Results: Antipsychotic treatment was superior to placebo across analyses. Time treatment interactions were statistically significant ($P < 0.05$) for both mixed (beta = 2.33) and joint (beta = 2.62) models. Compared with mixed modeling, joint modeling reduced the estimated change score for treatment (21.24 vs 19.74) and placebo (1.64 vs -1.11). The effect size differences between placebo and treatment groups were greater for joint (ES = 0.89) than mixed (ES = 0.83) models. Sensitivity analyses replicated this trend of results within each of the three trials.
Discussion: Compared to mixed models, the results of joint models provide a greater separation between treatment and placebo groups. This offers preliminary evidence that joint modeling may be useful in the analysis of antipsychotic placebo controlled RCTs.

M58. A possible role for prolactin in emerging psychosis

Sarah Ittig[1], Erich Studerus*[2], Anita Riecher-Rössler[3]

[1]*University Psychiatric Clinics,* [2]*University Hospital of Psychiatry Basel,* [3]*Center for Gender Research and Early Detection*

Background: Hyperprolactinemia is frequently found in patients with schizophrenic psychoses and is usually considered to be an adverse effect of antipsychotic medication. However, there have also been recent reports on hyperprolactinaemia in antipsychotic-naïve first-episode psychosis (FEP) patients and in antipsychotic-naïve at-risk mental state (ARMS) individuals.
Prolactin secretion is not only stimulated by sucking, but also by psychosocial stress. The main regulatory mechanism acting on prolactin is the inhibition of its synthesis by dopamine. Furthermore, there is strong evidence that psychosocial stress is implicated in the development of psychotic symptoms. To corroborate the role of prolactin in emerging psychosis we want to i) replicate the existing findings of elevated prolactin levels in ARMS and FEP subjects (% hyperprolactinaemia) ii) analyze if FEP patients have higher prolactin levels than ARMS individuals, and iii) analyze if prolactin levels differ between men and women after normalization.
Methods: The data analyzed in this study were collected within the prospective Früherkennung von Psychosen (FePsy) study, which aims to improve the early detection of psychosis. From January 2012 until October 2015, 38 antipsychotic-naïve ARMS individuals and 12 antipsychotic-naïve FEP patients met the requested criteria for prolactin analyses and agreed to special blood withdrawal. This took place between 8 and 10 a.m. after overnight fast and 30 min of rest. Patients were asked to avoid stress, sports, physical activity, stimulation of the breast and smoking during at least 12 hours before blood taking. For analyses with continuous variables, we normalized prolactin values to correct for the biological variation between the sexes. We performed an ANOVA analysis to evaluate the main effects of group (ARMS, FEP) and sex (men, women), as well as their interactions on prolactin levels.
Results: Hyperprolactinaemia, i.e.blood levels higher than the normal range, was shown in 24% of ARMS individuals (22% of men and 33% of women) and 8% of FEP patients (0% of men, 50% of women). Mean prolactin values did not show a difference between ARMS and FEP subjects ($F = 0.122$; $P = 0.727$) but there was a main effect of sex ($F = 5.2533$; $P = 0.023$) describing higher normalized prolactin levels in women as compared to men. There was no interaction effect of group (ARMS, FEP) and sex (men, women).
Discussion: We could replicate the finding of elevated prolactin levels in ARMS individuals and FEP patients with a relatively high percentage of hyperprolactinemia using very sound methodology when taking blood samples and regarding exclusion criteria. These findings support a possible role for prolactin in emerging psychosis. The fact that we could not find higher prolactin levels in FEP than in ARMS individuals might be due to methodological problems, as we could not examine the FEP patients directly in their acute psychotic episode. We could also show that prolactin values are higher in our female as compared to our male patients even after correcting for the normal biological variation between the sexes. Thus, it could be speculated that stress, which can induce hyperprolactinaemia, has a stronger effect on women than on men with emerging psychosis.

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M59. Enhancing computer-assisted cognitive remediation for schizophrenia: an open-label study with anodal tdcs on left lateral prefrontal cortex

Giorgio Di Lorenzo*[1], Emiliano Santarnecchi[2], Dario Serrone[1], Cherubino Di Lorenzo[3], Fabiola Ferrentino[1], Valerio De Lorenzo[1], Andrea Daverio[1], Cinzia Niolu[1], Stefano Seri[4], Simone Rossi[5], Alberto Siracusano[1]

[1]*University of Rome Tor Vergata, Rome, Italy,* [2]*Harvard Medical School,* [3]*Don Carlo Gnocchi Onlus Foundation,* [4]*Aston University,* [5]*University of Siena*

Background: The aim of this study was the application of a specific intervention that combined a neuromodulation technique (transcranial Direct Current Stimulation, tDCS) and a computer-assisted cognitive remediation (CACR) strategy in order to obtain a fast and long-lasting cognitive enhancement in people affected by Schizophrenia (SCZ).
Methods: A group (enhanced CogPack®, eCP group) of fourteen SCZ patients was treated for eight sessions (twice-weekly) of anodal tDCS over F3, roughly corresponding to the lateral prefrontal cortex (electrode delivering cathodal tDCS was placed on the ipsilateral arm; stimulation intensity: 1mA; duration: 20'), followed by a CACR intervention with CogPack® (duration: 50'-60'). A second group (CP group) of fifteen SCZ patients was treated with eighteen CogPack® sessions without neuromodulation (twice-weekly). Clinical, cognitive, and functioning assessments were done the week before (T0) and after (T1) the CACR intervention, as well as three and six months after the CACR end (respectively, T2 and T3).
Results: At T0, clinical, cognitive and functioning indices did not differ between eCP and CP groups. Respect to T0, a significant improvement in several cognitive domains and in the functioning was observed at T1, T2, and T3 for both intervention groups, as revealed by the repeated measures ANOVA models. No difference emerged in the efficacy on the cognitive and functioning indices between the two intervention group, as indicated by the absence of significant group × time interaction effect ("eCP vs.CP" × "T0 vs. T1 vs. T2 vs. T3).
Discussion: Anodal tDCS possibly enhanced cognitive performance during CogPack®, reducing the amount of time needed to elicit a significant, long-lasting effect using CACR treatment in Schizophrenia. The present findings confirmed cognitive remediation intervention as potentially activating learning processes, with tDCS amplifying such effect by means of neuroplasticity mechanisms leading to a substantial shortening of the time required to induce clinically appreciable effects.

M60. Safety, tolerability, and pharmacokinetics of a novel PDE10A inhibitor, TAK-063, following multiple dosing in subjects with stable schizophrenia and healthy japanese subjects

Paul Goldsmith*[1], John Affinito[2], Tom Macek[2], Max Tsai[2], Jinhui Xie[2], Lev Gertsik[3]

[1]*Takeda Development Centre Europe,* [2]*Takeda Development Center Americas, Inc.,* [3]*Parexel*

Background: TAK-063 selectively inhibits phosphodiesterase 10A (PDE10A), which hydrolyzes both cyclic adenosine monophosphate and cyclic guanosine monophosphate. PDE10A inhibition may aid schizophrenia treatment by modulating, indirectly or directly, the effects of glutamatergic and dopaminergic systems. The objective was to characterize the safety, tolerability, and pharmacokinetics (PK) of TAK-063 following repeated dosing.