T56. Plasma and serum brain derived neurotrophic factor levels and their association with neurocognition in at-risk mental state, first episode and chronic schizophrenia patients

Ulrike Heitz*[1], Martina Papmeyer[2], Erich Studerus[3], Tobias Vogel[3], Konstanze Römer[3], Sarah Ittig[3], Stefan Borgwardt[4], Marc Graf[3], Anne Eckert[3], Anita Riecher-Rössler[3]

[1]Psychiatric University Clinics Basel; [2]University Hospital of Psychiatry, University of Bern; [3]University of Basel Psychiatric Clinics; [4]Psychiatric University Hospital Basel

Background: Brain derived neurotrophic factor (BDNF) is known to be involved in numerous cognitive processes. Peripheral BDNF levels in plasma and serum are used as in-vivo correlates of cortical BDNF. Since cognitive deficits are recognized as core feature of psychotic disorders, preceding the onset of the illness (Pflueger, Gschwandtner, Stieglitz, & Riecher-Rössler, 2007), it is of utmost importance to investigate the relation between BDNF levels in emerging psychosis and their correlation with cognition to elucidate this matter. However, there are so far no studies investigating BDNF levels in individuals with an at-risk mental state (ARMS) for psychosis. The aims of the present study were hence the following: first to assess peripheral BDNF levels across different stages of potentially emerging psychosis, and second to investigate their association with cognitive performances.
Methods: Plasma and serum BDNF levels were measured and correlated with neuropsychological performance in ARMS ($n = 18$), first episode psychosis (FEP; $n = 6$), and chronic schizophrenia patients (CS; $n = 11$) within the project "Vulnerability and Resilience Factors of Schizophrenia" funded by the Swiss National Foundation. Neuropsychological domains assessed were intelligence, verbal memory, working memory, attention and executive function.
Results: Plasma ($P = .001$) and serum ($P < .001$) BDNF levels differed significantly between groups and were highest in CS, intermediate in FEP and lowest in ARMS. Across all groups, plasma BDNF and verbal learning and memory were negatively correlated ($r = -.361$; $P = .064$), while a positive correlation was found between plasma BDNF and executive functioning ($r = .356$; $P = .069$), with both correlations being at a trend level. A hierarchical step-wise multiple regression revealed that both BDNF parameters significantly predicted the outcome of the ToH task ($P = .023$; $R^2 = .433$).
Discussion: The low BDNF levels in ARMS compared to the other two groups were surprising, as based on the literature decreased levels with progression of the illness were expected. The low BDNF level in ARMS implies an important drop of this neurotrophin prior to the onset of the disorder. The associations of peripheral BDNF with neuropsychological performances preceding the onset of the disorder are so far inconsistent but could, if these findings are replicated, point towards a link of these variables. However, as this is the first study to investigate peripheral BDNF levels in ARMS and their correlation to neuropsychological performances, no firm conclusions can be drawn and more research is needed.

Reference:

1. Pflueger, M. O., Gschwandtner, U., Stieglitz, R. D., & Riecher-Rössler, A. Neuropsychological deficits in individuals with an at risk mental state for psychosis - working memory as a potential trait marker. Schizophr Res, 97(1-3), 14-24. doi: DOI 10.1016/j.schres.2007.09.003 (2007)

T57. Long-term tolerability of aripiprazole once-monthly in patients with schizophrenia following treatment of an acute exacerbation

John Kane[1], Timothy Peters-Strickland[2], Na Jin[2], Pamela Perry[2], Michelle Gara[2], Peter Hertel[3], Phyllis Salzman*[2], Anna Eramo[4], Raymond Sanchez[2], Robert D. McQuade[2]

[1]The Zucker Hillside Hospital and The Hofstra North Shore LIJ School of Medicine; [2]Otsuka Pharmaceutical Development & Commercialization, Inc.; [3]H. Lundbeck A/S; [4]Lundbeck LLC

Background: Aripiprazole once-monthly 400 mg (AOM 400) is a long-acting injectable antipsychotic, which is available for the treatment of schizophrenia. Aripiprazole exhibits partial agonism at the dopamine D2 receptor and serotonin 5-HT1A receptor and antagonism at the 5HT2A receptor. The efficacy of AOM 400 was demonstrated in adults experiencing an acute psychotic episode where significant improvements were shown in symptoms and functioning versus placebo in a double-blind, placebo-controlled 12-week study (NCT01663532, Kane *et al.* 2014). The present open-label safety extension study investigated the long-term tolerability of AOM 400 in patients with schizophrenia who initiated treatment following an acute episode.
Methods: This was a 26-week, multicenter, open-label, extension study (NCT01683058) in adult patients with schizophrenia who completed the lead-in study (NCT01663532) for the acute treatment of schizophrenia. Only patients completing the lead-in study with outpatient status were eligible for inclusion in the extension, and the last visit in the lead-in study served as the baseline visit for the extension. Patients from the placebo arm of the lead-in study received blinded oral aripiprazole 10-20 mg/day for 14 days after the first injection of AOM 400. To maintain blinding of the lead-in study, patients from the AOM 400 group of the lead-in received double-blind placebo tablets for the first 14 days. In the extension, patients received 6 injections with AOM 400 (dose reduction to 300 mg was permitted based on the investigator's judgment) every four weeks. Due to the open-label, single-treatment design, data from treated patients were summarized using descriptive statistics. No efficacy data were collected.
Results: Of the 74 patients who enrolled in the in the extension study, 46 had received AOM 400 and 28 had received placebo in the lead-in study. A total of 45 (60.8%) patients completed the 26-week extension, and of the 29 (39.2%) patients who discontinued the study, most were lost to follow-up ($n = 9$, 12.2%). Overall, 49/74 (66.2%) patients reported treatment-emergent adverse events (TEAEs) during the study, with the majority being mild to moderate in severity. TEAEs occurring in $\geq 5\%$ of patients were weight increased (29.7%, 22/74), akathisia (12.2%, 9/74), headache (8.1%, 6/74), weight decreased (8.1%, 6/74), and hyperlipidemia (5.4%, 4/74). The incidence of potentially clinically relevant weight gain ($\geq 7\%$ increase in body weight) at the last visit was 15.5% (11/71). Serious TEAEs and TEAEs resulting in discontinuation were reported by 6.8% (5/74) and 8.1% (6/74) of patients, respectively. The only serious TEAEs reported in $\geq 2\%$ of patients were depression and schizophrenia, each in 2.7% (2/74) of patients. There were no other clinically relevant findings regarding vital signs, injection site, laboratory values, or suicidality scales.
Discussion: Long-term treatment with AOM 400 following an acute exacerbation of schizophrenia was well tolerated with low rates of discontinuation due to adverse events or lack of efficacy. The instances of increased body weight and akathisia are consistent with the safety profile of AOM 400. For 8 of the 22 patients with TEAEs of increased weight in the extension study, the event began during the lead-in study. Note that drug-related, continuing TEAEs of the lead-in study were also counted in the extension study. Long-term treatment with AOM 400 was well tolerated in patients with schizophrenia whether treatment began during acute exacerbation of symptoms, or upon entering the extension study. No new safety signals were noted.

References:x

1. Kane JM *et al.* J Clin Psychiatry. 2014 Nov;75(11):1254-60.

T58. Results of an FDA device clearance trial for plasticity-based adaptive cognitive remediation (PACR)

Henry Mahncke*[1], Sarah-Jane Kim[1], Catherine Stasio[1], Trina Walker[2], Peter Buckley[3], Stanley Caroff[4], Erica Duncan[5], Philip D. Harvey[6], L. Fredrik Jarskog[7], Steven Lamberti[8], Keith Neuchterlein[9], Martin Strassnig[6], Dawn Velligan[10], Joseph Ventura[9], Sarah Yasmin[11], Richard Keefe[2]

[1]Posit Science; [2]Duke University; [3]Medical College of Georgia; [4]Philadelphia Veteran's Administration Hospital; [5]Emory University; [6]University of Miami; [7]UNC-Chapel Hill; [8]University of Rochester; [9]University of California, Los Angeles; [10]University of Texas Health Science Center at San Antonio; [11]Stanford University

Background: Computerized cognitive remediation programs have consistently demonstrated benefit to cognitive function in people with schizophrenia in several single-site studies and a few multi-site studies. Much of this work was limited to specific interventions focused on auditory processing speed and accuracy. The current study