it is still unknown whether these behavioral impairments are predisposed, cocaine-induced, or both, and, thus, reflect stable trait vs. state markers of cocaine use disorder. Therefore, we examined the relation between changing intensity of cocaine use and the development of decision-making and impulsivity measures within one year.

Methods

We conducted a longitudinal study with two test sessions at a one-year interval. We compared the course of impulsivity and decision-making in 19 cocaine users with increased, 19 users with decreased, and 19 users with stable cocaine use, as well as in 48 psychostimulant-naïve controls. Intensity of cocaine use was objectively determined by quantitative hair toxicology. Impulsivity and decision-making performance were assessed by the Barratt Impulsiveness Scale (BIS-11), the Iowa Gambling Task (IGT), the response bias B'' in the sustained attention task Rapid Visual Processing (RVP), and the Delay Discounting task (DD). To analyze the longitudinal data, linear multilevel models were applied.

Results

Results showed significant group*time interactions for the BIS-11 total score and the IGT total card ratio.Increasers showed enhanced, whereas decreasers displayed reduced self-reported impulsivity within one year. Surprisingly, increaser’s IGT ratios were improved during the interval, whereas decreaser’s ratios got worse. By contrast, neither the response bias B” nor the DD total score showed substantial group*time interactions.

Discussion

These results indicate that self-reported impulsivity and decision-making performance clearly co-vary with changing cocaine use, while response bias and delay discounting remain largely unaffected. Accordingly, self-reported impulsivity and gambling decision-making measures are less suitable to predict the risk for cocaine addiction but might be used to monitor treatment success. By contrast, delay of gratification seems to be a reliable trait marker for cocaine addiction.
Title

Vulnerability to Mental Health Problems, Chronic Stress, and Regular Exercises

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Background
Chronic stress can lead to serious health problems and can affect nearly every system of the human body, as suggested by physical, cognitive, affective and behavioral symptoms. Indeed, for a certain percentage of the general population, chronic stress raises blood pressure, increases the risk of heart attack and stroke, suppresses the immune system, and increases the vulnerability to psychiatric disorders, such as anxiety, depression, or schizophrenia.

Aim of Study
Based on a sample of 2,517 college/university students from the United States, Europe, and Argentina, this study investigated the interrelationships between insufficient coping skills under chronic stress on the one hand, and impaired physical and mental health on the other. Specifically, we addressed the following questions: (1) inter-relationship between coping behavior and the factors "regular exercises", "consumption behavior", "impaired physical health", "psycho-somatic disturbances", and "impaired mental health"; (2) how to draw a line between risk and non-risk cases; and (3) extent to which insufficient coping skills are influenced by socio-cultural factors.

Methods and Materials
All students completed 2 self-report questionnaires: the Coping Strategies Inventory "COPE" and the Zurich Health Questionnaire "ZHQ" which assesses "regular exercises", "consumption behavior", "impaired physical health", "psychosomatic disturbances", and "impaired mental health". The data were subjected to structure analyses by means of Neural Network techniques, using the different study sites as independent "learning" and "test" samples.

Results
We found 2 highly stable COPE scales that quantified basic coping behavior in terms of "activity-passivity" and "defeatism-resilience". Excellent reproducibility across study sites suggested that the new scales represent socio-culturally independent personality traits. The ZGF factors were used to externally validate the newly constructed scales and to estimate the extent to which the new scales are inter-related with consumption behavior and health problems. We found a highly significant and consistent relationship between insufficient coping skills on the one hand, and the state of physical and mental health on the other: The higher a person's defeatism score the higher his/her impairment in terms of physical and mental health, combined with a higher consumption of illegal drugs as well as a significant lack of physical activity.
Conclusions
Our results suggested that (1) the proposed method provides powerful screening tools in the field of early detection and prevention of psychiatric disorders; and (2) physical activity (regular exercises) plays a significant role not only in the prevention of health problems but also in early intervention programs.

References

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Title

The operational definition of subtypes makes a big difference: Distinctive versus fuzzy subtypes in specific phobias

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Background

Research on subtypes of mental disorders is growing. However, too little attention has been paid to the operational definition of the subtypes. The aim of this study was to examine distinctive or pure subtypes in specific phobias and to contrast them with fuzzy or overlapping subtypes. The analysis focused on pure animal phobias, pure other specific phobias and a mixed subtype. We examined the outcomes with regard to the most relevant epidemiological parameters, risk factors and sociodemographic marker variables.

Data and Methods

The data come from the ZIInEP Epidemiology Survey which was carried out between August 2010 and September 2012. After a screening CATI interview, 1’500 participants aged 20-41 years were selected for a comprehensive face-to-face interview. In analogy to the Zurich Study the sample was stratified, in this instance enriched by participants with high scores on the SCL-27. The participants were interviewed in the face-to-face interview with the Mini-SPIKE, a short version of the instrument used in the Zurich Study covering most psychiatric syndromes. The analyses comprised basic statistical descriptive models.

Results

Pure animal phobias consistently displayed a low age at onset of first symptoms (8-12 years) and clear preponderance of females (OR>3). Pure other specific phobias started up to 10 years later and displayed almost a balanced sex-ratio. With regard to risk factors and comorbid disorders, pure animal phobias showed virtually no associations, in contrast to numerous associations in pure other phobias. Comparing the results with respect to fuzzy subtypes it became apparent that the latter allowed for much less differentiation.

Discussion

Across the whole range of epidemiological parameters examined in this study, pure animal and pure other phobias represented two completely different entities. This was not obvious if overlapping subtypes were analysed. In this instance, the choice of operational definitions makes a big difference.
**Title**

*Trichotillomania - A randomized controlled trial on internet based self-help*

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**Introduction**

Online interventions are a low threshold option for people who suffer from psychiatric disorders, such as depression and anxiety. For Trichotillomania (TTM) a pilot study (Moritz & Rufer 2011) assessed the feasibility and effectiveness of a new self-help method, entitled decoupling (DC), with promising results. The current study, aimed at confirming the pilot study and comparing DC to Progressive Muscle relaxation (PMR) in patients with TTM.

**Methods**

A sample of 105 participants with TTM was recruited via the Internet. All participants were diagnosed by an experienced clinician via phone-interview and randomly allocated to receiving DC or PMR. Severity of TTM was assessed with Massachusetts General Hospital Hair-Pulling Scale (MGH-HPS). Intention to treat analyses (ITT) and completer analyses were conducted for testing effects of the 4-week-interventions and after 6-months (follow up).

**Results**

The primary outcome (MGH-HPS) showed that DC as well as PMR, both after comprehensive psycho-education, decreased hair pulling symptoms significantly. This decrease was found from pre- to post (η² partial = 0.31) and was stable between post and 6 months follow-up (η² partial = 0.03). There was no significant difference in MGH-HPS between DC and PMR (p=0.28). In retrospect TTM patients rated DC more helpful than PMR (p=0.035) and would recommend DC significantly more often to a friend (p=0.004).

**Discussion**

In contrast to our hypothesis, DC was not superior to PMR but showed similar results in the primary outcome. This unexpected result and possible reasons will be discussed in the poster.