F24. OMEGA-6 PUFA METABOLISM DISTURBED IN PHOSPHO- AND SPHINGOLIPIDS IN NEUROLEPTIC-NAÏVE FIRST-EPISODE SCHIZOPHRENIA PATIENTS – A FATTY ACID PROFILING STUDY IN FIVE LIPID FRACTIONS

Kerstin Langbein*,[1], Christian Fleischer[1], Katrin Kuhnt[2], Stefan Smesny[1]

[1]Jena University Hospital; [2]Friedrich-Schiller-University Jena

Background: Alterations of polyunsaturated fatty acid (PUFA) levels are a well-replicated finding in schizophrenia research. There is however a controversy about the origin of this abnormality and its importance in the pathogenesis of schizophrenic illness. To investigate the influence of nutrition, in this study we investigate different aspects of fatty acid metabolization in a cohort of neuroleptic naïve first-episode schizophrenia patients (FEP) and a group of healthy controls (HC) matched for age and gender.

Methods: In 33 FEP (25.8 ± 4.8y, male 60.6% 20/33) and 32 HC (24.9 ± 4.6y, male 53.1% 17/32) fatty acid profile was investigated by gas chromatography in blood plasma lipids of the triacylglycerol (TAG) fraction (closely related to fat consumption within recent days, rich in SFA, MUFA (~50%), and LA (C18:2n6)), the cholesterol ester (CE) fraction (dependent on fat consumption within recent days, rich in LA (C18:2n6)(~51%), SFA and PUFA), and the plasma phospholipid (PL) fraction (reflecting fat consumption of the last weeks to month, rich in SFA (~50%), AA (~7%), and LA (C18:2n6). In erythrocyte membranes (sensitive to fat consumption within weeks to month), fatty acid profile was investigated in phospholipids of the phosphoethanolamin (PE) fraction (rich in PUFA (~45%), AA (C20:4n6) and SFA) and of the sphingomyelin (SM) fraction (rich in long chain SFA (>70%) and MUFA (including NA C24:1c15). Psychopathology was assessed using the PANSS, BPRS-E and SCL-90-R ratings. Statistical analysis included multi- and univariate ANOVA, non-parametric tests and correlation analysis.

Results: In the plasma PL fraction and in the lipid fractions of erythrocyte membranes (PE, SM) that are less influenced by recent nutrition, patients showed generally reduced omega-6 PUFA levels, particularly in terms of AA in the SM fraction. While PUFA of the PL and PE fraction were positively correlated in HC, this was not the case in the FEP group.

Discussion: Our results support the previous finding of a general omega-6 PUFA deficit in FEP. The decrease points towards an endogenous regulation deficit that is independent of recent nutrition, might affect the metabolism of grey and white matter structural components, and could cause alterations of AA downstream functions. While correlation analysis in HC strongly suggests that nutrition and supplementation have the potential to influence PUFA availability, inner transport and metabolization pathways seem to be disturbed in FEP.

F25. NEURAPRO REVISITED: INCREASES IN LONG-CHAIN OMEGA-3 FATTY ACIDS IMPROVE FUNCTIONAL AND SYMPTOMATIC OUTCOMES IN ULTRAHIGH RISK PATIENTS

G. Paul Amminger*,[1], Barnaby Nelson[1], Hok Pan Yuen[1], Connie Markulev[1], Miriam R. Schäfer[1], Monika Schlögelhofer[2], Nilufar Mossaheb[2], Stephan Smesny[3], Ian Hickie[4], Gregor Berger[5], Eric Chen[6], Lieuwe de Haan[7], Dorien H. Nieman[7], Merete Nordentoft[8], Anita Riecher-Rössler[9], Swapna Verma[10], Maximus Berger[1], Andrew Thompson[11], Alison Yung[12], Patrick D. McGorry[1]

[1]Orygen, National Centre of Excellence in Youth Mental Health; [2]Medical University of Vienna; [3]University Hospital, Jena; [4]University of Sydney; [5]Child and Adolescent Psychiatric Service of the Canton of Zurich; [6]University of Hong Kong; [7]Academic Medical Center, Amsterdam; [8]Psychiatric Centre Bispebjerg;

[9]Psychiatric University Clinics Basel; [10]Institute of Mental Health, Singapore; [11]Warwick Medical School; [12]Institute of Brain, Behaviour and Mental Health, University of Manchester

Background: The NEURAPRO multicentre randomised controlled trial (RCT) of long-chain polyunsaturated omega-3 fatty acids (ω-3 PUFAs) ('fish oil') in combination with high-quality psychosocial intervention (cognitive behavioural case management [CBCM]) vs. placebo in combination with CBCM in young people at ultrahigh risk (UHR) of psychosis showed that the group allocated to fish oil had no clinical benefits over the placebo group. However, a limitation of the trial was that adherence with the study medication was relatively low. Furthermore, although RCTs are placed at the top of the evidence hierarchy, this methodology has limitations in fish oil RCTs, since the test agent is not only present in the intervention group, but ω-3 fats are present in the diet and in the tissues of all participants. A biomarker analysis of ω-3 changes during the trial can ultimately determine the efficacy of ω-3 supplementation in this trial.

Methods: The NEURAPRO study was conducted from March 2010 to September 2014, in 10 specialized early psychosis treatment services in Australia, Asia, and Europe. In this study of 304 young people at UHR for psychotic disorders, 153 (50.3%) were allocated to ω-3 PUFAs and 151 (49.7%) to placebo. In all, 139 (45.7%) were male; mean (SD) age was 19.1 (4.6) years. The primary outcome was transition to psychosis assessed with the Comprehensive Assessment of the At-Risk Mental State. Secondary outcomes were levels of psychopathology and functioning assessed by the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Negative Symptoms (SANS), the Montgomery Asberg Depression Rating Scale (MADRS), the Young Mania Rating Scale (YMRS), the Social and Occupational Functioning Assessment Scale (SOFAS), and the Global Functioning: Social and Role scales. Levels of ω-3 PUFAs in fish oil, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (amongst other fatty acids) were measured as percentage of total fatty acids in erythrocytes at baseline and at month 6 (end-of-intervention). We examined changes in cell membrane levels of EPA and DHA, as measures of ω-3 intake independent of source. Data were analysed as a single cohort. Cox proportional hazards models and linear regression analyses were used to examine relationships between the ω-3 index (EPA+DHA) with clinical outcomes at month 6 and 12.

Results: When analysed as a single cohort, no association was observed between the ω-3 index and transition to psychosis at any follow-up time point but increase of the ω-3 index was found significantly related with most of the functional and symptomatic measures at month 6 and 12, in linear regression models adjusting for relevant baseline factors (i.e., functioning, psychopathology, ω-3 index and smoking). The models revealed consistent results, with low functioning or high psychopathology at baseline, low levels of ω-3s at baseline and increase of the ω-3 index independently predicting clinical improvements at in this sample.

Discussion: In contrast to our RCT analysis, this study using biomarkers shows that increase in erythrocyte ω-3 PUFAs may improve clinical outcomes of UHR patients. The results also imply that people with low DHA and EPA levels may benefit more from supplementation with fish oil. The analysis also highlights shortcomings of the RCT design in situations when the tested intervention is available outside the study.

F26. THE NATURE OF CLINICAL HIGH-RISK SYMPTOMS: NEW INSIGHTS GAINED FROM AGE EFFECTS

Frauke Schultze-Lutter*,[1], Chantal Michel[2], Stefanie Schmidt[2]

[1]Heinrich-Heine University Düsseldorf; [2]University Hospital of Child and Adolescent Psychiatry, University of Bern

Background: Early detection of psychosis is an important topic in psychiatry and is involving ever younger patient groups. Yet, developmental issues are still under researched. Thus, we examined risk symptoms and criteria in 8-40-year-olds from the general population.

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Methods: Clinical high-risk symptoms, i.e. attenuated and transient psy-cvhotic symptoms (APS, BIPS) as well ascognitive and perceptive basic symptoms (BS), were assessed by well-trained psychologists performed assessments of risk symptoms, using established interviews. Differentiating between perceptive and non-perceptive/cognitive phenomena, impact of age groups on risk symptoms and their clinical significance (current psychosocial functioning deficits or non-psychotic DSM-IV axis-I disorder) was assessed by logistic regression analyses.

Results: Altogether, 9.9% of interviewees (N=689) reported APS, and 18.1% BS; 1.3% met APS, 3.3% COPER and 1.2% COGDIS criteria. For APS, an age effect was detected around age 16: compared to 16-40-year-olds, 8-15-year-olds reported more perceptive APS and lesser clinical significance of non-perceptive APS. Similar age effects of BS on prevalence and clinical significance that differed between perceptive and cognitive BS and followed brain maturation patterns were also detected: around age 18 for perceptive and in the early twenties for cognitive BS.

Discussion: These findings strongly suggest differential developmental factors affecting prevalence and clinical significance of APS and BS: While neurocognitive maturation might influence the presence of APS, brain maturation seems to influence the presence of BS. These findings emphasize the need to address the differential effects of perceptive and non-perceptive risk phenomena, and their interaction with age, also in terms of conversion to psychosis, in future studies.

F27. LATENT PROFILES OF DEVELOPMENTAL SCHIZOTYPY IN THE GENERAL POPULATION: ASSOCIATIONS WITH CHILDHOOD TRAUMA AND FAMILIAL MENTAL ILLNESS

Melissa Green*,[1], Richard J. Linscott[2], Kristin R. Laurens[3], Stacy Tzoumakis[4], Kimberlie Dean[4], Johanna C. Badcock[5], Vaughan J. Carr[4]

[1]University of New South Wales Prince of Wales Hospital; [2]University of Otago; [3]Australian Catholic University; [4]University of New South Wales; [5]University of Western Australia

Background: Latent liability for schizophrenia (schizotypy) is expressed in various combinations of cognitive, psychological, and behavioural characteristics evident in the general population. Historical models propose that distinct classes of individuals expressing different forms of schizotypy may represent manifestations of differential levels of genetic and environmental risk for schizophrenia (or related illness). However, there has been little investigation of developmental models of schizotypy in childhood. Here, we sought to delineate latent profiles of schizotypy among children aged 11–12 years, and to examine associations between emerging schizotypal profiles and parental history of mental illness (as a proxy for genetic risk), early life trauma, and childhood contact with health services for mental illness up to age 13 years.

Methods: Latent profiles of schizotypy were distinguished among 22,137 children (mean age=11.9 years) for whom intergenerational records of health service contact for mental illness and child protection reports were linked to the Middle Childhood Survey (MCS) within the NSW Child Development Study.[1] Selected MCS items were used to index schizotypy across six domains (Unusual Experiences, Cognitive Disorganisation, Impulsive Nonconformity, Introversion, Dysphoria and Self-Other disturbance). Using Latent Profile Analyses (LPA), four groups emerged according to patterns of expression across these domains; membership of three putative schizotypy groups were examined in relation to the likelihood of being exposed to childhood maltreatment and parental mental illness, and the child's own mental illness up to age 13 years, relative to the no risk group.

Results: Four classes emerged from the LPA: (1) 'schizotypy' (n=1323; 6%); (2) 'dysphoric pseudo-schizotypy' (n=4261, 19%); (3) 'introverted pseudo-schizotypy' (n=4473; 20%) and; (4) 'no psychopathology' (no-risk, n=12,080; 55%). Children in the schizotypy group had the greatest odds of being the

subject of a child protection report (OR=2.9, 95% CI 2.6–3.3) and in contact with health services for mental illness by age 13 years (OR=2.7, 95% CI 2.2–3.3), relative to the no-risk group. The odds of child protection reports and childhood mental disorders were smaller, yet significantly increased, among dysphoric pseudo-schizotypy (ORs=1.9 and 1.8, respectively) and introverted pseudo-schizotypy (ORs=1.7 and 1.4, respectively), relative to the no-risk group. Parental mental illness exposure was greatest among the schizotypy (OR=2.3, 95% CI 2.0–2.6) subgroup, and was also increased in dysphoric pseudo-schizotypy (OR=1.6, 95% CI 1.5–1.8) and introverted pseudo-schizotypy (OR=1.4, 95% CI 1.3–1.5), relative to the no-risk group.

Discussion: We provide evidence for distinct subtypes of children expressing different forms of schizotypy among a large Australian sample from the general population. The subgroup of children labeled 'schizotypy' (6%) characterized by high levels of cognitive disorganisation, impulsive non-conformity, introversion, and self-other disturbance may be at highest risk for developing schizophrenia or other mental illness in adulthood, and had a greater likelihood of childhood maltreatment and parental mental illness history, than other 'pseudo-schizotypy' groups.

Reference:

1. Carr, V.J., Harris, F., Raudino, A., Luo, L., Kariuki, M., Liu, E., Tzoumakis, S., Smith, M., Holbrook, A., Bore, M., Brinkman, S.A., Lenroot, R.K., Dix, K., Dean, K., Laurens, K.R., Green, M.J. (2016) Cohort Profile: The New South Wales Child Development Study (NSW-CDS) – An Australian multi-agency, multi-generational, longitudinal record linkage study. 6:e009023 doi:10.1136/bmjopen-2015–009023.

F28. PROGRESSIVE POST-ONSET REORGANISATION OF MRI-DERIVED CORTICAL THICKNESS IN ADOLESCENTS WITH SCHIZOPHRENIA

Lena Palaniyappan*,[1], Anthony James[2]
[1]University of Western Ontario; [2]University of Oxford

Background: Cortical thickness changes continuously throughout healthy adolescence reflecting ongoing maturation. In schizophrenia, distributed abnormalities in cortical maturation are suspected. To study if these distributed changes are a result of a co-ordinated process, we investigated the structural covariance among the longitudinal post-onset thickness changes that occur across various brain regions in adolescent-onset schizophrenia.

Methods: 19 healthy adolescents and 18 age-matched patients with early-onset schizophrenia were scanned twice (~2 years' interval). The rate of change in cortical thickness was estimated both at lobar and sulcogyral level. Group level structural covariance was studied using a graph theoretical framework.

Results: At baseline, patients had distributed reduction in cortical thickness compared to controls, though this deviation was abolished over the next 2 years. Occipital cortex had a significantly deviant rate of change in patients (0.8% increase per year) compared to controls (2.5% thinning/year). Patients had a significant increase in covariance of right anterior insula and calcarine sulcus with rest of the brain.

Discussion: Post-onset structural changes in EOS are not a result of random, mutually independent processes. A spatially interconnected reorganization process, distinct from normal maturational events may underlie these distributed changes.

F29. HIGH-RISK SYMPTOMS FOR PSYCHOSIS IN ADOLESCENTS AND ITS RELATIONSHIP WITH FAMILY BURDEN

Olga Puig-Navarro*,[1], Elena De la Serna[2], Jordina Tor[3], Anna Sintes[3], Gisela Sugranyes[1], Marina Redondo[1], Marta Pardo[3], Montse Dolz[3], Inmaculada Baeza[1]
[1]Hospital Clinic of Barcelona; [2]Centro de Investigación Biomédica en Red de Salud Mental; [3]Hospital St Joan de Déu