psychosis at 12 and 24 months after the beginning of the intervention. This cohort will be compared to patients with first-psychosis episodes without group psychotherapeutic intervention.
Methods: Longitudinal, observational, retrospective study on a cohort of N=46 patients with first-episode psychosis within the last 5 years. Two groups of 23 patients each were formed. The participants of one of those groups received group psychotherapy in the context of the AGES-Mind study and the other group received treatment as usual without group intervention. Non-exposed patients were matched by age, gender and time elapsed since first-episode psychosis with those exposed to the intervention. Sociodemographic data, clinical status and use of clinical resources outcome variables were assessed.
Results: No significant differences were found in clinical status and use of resources between participants and non-participants in the psychotherapeutic group intervention after 12 and 24 months.
Conclusions: After controlling for potentially confounding variables as sociodemographic, age and time since first-episode, participating in a group psychotherapeutic program does not seem to improve clinical variables or use of resources. Further studies with larger samples would be necessary to explore other variables, such as symptoms, satisfaction with the intervention or social functioning.

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EPP1049

Non-schizophrenic psychotic disorders: Cycloid psychosis. Case report and literature review

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Introduction: Cycloid psychosis is a clinical entity with defining traits which emerged from the Wernicke-Kleist-Leonhard school of psychiatry and has a long history in Europe. Leonhard distinguished three clinical forms: anxiety-happiness, confusion and motility psychosis. It is a condition with high clinical heterogeneity and favorable prognosis.
Objectives: To describe a case of cycloid psychosis and review in literature the heterogeneity of this phenomena and its clinical management.
Methods: Clinical case report and brief review of literature.
Results: 57-year old male with previous diagnosis of paranoid schizophrenia and severe congenital hearing loss. Preserved autonomy and adequate real-life and interpersonal functioning. Along the past few years the patient has presented episodes of a significant clinical global worsening in context of mainly somatic symptoms (intestinal obstruction and volvulus) and minor stressful life events. On this occasion he appears in the emergency room with a new episode of abdominal pain and is admitted to Internal Medicine with presumptive diagnosis of intestinal volvulus. The patient gathered heterogeneous symptoms including disorientation, confusion, generalized tremor, gait disorder, profuse sweating, regressive and oppositional behaviors (refusal to eat or drink liquids) and sudden behavioral oscillations (from agitation to prostration). From the psychic point of view he showed thought blocking, mutism, significant anxiety, fear of death, delusional prejudice ideas and sensoperceptive disturbance which seemed otherwise related to previous sensorial problems. We introduced treatment with Olanzapine 30 mg and after 4 weeks, the patient suddenly showed a significant clinical improvement until the complete remission of the symptoms and restitution of his previous state. In coordination with his regular psychiatrist was proposed the controversial diagnosis of cycloid psychosis. Cycloid psychosis gather a few clinical features which differentiate it from other entities: acute onset, polymorphic symptomatology, global disturbance of psychic life, remitting and recurrent course and favorable prognosis. Regarding its clinical management no controlled studies have been conducted to this date of the treatment of this phenomena. According to literature ECT seems to be an effective treatment as well as low-doses of atypical antipsychotics. Some authors propose pharmacological maintenance treatment with mood stabilizers.
Conclusions: The diagnosis of cycloid psychosis can be useful as well as necessary to describe certain patients with similar clinical features, recurrent course and favorable prognosis. Future studies on pharmacological approach would be useful to ensure the appropriate clinical management of these patients.

Disclosure of Interest: None Declared

EPP1050

The response to unfolded proteins in schizophrenia and bipolar disorder

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Introduction: Schizophrenia (SCH) and bipolar disorder (BD) are severe mental disordes, which have high incidence (Whiteford *et al.* Lancet 2013; 381 1575-86) and are the main causes of diasibility in young people (WHO 2022; https://www.who.int/news-room/fact-sheets/detail/mental-disorders).
Psycological stress appears in different mental disorders, and this is directly related to oxidative stress (Moller *et al.* Chem Biol Interact. 1996; 102 17-36)(Pupic-Bakrac *et al.* 2020; Psychiatr Danub. 32 412-9). Oxidative stress causes reticulum edoplasmic stress (ER stress) and this produces high levels of misfolded proteins. Defective proteins are degraded by the proteasome, but but when the density of misfolded proteins exceeds the capacity of the proteosome, the Unfolded and Misfolded Protein Response (UPR) is triggered through three main pathways: Inositol-requiring enzyme 1α (IRE1α); transcription factor 6 alpha (ATF6α) and protein kinase RNA-Like ER kinase (PERK), trying to recover normal protein synthesis capacity (Bermejo-Millo *et al.* 2018; Mol Neurobiol. 55 7973-86) (González-Blanco *et al.* 2022; J Cachexia Sarcopenia Muscle 13 919-31).
Objectives: Characterizing ER stress and UPR in SCH and BD.

Methods: We studied ER stress and UPR in peripheral blood mononuclear cells (PBMC) from 50 patients with SCH and an equal number of patients with BD compared to their corresponding controls in order to achieve our objectives.
Western Blot assay were performed following classical procedure () and the results was normalized to Ponceau as loanding control (Nie *et al.* 2017; BiochemByophys Resp 12 10-13) (Sander *et al.* 2019; Anal Biochem 575 44-53). Proteasome activity was assessed using Proteasome Activity Assay Kit (ab107921, Abcam, Cambridge, UK).
Results: ER stress was evaluated with BiP/GRP78. Our results showed significantly increased expression in SCH (p<0,01) and BD (p<0,05), being more increased in SCH. Proteasome activity was increased in SCH and BD, being only statistically significant in SQZ (p<0,05). UPR study showed IRE1a cascade significantly activated in SCH (p<0,001) and only slight increased in BD showed without statistical differences. ATF6a pathway is measured by cleavage to active protein (50-kDa). Results showed higher expression in SCH than in BD and controls (p<0,001). In addition, PERK pathway showed higher statistical levels of p-eIF2a/eiF2a ratio in SCH than in BD and control respectively (p<0,05 and p<0,01).
Conclusions: Our results showed a greater alteration in SCH than in BD at the level of protein synthesis, which implies a greater toxicity at the cellular level and, therefore, a clear risk for the survival of cells in this pathology.

Disclosure of Interest: None Declared

EPP1051

Efficacy and safety of iclepertin (BI 425809) in patients with schizophrenia: CONNEX, a Phase III randomised controlled trial programme

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Introduction: Cognitive impairment (CI) is a major determinant of poor functional outcome in schizophrenia and there are currently no available pharmacotherapies. Deficits in glutamatergic signalling play a key role in the neuropathology of cognitive symptoms. Iclepertin (BI 425809), an inhibitor of glycine transporter-1, enhances glutamatergic signalling by increasing synaptic levels of the *N*-methyl-D-aspartate receptor co-agonist, glycine. A 12-wk, Phase II trial (NCT02832037) in 509 patients (pts) with schizophrenia demonstrated that iclepertin was well tolerated and significantly improved cognition.
Objectives: The Phase III CONNEX programme aims to confirm the efficacy, safety and tolerability of iclepertin in improving cognition and functioning in a larger cohort of pts.
Methods: CONNEX consists of three replicate randomised, double-blind, placebo-controlled parallel-group trials in pts with schizophrenia (NCT04846868, NCT04846881, NCT04860830) currently stable on antipsychotic treatment. Each trial aims to recruit ~586 pts, 18–50 years old, treated with 1–2 antipsychotic medications (≥12 wks on current drug; ≥35 days on current dose prior to treatment), who have functional impairment in day-to-day activities and interact ≥1 hr per wk with a designated study partner. Pts with CI due to developmental, neurological or other disorders, or receiving cognitive remediation therapy within 12 wks prior to screening, will be excluded. Pts will be recruited from 39 countries in Asia, Australia, New Zealand, North and South America and Europe, and randomised 1:1 to receive either oral iclepertin 10 mg (n=293) or placebo (n=293) once daily over 26 wks. The primary efficacy endpoint is change from baseline (CfB) in the MATRICS Consensus Cognitive Battery overall composite T-score. Key secondary efficacy endpoints are CfB in Schizophrenia Cognition Rating Scale total score and CfB in the adjusted total time in the Virtual Reality Functional Capacity Assessment Tool. Long-term safety and tolerability data will be collected in an open-label safety extension study (CONNEX-X).
Results: The studies are currently recruiting (first pts enrolled Aug–Sept 2021), with completion expected in Q2 2024. Here we present an overview of the current study status, including any information relating to screening failures and the experience of collecting these data as part of a large multicountry, multicentre study.
Conclusions: To date, most large, industry-sponsored studies testing various compounds to address cognitive function have failed to show proof-of-clinical concept. Demonstration of efficacy of iclepertin in improving cognition in this Phase III programme would provide important insight into the role of glutamate in cognitive symptoms, that may also have relevance for other cognitive disorders. Iclepertin may represent the first efficacious medication for CI associated with schizophrenia.

Disclosure of Interest: P. Falkai Consultant of: Advistory board Boehringer Ingelheim Pharma GmBH & Co. KG, C. Reuteman-Fowler Employee of: Boehringer Ingelheim Pharma GmBH & Co. KG, Z. Blahova Employee of: Boehringer Ingelheim Pharma GmBH & Co. KG, S. Ikezawa Consultant of: Financial agreements with Boehringer Ingelheim Pharma GmbH, Merck, Biogen and Sunovion, S. Marder Grant / Research support from: Boehringer Ingelheim, GW Pharma, Consultant of: Boehringer Ingelheim, Merck, Sunovion, J. Krystal Shareolder of: Co-founder of Freedom Biosciences, Inc Investments in Biohaven Pharmaceuticals, Sage Pharmaceuticals, Spring Care, Biohaven Pharmaceuticals Medical Sciences, EpiVario, RBNC Therapeutics, Terran Biosciences and Tempero Bio., Consultant of: Aptinyx, Atai Life Sciences, AstraZeneca Pharmaceuticals, Biogen, Biomedisyn Corporation, Bionomics, Boehringer Ingelheim International, Cadent Therapeutics, Clexio Bioscience, COMPASS Pathways, Concert Pharmaceuticals, Epiodyne, EpiVario, Greenwich Biosciences, Heptares Therapeutics, Janssen, Jazz Pharmaceuticals, Otsuka America Pharmaceutical, Perception Neuroscience Holdings, Spring Care, Sunovion Pharmaceuticals, Takeda Industries, Taisho Pharmaceutical Co Advistory board: Biohaven Pharmaceuticals, BioXcel Therapeutics, Cadent Therapeutics, Cerevel Therapeutics, Delix Therapeutics, EpiVario, Eisai, Jazz Pharmaceuticals, Novartis, PsychoGenics, RBNC Therapeutics, Tempero Bio and Terran Biosciences;