Objectives: scientific publications
Methods: analytical review
Results: The central nervous system has evolved a conserved unfolded protein response mechanism to cope with the accumulation of misfolded proteins. As one of the main intracellular redox systems involved in neuroprotection, the vitagene system becomes a potential neurohormetic target for novel cytoprotective interventions. Vitagens encode the cytoprotective heat shock proteins (Hsp) Hsp70 and heme oxygenase-1, as well as thioredoxin reductase and sirtuins. The cellular stress response is the ability of a cell to withstand stressful conditions, including the heat shock response. The production of heat shock proteins, including protein chaperones, is necessary for the folding and repair of damaged proteins, which promotes cell survival to avoid apoptosis.«Molecular chaperone» are proteins that function as part of an ancient defense system in our cells. They promote cell survival by sequestering damaged proteins and preventing their aggregation. Chaperone complexes are involved in the regulation of mitochondrial functions, assembly of the cytoplasmic proteolytic system of brain cells. The cellular response to stress requires the activation of survival pathways that are under the control of protective genes called vitagens. Vitagens are involved in the production of heat-shock protein molecules, glutathione, and bilirubin. They have antioxidant and anti-apoptotic activity and provide protection against oxidative stress.
Conclusions: Studies have shown that the heat shock response contributes to the maintenance of cellular homeostasis, the establishment of a cytoprotective state in a wide range of human diseases, including inflammation, cancer, aging, and neurodegenerative disorders. Endogenous proteins can be manipulated by food or pharmacological compounds, which represents an innovative approach to therapeutic intervention in neurodegenerative disorders, actually influencing reserve mechanisms and adaptive capacity.

Disclosure of Interest: None Declared

EPV0686

Platelet enzymatic activities in patients with late-onset schizophrenia spectrum disorders

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Introduction: Impairments in energy metabolism, glutamate neurotransmitter and antioxidant systems contribute substantially in development of schizophrenia spectrum disorders, especially in late-onset psychosis (LOP).
Objectives: Revealing subgroups of patients with LOP by determining activity of platelet enzymes of energy, glutamate, and glutathione metabolism.
Methods: 62 women of 52-89 years old were studied, with late onset schizophrenia spectrum disorders (F20.0, F25, F22.0, F06.2 by ICD-10). PANSS with its subscales was used to assess the severity of psychotic symptoms. Scores by PANSS and activity levels of platelet cytochrome *c*-oxidase (COX), glutamate dehydrogenase (GDH), glutathione reductase (GR) and glutathione-S-transferase (GST) were evaluated twice: before and on the 28-th day of antipsychotic treatment. Activities of COX, GDH, GR, and GST were measured in 37 women of 50-84 years old comprising the control group.
Results: Clustering of patients by the enzymatic activities resulted in 2 clusters (C1 and C2) significantly different by COX and GST ($p<0.001$). In C1 (n=40), as compared with control, reduced level of GDH activity before and after treatment ($p=0.049$ and $p=0.032$, respectively) and a reduced level of GR activity before treatment ($p=0.026$) were revealed. In C2 (n=22), as compared with the control, COX activity was increased before and after treatment ($p=0.0001$), GDH activity was decreased before and after treatment ($p=0.0002$ and $p=0.0001$, respectively), and GST activity was decreased before and after treatment ($p=0.029$ and $p=0.0029$, respectively). GR activity was not significantly changed in both clusters. Significant correlations were found between enzymatic activities and scores by psychometric scales: in C1, GR activity positively correlated with the score reduction (delta) by PANSS-Pos ($R=0.45$, $p=0.004$), by PANSS-Psy ($R=0.44$, $p=0.005$), and by PANSS ($R=0.47$, $p=0.002$), and GST activity – with the score reduction by PANSS-Psy ($R=0.315$, $p=0.048$). In C2 (n=22), GDH activity negatively correlated with the score reduction by PANSS-Pos ($R=-0.41$, $p=0.050$) and by PANSS ($R=-0.49$, $p=0.021$).
Conclusions: The different correlations revealed in two separated clusters between enzymatic activity levels and clinical measures characterizing the antipsychotic treatment efficacy will allow us to approach differentiated predicting the effectiveness of pharmacotherapy using the biochemical parameters.

Disclosure of Interest: None Declared

EPV0687

Clustering patients with late-life depression by blood glutathione-dependent enzymatic activities for stratification of a heterogeneous group

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Introduction: We have previously found significant alterations in activities of glutathione dependent enzymes in blood cells of patients with late-life depression (LLD) compared with age-matched controls.
Objectives: The revealing subgroups of LLD patients by glutathione-metabolism enzymes' activities in blood cells using cluster analysis.
Methods: LLD patients (n=101) of 60-86 age (69 patients with recurrent depression (RD), 23 with bipolar disorder (BD) and 9 patients with a single depressive episode (DE)) were assessed by Hamilton depression rating scale (HAMD-17), and Hamilton Anxiety Rating Scale (HARS). Activity levels of glutathione reductase (GR) and glutathione S-transferase (GST) were

determined in patients' platelets (-pl) and erythrocytes (-er). The control group consisted of 51 peoples 55-84 years old without mental pathology. Cluster analysis module of the STATISTICA software was used for clustering the patients by baseline blood parameters.

Results: Three clusters of patients were obtained: C1, n=39, C2, n=31, C3, n=31, differing significantly in all biochemical parameters (Kruskal-Wallis test, $p<0.001$), except GST. When compared with control group by Mann-Whitney test, GST-pl, GST-er, and GR-er were significantly decreased in C1; GST-er was significantly increased in C2; GST-pl, GR-pl, and GR-er were significantly decreased in C3. Several significant correlations were found between the measured parameters and scores by HDRS or HAMD-17. In C1, baseline activity of GST-er correlated with total scores by HAMD-17 (R=0.335, p=0.043) after treatment. In C2, baseline activity of GR-er correlated with total scores by HARS (R=-0.376, p=0,037) after treatment and GR-pl correlated with delta scores by HAMD-17 under the treatment (R=0.484, p=0.006). No significant correlations were found in C3. Patients with BD distributed significantly unevenly between C1, C2, and C3, with significantly more BD patients clustering in C1 (61%) compared with C2 and C3 (Yetes-corrected Chi-square =7.73, p=0.0054), whereas patients with RD and DE distributed evenly.

Conclusions: Patterns of activity levels for glutathione-dependent enzymes in patients with BD differ from those in patients with RD and DE. Significant correlations of the measured biochemical parameters with scores by HDRS or HAMD-17 assessed after the treatment and evidenced for the treatment efficacy seem to be promising biomarkers for further evaluation of the treatment efficacy in heterogeneous group of LLD patients using the proposed approach to their stratification into subgroups.

Disclosure of Interest: None Declared

EPP0529

Aberrant Functional Connectivity Between Regions Involved in Belief Evaluation and Processing of Bodily Information in Patients with Somatic Delusions

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Introduction: According to the two-factor theory of delusional belief (Coltheart. Ann N Y Acad Sci 2010; 1191 16-26), explaining the presence of a delusion requires a combination of two neuropsychological impairments. The first deficit initially prompts the delusional belief and defines its content, whereas the second deficit – aberrant belief evaluation – interrupts the rejection of a delusional belief and is common for different types of delusions. The second deficit is associated with compromised functioning of the right ventral frontal/anterior insular cortex (r-VF/AI; Darby et al. Brain 2017; 140 497-507). However, neural correlates of the first deficit in different types of delusions remain obscure.

Objectives: The aim of the study was to search for regions whose functional connectivity with r-VF/AI is different between patients with somatic delusions (SD) and persecutory delusions (PD) and to further clarify the results by comparing clinical groups with healthy controls. We hypothesized that each clinical group is characterized by aberrant functional connectivity between a region, associated with poor belief evaluation (r-VF/AI), and a region, presumably associated with a neuropsychological impairment specific to the corresponding type of delusions.

Methods: Patients with delusional disorder or paranoid schizophrenia (n = 23) and healthy controls (n = 9; 5 females; mean age 36.2 ± 1.3) underwent resting-state fMRI (Philips Ingenia 3T). Nine patients had SD (5 females; mean age 40.3 ± 7.9) and fourteen patients had PD (3 females; mean age 35.6 ± 10.2). The clinical groups were compared in terms of whole-brain functional connectivity of r-VF/AI (ROI-to-voxel analysis in CONN; RRID: SCR_009550; www.nitrc.org/projects/conn). Statistical thresholds were p < .005 voxelwise, p[FDR] < .05 clusterwise. Each clinical group was compared with controls in terms of functional connectivity between r-VF/AI and previously identified regions with between-group differences in connectivity (ROI-to-ROI analysis). Age was a covariate of no interest in all analyses.

Results: Patients with SD compared to patients with PD and healthy individuals had higher functional connectivity between the r-VF/AI and a cluster in the right precentral and postcentral gyri extending to supramarginal and superior frontal gyri (Figure 1).

Image: