differences in outcomes after initiation indicates that the effectiveness of paliperidone palmitate was similar to that of other LAI antipsychotics. However, paliperidone palmitate may be better tolerated than other 1st generation LAI antipsychotics with a lower rate of discontinuation. These findings merit consideration in relation to the high cost of paliperidone palmitate compared to other LAI antipsychotics.

F229. THE BIOLOGICAL UNDERPINNINGS OF TREATMENT RESPONSE IN DELUSIONAL DISORDER: A SYSTEMATIC REVIEW OF QUALITATIVE EVIDENCE-TO-DATE

Alexandre González-Rodríguez*[,1], Francesc Estrada[2], Itziar Montalvo[1], José Antonio Monreal[3], Diego Palao[3], Javier Labad[3]
[1]Parc Tauli University Hospital, Institut d'Investigació i Innovació Parc Taulí (I3PT); [2]Parc Tauli University Hospital; [3]Parc Tauli University Hospital, Institut d'Investigació i Innovació Parc Taulí (I3PT), Autonomous University of Barcelona (UAB)

Background: The dopamine hypothesis of schizophrenia has been extensively proposed as a neurobiological mechanism that explains the relationship between schizophrenic symptoms and hyperdopaminergic states. This hypothesis is supported by direct and indirect evidence, and it mainly postulates that antipsychotics act blocking dopamine receptors. When focusing on delusional disorder patients, especially delusional disorder somatic type, a great effort towards the search for a biological basis of treatment response has been recently demonstrated. Thus, the main goal of this systematic review was to examine the evidence explaining the biological underpinnings of treatment response in delusional disorder.
Methods: A systematic review was performed using Pubmed, Scopus and PsycINFO databases (from 1990 to October 2017), according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The following search terms were used: [('treat*' OR 'therap*' OR 'biol*') AND ('delusional disorder')]. This systematic computerized search was completed by additional studies hand-checked through reference lists from the included studies and review articles. Studies were only included if the met our inclusion criteria: (a) the International Classification of Diseases (ICD) or Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnosis for delusional disorder, (b) be published in peer-reviewed journals, (c) in English, German or Spanish, (d) and reporting a hypothesis for the biological basis of treatment response in delusional disorder, irrespective of method and study design. Exclusion criteria were: (a) studies including organic delusional disorder or (b) somatic delusions secondary to other psychiatric diagnoses. The literature search strategy, data extraction and synthesis was conducted independently by two authors (A.G.R, F.E.). When disagreement, it was solved by consensus.
Results: A total of 59 articles were identified, of which 12 met our inclusion criteria. Four hypotheses were addressed: (1) Dopaminergic dysfunction (n=4): ziprasidone-induced supersensitivity psychosis by chronic blockade of D2 Dopamine Receptor (DRD2) (n=1); pretreatment levels of plasma homovallinic acid (pHVA) (n=1); dopamine transporter (DAT) dysfunction (n=1) and effectiveness of aripiprazole (DRD2 agonist) (n=1). (2) Serotonergic dysfunction (n=6): drug occupancy in 5-HT1A and 5-HT2A receptors (n=3) and efficacy of 5-HT2 antagonists (n=3). Brain dysfunction (n=7): hypoperfusion in cerebral blood flow in temporal and parietal lobes, left side (n=5), right side (n=1) and lack of basal ganglia and subcortical gray matter lesions (n=1). Genetic evidence (n=1): implications of DRD2 Ser311Cys, DRD3 Ser9Gly and TH VNTR polymorphisms.
Discussion: The strongests biological contributors for treatment response in delusional disorder seem to be those implicating monoaminergic systems, particularly dopamine and serotonergic neurotransmitters. Although the low level of evidence, the serotonergic dysfunction may be associated with response rates, especially in delusional disorder somatic type. The link between genetic variants of dopamine receptors and neuroimaging findings in delusional disorder may open new avenues for the search of the biological underpinnings of treatment response. The evidence for an integrated model involving dopamine and serotonin systems bears further investigations.

F230. COMPARISON OF PALIPERIDONE PALMITATE 3-MONTH AND PALIPERIDONE PALMITATE 1-MONTH FORMULATION FOR NEGATIVE SYMPTOMS IN SCHIZOPHRENIA: A PHASE 3 NON-INFERIORITY STUDY

Maju Mathews[1], Srihari Gopal*[,1], Arun Singh[1], Jagadish Gogate[2], Edward Kim[2], Katalin Pungor[2]
[1]Janssen Research & Development, LLC; [2]Janssen Scientific Affairs, LLC

Background: Negative symptoms of schizophrenia are key predictors of long-term disability. It is important to understand whether treatment with long-acting injectable antipsychotics can improve negative symptom psychopathology. Paliperidone palmitate 3-month formulation (PP3M) provides a sustained release of paliperidone, permitting a significantly extended dosing interval of only 4 doses per year in patients with schizophrenia. The efficacy of PP3M as assessed by relapse rate is comparable to the paliperidone palmitate 1-month formulation (PP1M). The purpose of this post-hoc analysis was to compare the improvement in negative symptoms in patients treated with PP1M and PP3M.
Methods: Data from a randomized, double-blind (DB), parallel-group, multicenter, phase 3 study in patients with schizophrenia were analyzed. Patients aged 18 to 70 years with schizophrenia (DSM-IV-TR) and a total Positive and Negative Syndrome Scale (PANSS) score of 70–120 at screening were enrolled. After screening (3 weeks), patients entered a 17-week open-label (OL) phase, to receive PP1M (day 1 [150 mg eq. deltoid], day 8 [100 mg eq. deltoid], weeks 5, 9 and 13 [50, 75, 100, or 150 mg eq., deltoid/gluteal]) and entered a 48-week DB phase and were randomized (1:1) to receive fixed doses of either PP1M (50, 75, 100, or 150 mg eq., stabilized in OL) or PP3M (175, 263, 350, or 525 mg eq.) in deltoid or gluteal muscle until they relapsed or withdrew from study. The PANSS total scores with emphasis on 7-item negative subscale scores for PP1M vs PP3M were assessed.
Results: Of 1429 patients enrolled, 1016 were randomized to receive PP3M (n=504) or PP1M (n=512) in DB phase. Majority of patients were men and white (both 55%), with a mean (SD) age of 38.4 (11.86) years. At baseline, the mean (SE) negative subscale total was 23.2 (0.12), indicating a moderate to severe level of negative symptoms. Negative subscale and negative symptoms factor scores showed continuous improvements throughout the OL and double-blind phases of the study - mean (SD) at OL baseline and DB endpoint for total negative subscale score and symptom factor score were 23.2 (4.60) and 22.3 (4.87), and 15.9 (4.99) and 14.9 (4.81), both R2:0.16, respectively. The mean (SD) PANSS negative subscale score changes from DB baseline for PP1M vs PP3M were similar over time (mean change from baseline to DB endpoint was -1.4 (3.67), R2:0.06 vs -1.4 (3.63), R2:0.05).
Discussion: Development of an LAI antipsychotic with less frequent dosing than those currently available would be of potential advantage to patients, caregivers, and prescribers. PP3M and PP1M demonstrated consistent and similar efficacy in patients with moderate to severe negative symptoms of schizophrenia over the observed timepoints, including impact on patients with predominantly negative symptoms. Longer continuous treatment with PP3M showed greater benefit. This indicates that long-acting therapies are associated with continued improvement in negative symptoms over time. Treatment with LAIs for longer than a year was associated with the greatest improvements in negative symptoms.