

**Discussion:** Adherence to study medication was relatively low in NEURAPRO. Poor functioning and lower levels of  $\omega$ -3 PUFAs at baseline were associated with non-adherence. Young people who were non-adherent had a significantly higher risk of progressing to first episode psychosis. Knowledge about factors associated with adherence could help to improve the delivery of interventions in young people at risk of psychosis.

#### T50. SYMPTOMATIC AND FUNCTIONAL RESPONSE TO BREXPIPRAZOLE TREATMENT IN PATIENTS WITH ACUTE SCHIZOPHRENIA BY AGE

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**Background:** Atypical antipsychotics are the mainstay of treatment for schizophrenia, and have a meaningful effect on positive symptoms and agitation/aggression. More recently, treatment goals have shifted to target functioning; a cycle of deterioration often occurs in early schizophrenia in which recurring relapse results in decreased functioning.

Brexpiprazole is a serotonin-dopamine activity modulator that is a partial agonist at 5-HT<sub>1A</sub> and dopamine D<sub>2</sub> receptors, and an antagonist at 5-HT<sub>2A</sub> and noradrenaline alpha<sub>1B/2C</sub> receptors, all at subnanomolar potency. The efficacy of brexpiprazole has been shown in both short- and long-term studies. In this post-hoc analysis from three short-term studies, the proportion of patients achieving symptomatic and functional response was assessed, grouped by age at baseline.

**Methods:** Efficacy and functioning data were pooled from three 6-week, double-blind, placebo-controlled studies in hospitalized patients with acute exacerbation of schizophrenia (Vector [NCT01396421]; Beacon [NCT01393613]; and Lighthouse [NCT01810380]), and stratified according to age at baseline (18–35 years; and 36–65 years). For the current analyses, response was defined as reduction in PANSS score of  $\geq 30\%$  from baseline; a CGI-I score of 1 or 2 (much improved or improved); or reduction in PANSS score of  $\geq 30\%$  OR CGI-I score of 1 or 2. Functional response was defined as an increase in PSP total score of at least 10 points. The analyses were conducted using a mixed-model repeated measures (MMRM) approach with all brexpiprazole doses pooled (2–4mg/day).

**Results:** 557 patients aged 18–35 years and 857 patients aged 36–65 years were analysed. For patients aged 18–35 years, a statistically significantly greater proportion of brexpiprazole-treated vs placebo-treated patients had symptomatic response after 6 weeks of treatment (PANSS  $\geq 30\%$ : 40.5% vs 28.7%,  $p < 0.01$ ; CGI-I 1 or 2: 39.9% vs 25.4%,  $p < 0.001$ ; PANSS  $\geq 30\%$  OR CGI-I 1 or 2: 46.2% vs 32.3%,  $p < 0.01$ ). Similar results were observed for patients aged 36–65 years (PANSS  $\geq 30\%$ : 48.7% vs 37.6%,  $p < 0.01$ ; CGI-I 1 or 2: 47.1% vs 32.7%,  $p < 0.0001$ ; PANSS  $\geq 30\%$  OR CGI-I 1 or 2: 54.8% vs 41.6%,  $p < 0.001$ ). For patients aged 18–35 years, a statistically significantly greater proportion of brexpiprazole-treated vs placebo-treated patients had functional response after 6 weeks of treatment (PSP 10 points change: 46.3% vs 33.0%,  $p < 0.01$ ); similar results were observed for patients aged 36–65 years (49.2% vs 38.2%,  $p < 0.01$ ).

The proportion of patients meeting both symptomatic (using  $\geq 30\%$  PANSS improvement or CGI-I score of 1 or 2) and functional response was statistically significantly greater in brexpiprazole-treated patients vs placebo-treated patients regardless of the age group (18–35 years: 37.4% vs 25.4%,  $p < 0.01$ ; 36–65 years: 41.8% vs 30.2%,  $p = 0.01$ ).

**Discussion:** The results of these analyses confirm that 6 weeks of treatment with brexpiprazole results in symptomatic and functional response in acutely ill schizophrenia patients in both younger patients (age 18 to 35 years) as well as older patients (age 36–65).

#### T51. TREATMENT OF NEGATIVE SYMPTOMS OF SCHIZOPHRENIA WITH TRANSCRANIAL CURRENT STIMULATION (TDCS): RESULTS OF RANDOMIZED, DOUBLE-BLINDED, SHAM-CONTROLLED TRIAL

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**Background:** The negative symptoms of schizophrenia cause significant distress and impairment. The treatment of them is a challenge, with medications having none or little effect. So, new treatments are necessary for this condition. The aim of the study was to ascertain the efficacy of tDCS in treating negative symptoms of schizophrenia

**Methods:** This study was designed to be a randomized, sham-controlled, double-blinded trial using tDCS for the treatment of negative symptoms of schizophrenia. One-hundred (here we analyzed only 70% of the sample, the remaining will be presented at the meeting) patients will be enrolled and submitted to ten tDCS session over the left dorsolateral prefrontal cortex (anodal stimulation) and left temporo-parietal junction-left (cathodal stimulation), over 5 consecutive days, with 2 mA of current. Participants were assessed with clinical and neuropsychological tests before and after the intervention. The primary outcome was change (over time and across groups) in the scores of the Negative Subscale of Positive and Negative Symptoms Syndrome (PANSS). Our secondary outcomes consist of others scales as SANSS (Scale of Assessment of Negative Symptoms), Calgary and the AHRS (Auditory Hallucinations Rating Scale).

**Results:** From 70% of the sample the active tDCS was significantly superior to sham at endpoint at 6 weeks by negative sub scale of PANSS (mean difference, 3,5 points; SD=6.2;  $P < .05$ ). The total PANSS and the hallucinations scale had no differences between both groups. The other times of analysis were not found differences between sham and active groups. The others scales (Calgary and SANSS have not being evaluated yet).

**Discussion:** The results of our studies suggests a potential role of tDCS for the treatment of negative symptoms of schizophrenia. The effect size was small. This is the biggest study with tDCS for treating negative symptoms of schizophrenia until now. At the meeting all the data will be analyzed (100 patients), it these could change our preliminary results.

#### T52. N-ACETYL-CYSTEINE ADD-ON TREATMENT LEADS TO AN IMPROVEMENT OF FORNIX WHITE MATTER INTEGRITY IN EARLY PSYCHOSIS

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**Background:** Beneficial effects of N-acetyl-cysteine (NAC) on negative symptoms in chronic schizophrenia have been reported in two studies. A recent study in early psychosis from our group, did not report significant improvement in negative symptoms (potentially linked to the modest baseline levels) but showed improvement in cognition (i.e. processing speed) and an increase in the brain antioxidant glutathione (GSH) levels, indicating good target engagement.<sup>1</sup> Indeed, research in animal models highlights the critical role of redox regulation by brain GSH for white matter maturation and maintenance. Given the strong evidence of white matter (WM) alterations in schizophrenia