EPV1853

Effect of Semaglutide versus placebo on prediabetes, psychotic symptoms, and quality of life (HISTORI): A randomized clinical trial among patients with schizophrenia

N. Uhrenholt[1,2*], A. Ganeshalingam[3,4], S. Arnfred[5,6], P. Gæde[7,8], J. Frystyk[3,4,9] and N. Bilenberg[2,9]

[1]Research Unit for Clinical Psychopharmacology, Psychiatry West, Region Zealand, Slagelse; [2]Child and Adolescent Psychiatry, Mental Health Services in the Region of Southern Denmark; [3]Endocrine Research Unit, Department of Endocrinology; [4]Steno Diabetes Center Odense, Odense University Hospital, Odense; [5]Psychiatric Research Unit, Copenhagen University Hospital, Psychiatry Region Zealand, Slagelse; [6]Department of Clinical Medicine, University of Copenhagen, Copenhagen; [7]Department of Cardiology and Endocrinology, Næstved, Slagelse & Ringsted Hospitals, Slagelse; [8]Department of Regional Health Research and [9]Department of Clinical Research, University of Southern Denmark, Odense, Denmark
*Corresponding author.
doi: 10.1192/j.eurpsy.2025.2278

Introduction: Individuals diagnosed with schizophrenia experience a 2- to 3-fold higher mortality rate compared to the general population, with cardiovascular disease being the primary cause. On average, they lose about 15 years of potential life. Additionally, up to 15% of individuals with schizophrenia develop type 2 diabetes, further exacerbating their health challenges.
Objectives: This study aimed to evaluate the efficacy of Semaglutide, a glucagon-like peptide-1 receptor agonist, as an adjunctive treatment to antipsychotic therapy in patients with schizophrenia spectrum disorders, prediabetes and overweight.
Methods: We conducted an investigator-initiated, randomized, placebo-controlled, double-blind trial across two clinical sites in Denmark. Out of 402 possible eligible participants, 154 were enrolled. Participants were receiving second-generation antipsychotic treatment, were overweight or obese, and had prediabetes (HbA1c 39-47 mmol/mol). Data collection spanned from January 1, 2022, to May 1, 2024. The primary outcome measure was changes in HbA1c, with secondary outcomes including psychotic symptoms, quality of life, BMI, and cardiometabolic parameters. A prespecified statistical analysis plan was registered with ClinicalTrials.gov prior to unblinding the treatment arms.
The trial is spear-headed by Odense University Hospital with recruitment from community psychiatry settings in the Region of Southern Denmark and Region Zealand.
Results: The last patient visit was May 1, 2024 and unblinding occurred primo September 2024. Results will be analyzed in Q4, 2024 and primary and secondary results presented at the conference.
Conclusions: Semaglutide holds potential as a novel therapeutic option for individuals with schizophrenia who experience prediabetes and antipsychotic-induced weight gain.

Disclosure of Interest: None Declared

EPV1851

Reward processing in schizophrenia: a pilot fMRI study for examining delusions using the monetary incentive delay task

A. Urkola[1*], I. Gomez-Alonso[1,2], M. Á. García-León[3], A. Karuk[1], N. Ramiro[4], P. McKenna[1,5], P. Fuentes-Claramonte[1,5] and E. Pomarol-Clotet[1,5]

[1]FIDMAG Hermanas Hospitalarias Research Foundation; [2]Universitat de Barcelona, Barcelona; [3]Universidad de Sevilla, Sevilla; [4]Hospital de San Rafael and [5]CIBERSAM, Barcelona, Spain
*Corresponding author.
doi: 10.1192/j.eurpsy.2025.2279

Introduction: Schizophrenia is a severe psychiatric disorder characterized by positive (delusions and hallucinations), negative and disorganization symptoms. According to the influential dopamine hypothesis, positive symptoms of schizophrenia are linked to increased dopamine transmission in subcortical regions, particularly the striatum. Kapur's aberrant salience theory further suggests that hyperdopaminergia leads to increased and disorganized reward prediction error signalling, leading to the misattribution of significance to irrelevant stimuli, which contributes to the development of delusions. Negative symptoms have been argued to reflect reduced reward prediction error signalling.
Objectives: To design an optimized monetary incentive delay (MID) task for use in fMRI studies of schizophrenia patients. For this, a pilot study was conducted in order to test the effects of monetary incentives on task performance in schizophrenia patients and healthy controls.
Methods: Nine healthy controls and seven patients with DSM-5 schizophrenia completed the MID task, including a training and test phase. This task evaluates reward processing by presenting cues that predict either rewarding or non-rewarding outcomes before a target that requires a speeded response. We investigated the effect of these cues on task performance (accuracy and reaction times) through a repeated measures ANOVA that compared rewarding and non-rewarding cues with a between-subjects factor for diagnosis.
Results: The patients with schizophrenia exhibited slower RT and lower accuracy compared to healthy controls (main effect of group, RT $p = 0.008$, accuracy $p = 0.047$). There was also a significant main effect of condition, with better accuracy and shorter RT in the rewarded condition in both the patients and controls (accuracy $p = 0.01$, RT $p = 0.003$). However, there was no significant group*-condition interaction. Both the patients and the controls showed significant improvements in task performance when rewards were offered, compared to when no rewards were provided.
Conclusions: Our MID task shows expected performance effects in patients with schizophrenia, producing effects comparable to those observed in healthy controls. This MID task design is therefore suitable for examining and understanding symptom profiles associated with reward processing, such as delusions and negative symptoms.

Disclosure of Interest: None Declared