proteins involved in intracellular trafficking, and dopaminergic receptors [long and short forms of the dopamine receptor D2 (DRD2) and dopamine receptor D1 (DRD1)] in several key brain regions of wild type adult mice exposed to social defeat stress.

Methods: C57BL/6J mice were subjected to chronic social defeat procedure for 10 consecutive days. The defeated mice were categorized into unsusceptible (UNS) and susceptible (SUS) groups based on performance in the social avoidance test. Animals were randomly divided into two groups, vehicle (VEH) and drug (DRUG) groups. Risperidone (RIS) was administered to the DRUG group at the dosage of 0.2 mg/kg, i.p. for 7days. After sacrifice and brain extraction, prefrontal cortex (PFC), hippocampus (HIP) and amygdala (AMY) were obtained. The mRNA levels of our target genes were measured by real time- PCR.

Results: In the VEH group, mRNA expression levels of GASP1 and ARF6 were decreased in the PFC and HIP, and AMY of UNS mice respectively compared to control mice. The mRNA expression of Rab4 was rather increased in the PFC of UNS mice compared to control mice. In the DRUG group, only mRNA expression level of GASP1 was decreased in the PFC of UNS mice compared to control mice.

Discussion: Our results indicate that social defeat stress induces changes in expression levels of GASP1, ARF6 and Rab4 in several key brain regions and these effects are blocked by risperidone. It may suggest that risperidone can prevent or treat an impairment of intracellular trafficking caused by defeat stress. As ARF6 is known to mediate recycling of D2 receptors and GASP-1 is involved in the lysosomal sorting of D2 receptor, our findings should be discussed with regard to the changes of mRNA expression levels of DRD2 and DRD1.

M207. REVEALING HYPOTHALAMIC PATHWAYS CONTRIBUTION TO OLANZAPINE- INDUCED METABOLIC SYNDROME: FROM MURINE MODEL TO HUMAN TRANSLATION

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Background: Olanzapine (OL) represents one of the main choices for the treatment of psychotic symptoms. However, OL increase the risk of metabolic syndrome (MS). The mechanism of Olanzapine induced MS remains still unclear but hypothalamic pathways seem to be involved. The purpose of our study is to validate an innovative approach for translational studies to investigate the hypothalamic pathways contribution to OL induced MS.

Methods: To establish a murine model of Olanzapine induced MS, OL compounded in chow (54mg/Kg of HFD food) has been administered for 30 days to C57BL/6J female mice of 10 weeks old (20 mice/group). Food intake and weight gain are tested.

After the 4 weeks of treatment, mice are sacrificed by rapid cervical dislocation. Blood is collected for Glucose, Insulin and Leptin evaluation. Hypothalamus and Liver are rapidly dissected and analyzed with qPCR. Fatty liver is histologically tested with Red Oil-O- staining.

The identification of mice hypothalamic coexpression network with a Genome-wide Weighted Genes Co-expression Network Analysis (WGCNA) is performed using a publicly available mice hypothalamic RNASeq a dataset.

From the RNASeq data obtained from Perez-Gomez et al. study (PMID: 30532051) a differential gene expression (DGE) analysis is performed to identify the gene impacted by Olanzapine and verified with qPCR on

our sample. The segregation of differentially expressed genes in specific modules of the mice hypothalamic network is tested.

Human hypothalamic network identification is performed using the publicly available GTEx dataset of Hypothalamic RNASeq data for a WGCNA. The segregation of differentially expressed genes of mice model in human network has been studied. An eigengene network approach is used to study the relationship between the human affected modules.

Results: From the 2nd week of treatment, the weight gain shows a significant increase (p= 0.02) in OL group compared to Control. The difference in weight gain remains unchanged until the 30th day. Likewise Blood glucose, Insuline and Leptine levels appear increased in Olanzapine group compared to control (p= 0,0089, p= 0,01, p= 0,0012 respectively). The percentage of liver parenchyma occupied by lipid droplets shows a statistically significant increase in OL treated group (p=0,0001).

14 of the 29 identified hypothalamic differentially expressed genes between OL- treated mice compared to control clusters in a single module of the WGCNA. The pathway analysis of this module reveals that Wnt signaling pathway reaches the statistical significance (FDR= 0,02 p value = 0,00006). The co-occurrence of OL-induced hypothalamic differentially expressed genes, previously identified in mice, is analyzed on human WGCNA on hypothalamic RNASeq data. The impacted module in humans seems to be three with no identifiable pathways involved. From the eigengene analysis results that two of the three impacted modules cluster in a single hierarchical module. The pathway analysis performed on the whole eigengine module reveals that Wnt signaling pathway reaches the statistical significance (FDR= 0,01 p value = 0,00003).

Discussion: Our study firstly demonstrates the full MS-phenotype induced by Olanzapine avoiding the use of weight gain as a proxy of OL-MS as shown in previous literature. The high comparability shows by hypothalamic network analysis in mice and humans underlines the highly interspecies conservation of hypothalamic functional pathways. So the present study represents an innovative approach for translational studies on hypothalamic pathway contribution to MS induced by OL. Combining a murine model, network analysis and human translation it proposes a reliable method for translation of pre-clinical studies.

M208. MEASURES OF COGNITION AND SOCIAL FUNCTIONING IN SCHIZOPHRENIA PATIENTS RECEIVING SEP-363856

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Background: SEP-363856 is a novel trace amine associated receptor-1 (TAAR1)/5-HT1A agonist with no dopamine-D2/5-HT2A antagonist activity. SEP-363856 showed significant antipsychotic efficacy in patients with schizophrenia, and a safety and tolerability profile similar to placebo and consistent with a non-D2 mechanism of action. Here, we examined measures of cognition and social functioning in schizophrenia patients receiving SEP-363856.

Methods: Patients aged 18–40 years with an acute exacerbation of schizophrenia were randomized, double-blind (DB), to 4-weeks of flexible-dose treatment with once daily SEP-363856 (N=120; 50 or 75 mg) or placebo (N=125). Patients (N=156) entering a subsequent 26-week open-label (OL) extension study were evaluated utilizing the Cogstate Brief Battery, administered at DB baseline and week 4, and OL baseline and weeks 12 and 26. Standardized z-scores were calculated for the Cogstate composite and subscale tasks (Detection task, Identification task, One Card Learning task, One Back task). The University of California San Diego Performance Based Skills Assessment (UPSA-B) scale was assessed at the same timepoints, as were the following psychiatric scales: Positive and Negative Syndrome Scale (PANSS), the Brief Negative Symptom Scale (BNSS), the Montgomery–Åsberg Depression Rating Scale (MADRS), the Clinical Global Impression Scale, severity scale (CGI-S), and the Pittsburgh Sleep

Quality Index global score (PSQI-global). Pearson correlation analyses were performed between DB baseline to Week 26 change in Cogstate composite and subscale scores and Week 26 change in the psychiatric scale scores.

Results: Small improvements, from DB baseline to Week 26, were observed in standardized scores on the Cogstate composite (+0.29), Identification task (+0.19), Detection task (+0.28); One Card learning task (+0.33); and One Back task (+0.33). Improvement from OL baseline at Week 26 was also observed on the mean [SD] UPSA-B total score (+6.2 [11.6]). At DB baseline, there were no correlations between CogState composite score and individual test scores with any of the psychiatric scales. Week 26 improvement in the following Cogstate composite and subscale tasks were correlated with Week 26 improvement in the following psychiatric scale scores: Cogstate composite score (PANSS total, r=-0.26; BNSS total, r=-0.31; CGI-S, r=-0.30; MADRS total, r=-0.23; PSQI-global, r=-0.23); Identification task (PANSS total, r=-0.30; BNSS total, r=-0.30), Detection task (BNSS total, r=-0.30; CGI-S, r=-0.28; PSQI-global, r=-0.23); One Card learning task (MADRS total, r=-0.29); and One Back task (PANSS total, r=-0.26).

Discussion: During 6-months of open-label extension treatment with SEP-363856, improvement in overall functioning was observed on the UPSA-B scale; and small but consistent improvement in cognition was noted in the Cogstate composite and subscale task scores. Endpoint reduction in the severity of schizophrenia-related symptomatology (eg, on the PANSS, BNSS, MADRS, insomnia) were associated with modest correlations, in the range of 0.2 to 0.3, in cognitive performance as measured by the Cogstate composite and subscale task scores.

M209. TO WHOM WE PRESCRIBE LONG ACTING ANTPSYCHOTICS AT DISCHARGE FROM HOSPITAL?

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Background: Although the growing evidence show the advantages of long acting injectable (LAI)antipsychotics on treatment of psychotic disorders, characteristics of the patients with psychotic disorders using LAI is not studied enough. The aim of this retrospective study is to understand the clinical characteristics of the patients with psychotic disorders to whom any LAI was prescribed at discharge from hospital

Methods: We screened the files of 400 inpatients with psychosis spectrum disorders who were treated in inpatient units of Istanbul Faculty of Medicine, Department of Psychiatry between 01.01.2014-01.016.2019. We recorded the last admission if the patient had more than one hospitalization. We compared the variables including illness duration, diagnosis, presence of involuntary hospitalization, insight, substance/alcohol abuse, forensic problems between those who were prescribed LAI and others. We also applied logistic regression analysis to detect the independent predictors of LAI prescription.

Results: Thirty-nine percent of the patients were given LAI at discharge. Patients with schizophrenia and schizoaffective disorders were more common compared to psychotic disorder NOS/schizophreniform disorder in LAI group (p<0.001). Those who prescribed LAI were older and had longer duration of psychotic disorder. Poor insight at admission, past and present noncompliance, involuntary admission (64,5% vs 35,5%, p=0.003) and history of forensi problems (63% vs 37%, p=0.01)were more common in LAI group. Past ECT treatment, antipsychotic polypharmacy and LAI treatment in past were more common in LAI group. Lack of insight at admission, history of LAI treatment before and noncompliance to medications before hospitalization were appeared as predictors of LAI prescription at discharge in logistic regression. We found no relationship between LAI prescription and drug abuse, treatment resistance and psychiatric comorbidity.

Discussion: Our findings suggest that LAIs were prescribed to chronic and older inpatients with lack of insight, and compliance at admission. The patients who were prescribed LAI also had indirect indicators of poor outcome, like previous ECT and polypharmacy. Contrary to previous reports, we found no difference in alcohol/substance abuse between those who were prescribed LAI and others.

M210. GRIN2B METHYLATION IS RELATED TO PANSS EXCITED COMPONENT (PANSS-EC) IN SCHIZOPHRENIA

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Background: Among the adversities found in schizophrenia, the dysfunctions in the glutamatergic system, specifically the N-methyl-D-aspartate receptor (NMDAR) are apparent. GRIN2B (coding a NMDAR subunit) has a critical role in synaptic plasticity and important participation in CNS neurodevelopment, this gene is closely associated with behavioural and cognitive impairments. One of the mechanisms that may underlie the deficiencies seen in the glutamatergic system in psychosis is DNA methylation as it is known to regulate gene expression. As part of a major study investigating the relationship of DNA methylation with schizophrenia and its symptom response to antipsychotic drug treatment, we determined whether methylation of the GRIN2B promoter region was associated with specific symptoms of schizophrenia determined by the Positive and Negative Syndrome Scale (PANSS).

Methods: Blood samples were collected from schizophrenia patients (n = 79) on admission to the study. Bisulphite conversion and pyrosequencing were used to determine methylation levels in 5 CpG sites in the GRIN2B promoter. PANSS score and the five factor subscores (Wallwork et al, 2012) at baseline and at 6 weeks was collected, and the change in PANSS following treatment was determined.

Results: Mean methylation at the five CpG sites was not associated with overall PANSS score or with the change in PANSS. However, a highly significant positive correlation of mean methylation with the baseline excited factor score (r=0.342, p=0.002), but with no other PANSS subscore, was found. No significant correlation with changes in PANSS, or in changes in subscores, over the treatment period was found.

Discussion: This is the first evidence showing GRIN2B methylation correlation with the excited component (EC) of schizophrenia symptoms. PANSS-EC is used to assess agitated patients (Lindenmayer et al., 2008, Montoya et al., 2011), and is valuable in identifying risks associated with agitation and aggression related to primary psychiatric disturbances. This result suggests that this GRIN2B epigenetic signature may relate to agitation and aggressive behaviour in schizophrenia.

M211. NEUROPROTECTIVE EFFECT OF SHI-ZHEN-AN-SHEN-TANG, A CHINESE HERB FORMULA ON MICE EXPOSED TO CUPRIZONE

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