**[Abstract:0665] Biological psychiatry and neuroscience**

**Blood microRNA dysregulation in schizophrenia**

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**Objective:** Schizophrenia is a devastating psychiatric disorder. Comprehensive research has been performed to identify biomarkers for this disease. Unfortunately we do not yet have a reliable biomarker for schizophrenia. MicroRNAs are 22-nucleotide-long RNA transcripts that regulate expression of genes at post-transcriptional level. To date, a limited number of studies has been done with peripheral tissue of schizophrenia patients. Here we demonstrate microRNA levels in plasma of schizophrenia patients.

**Methods:** Peripheral blood samples were collected from 16 schizophrenia patients and 16 healthy controls. Total RNA was extracted from Peripheral Whole Blood using Tri-Reagent (Sigma). Reverse transcriptase reactions contained 5 µl of extracted total RNA. Quantitative-Comparative CT (ΔΔCT) Real-time PCR was performed in an ABI Prism 7500 Real-Time PCR System (Applied Biosystems) using SDS 2.0.6 software.

**Results:** Schizophrenia patients showed significant upregulation of five microRNAs: miR9-5p (p=0.002), miR29a-3p (p<0.001), miR106b-5p (p=0.002), miR125a-3p (p<0.001) and miR125b-3p (p=0.018).

**Conclusion:** We found miR106b-5p upregulated in schizophrenia patients. Liu et al. compared 14 healthy controls with 16 depressed patients and found that miR-106b-5p and four other microRNAs were up regulated in the plasma of depressed patients. Additionally miR106b-5p was found to be downregulated in children with attention deficit / hyperactivity disorder(ADHD). In their unpublished study, Karababa et al. found miR106a-5p and miR106b-5p upregulated in manic patients. Perkins et al. found that miR-9-3p and miR-29a were downregulated and miR-106a was upregulated in the prefrontal cortex of individuals with schizophrenia. We believe combining our results with previous findings increases the likelihood the miR-106 family is disrupted in psychiatric disorders.

Limitations of our study are small sample size, cross sectional design, and limited number of microRNA types. Despite these limitations, our study contributes to revealing potential peripheral microRNA signatures and encourages researchers to focus on this field.

**Keywords:** schizophrenia, microRNA, blood

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**Effect of subacute agomelatine treatment on diabetic neuropathic pain**

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**Objective:** Diabetic neuropathy is a syndrome that develops with Diabetes mellitus only, in the absence of other factors that can cause neuropathy; it affects different components of the nervous system and can involve all types of nerve fibers. The drug groups most widely preferred for treating neuropathic pain in clinics are anticonvulsants and antidepressants. Based on the ability of antidepressants in the treatment of neuropathic pain, we planned to investigate possible effect of agomelatine, a new antidepressant drug, on hyperglycemia, metabolic alterations and neuropathic pain observed in diabetic rats.

**Methods:** Male Sprague-Dawley rats of the same age (weight: 250-300 g) were used for the experiments. Diabetes was induced by a
single 50 mg/kg dose of intravenous streptozotocin administration. The experimental protocol was approved by the Anadolu University Animal Experiments Local Ethics Committee. Effects of 7 and 14 days agomelatine (40 and 80 mg/kg) administration on hyperglycemia were assessed by measuring fasting blood glucose levels and conducting oral glucose tolerance tests (OGTT). Changes in metabolic parameters such as food and water consumption and excretion of urine and feces were monitored using metabolic cages. Weekly changes in the body weights of animals were recorded as well. The effect of agomelatine treatment on hyperalgesia occurring due to peripheral diabetic neuropathy was examined using Randall-Sellito (mechanical nociceptive stimulus), Hargreaves (thermal nociceptive stimulus), and cold-plate (4°C, thermal nociceptive stimulus) tests. The dynamic plantar esthesiometer, which measures the threshold values for mechanical stimuli, was used for allodynia studies; in addition, thermal allodynia was evaluated using warm-plate (38°C) test. Agomelatine administration was initiated 4 weeks after the induction of diabetes to permit development of nociceptive perception deficits in rats.

**Results:** Subacute administration of agomelatine did not cause any alterations in the blood glucose levels or metabolic parameters of diabetic rats with respect to the untreated diabetic animals. Moreover, body weights of diabetic rats were not affected by the agomelatine treatment. In contrast, subacute administration of agomelatine caused a significant increase in the reduced paw-withdrawal threshold, decreased paw-withdrawal latency and shortened reaction period of diabetic rats. Data obtained from OGTT, as well as blood glucose and metabolic cage measurements, suggest that agomelatine treatment does not induce a significant anti-hyperglycemic effect. On the other hand, findings of neuropathy tests suggested that subacute administration of agomelatine at doses of 40 and 80 mg/kg restored hyperalgesia and allodynia responses of the diabetic rats to the levels of normoglycemic control animals. Anti-hyperalgesic and anti-allodynic effects of this new antidepressant were comparable to the reference drug pregabalin (10 mg/kg).

**Conclusion:** Considering its antidepressant, anxiolytic and antinociceptive effects, it seems that agomelatine may propose clinical advantages for providing an ability to avoid polypharmacy in treatment of painful diabetic neuropathy and diabetes-induced affective disorders such as depression and anxiety.

**Keywords:** diabetes mellitus, agomelatine, neuropathy

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**Beneficial effect of mianserin in experimentally-induced chronic hyperglycemia: evidence of increased Ins1 mRNA expression**

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**Objective:** The aim of this study was investigating the potential effect of subacute mianserin administration on diabetes-induced chronic hyperglycemia and metabolic alterations.

**Methods:** Male Wistar rats of the same age (weight: 250-300 g) were used for the experiments. Diabetes was induced by a single 50 mg/kg dose of intravenous streptozotocin (STZ) administration. Effects of 14 days mianserin (30 and 45 mg/kg) administration on hyperglycemia arising in 6-week-diabetic rats were assessed by conducting oral glucose tolerance tests (OGTT) and by measuring glycated hemoglobin (HbA1c) levels. Changes in metabolic parameters such as food and water consumption and urine and feces excretion were observed using metabolic cages. Body weights of the animals were recorded weekly. Possible effect of mianserin treatment on Ins1 mRNA expression of diabetic rats was evaluated by real-time polymerase chain reaction (PCR) method. The experimental protocol was approved by the Anadolu University Animal Experiments Local Ethics Committee.

**Results:** Fourteen-daysubacute administration of mianserin did not alter the OGTT results or HbA1c levels of normoglycemic animals. Similarly, mianserin caused significant alterations neither in the measured metabolic parameters nor in the body weights of normoglycemic rats. On the other hand, subacute administration of this drug to the diabetic animals significantly reduced the augmented HbA1c levels with respect to the untreated diabetic groups. Further, mianserin treatment caused significant reduction in the increased urine discharge, fecal output, water, and food consumption characteristic of diabetic animals. Weight loss of diabetic animals was also improved. With regard to the anti-hyperglycemic effect, mianserin administered at a dose of 30 mg/kg was found to be as effective as the reference drug metformin (dose, 1g/kg). Moreover, our real-time PCR results indicated that Ins1 mRNA expression levels of diabetic rats significantly decreased with respect to the normoglycemic rats, as expected. Mianserin administration significantly increased the reduced