Three patients diagnosed with both schizophrenia spectrum multiple sclerosis [1]. Immune-related single-nucleotide polymorphisms hypothesis about a common etiology in a subgroup of schizophrenia and bipolarity factor for schizophrenia and other psychotic disorders, and there is a history of psychotic disorder for at least one year, were monitored during 6 months using Positive and Negative Syndrome Scale (PANSS), Global Assessment of Functioning (GAF), Clinical Global Impressions – Severity (CGI-S), Columbia-Suicide Scale for Schizophrenia (CSSRS), Calgary Depression Scale (CDS), Multiple Schizophrenia Severity Scale (MSSS), and the Extrapyramidal Symptom Rating Scale (ESRS). None of these patients presented other organic or psychiatric co-morbidity, and they were on active treatment for their multiple sclerosis throughout the 6-month duration of psychiatric evaluation. All patients were initiated on a new antipsychotic, because of the lack of efficacy of the previous agents, or due to their lack of therapeutic adherence. A patient was initiated on olanzapine 15 mg/day, while the other two received risperidone 4 mg/day. The antipsychotic doses were flexible during the 6 months of the treatment, with olanzapine between 10 and 20 mg daily, and risperidone between 3–6 mg daily. The initial PANSS mean score was 92.2, with a GAF of 35.3 and a CGI-S of 5.1.

Results: All patients reached the week 24 visit of their evaluation, and the overall tolerability of the antipsychotic treatment was good. All patients had lower PANSS scores at week 24 (the mean decrease was -25.6 points compared to baseline), higher GAF scores (+27.7 points), and lower CGI-S (-2.5 points). CSSRS did not change significantly during the 6 months, the score remained significantly increased reported at the baseline values, and no corrective medication was recommended throughout the 6 months for extrapyramidal symptoms. MSSS mean score did not change significantly at week 12 compared to its baseline values.

Discussion: Atypical antipsychotics are efficient and well tolerated in patients with schizophrenia and multiple sclerosis dual diagnosis. The positive effects of atypical antipsychotics maintained during the 6 months of monitoring and they had no significant impact over the multiple sclerosis symptoms.

References
1. Arneth BM. Multiple sclerosis and schizophrenia. Int J Mol Sci 2017;18(8):1760.
2. Andreassen OA, Harbo HF, Wang Y, et al. Genetic pleiotropy between multiple sclerosis and schizophrenia but not bipolar disorder: differential involvement of immune-related gene loci. Mol Psychiatry 2015;20(2):207–14.
3. Kroken RA, Sommer IE, Steen VM, et al. Constructing the immune signature for schizophrenia for clinical use and research; an integrative review translating descriptives into diagnostics. Front Psychiatry 2018;9:753.

T197. TREATMENT STRATEGIES FOR ULTRA-RESISTANT SCHIZOPHRENIAS

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Background: Treatment-resistant schizophrenias include a heterogeneous group of patients with significant individual and societal consequences, and a high number of these patients fail to respond to clozapine (almost 50%). Patients who did not respond to the second line antipsychotics are

T196. THERAPEUTIC MANAGEMENT IN MULTIPLE SCLEROSIS AND SCHIZOPHRENIA SPECTRUM DISORDERS DUAL DIAGNOSIS

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Background: Multiple sclerosis has been suggested as a potential vulnerability factor for schizophrenia and other psychotic disorders, and there is a hypothesis about a common etiology in a subgroup of schizophrenia and multiple sclerosis [1]. Immune-related single-nucleotide polymorphisms have been associated with schizophrenia and genetic pleiotropy between schizophrenia and multiple sclerosis has been reported, but not between bipolar disorder and multiple sclerosis (at the level of major histocompatibility complex) [2]. As new data about the involvement of genetically-determined immune factors in the susceptibility to schizophrenia appear (e.g., variants of complement factor 4 possibly linked to synaptic pruning during brain development) [3] the interest for finding therapeutic targets within the immune system for psychotic disorders is also increasing.

Methods: Three patients diagnosed with both schizophrenia spectrum disorders (schizophrenia n=2, or schizoaffective disorder, depressive type n=1), female, mean age 43.7, with a history of psychotic disorder for at least one year, were monitored during 6 months using Positive and Negative Syndrome Scale (PANSS), Global Assessment of Functioning (GAF), Clinical Global Impressions – Severity (CGI-S), Columbia-Suicide Scale for Schizophrenia (CSSRS), Calgary Depression Scale (CDS), Multiple Schizophrenia Severity Scale (MSSS), and the Extrapyramidal Symptom Rating Scale (ESRS). None of these patients presented other organic or psychiatric co-morbidity, and they were on active treatment for their multiple sclerosis throughout the 6-month duration of psychiatric evaluation. All patients were initiated on a new antipsychotic, because of the lack of efficacy of the previous agents, or due to their lack of therapeutic adherence. A patient was initiated on olanzapine 15 mg/day, while the other two received risperidone 4 mg/day. The antipsychotic doses were flexible during the 6 months of the treatment, with olanzapine between 10 and 20 mg daily, and risperidone between 3–6 mg daily. The initial PANSS mean score was 92.2, with a GAF of 35.3 and a CGI-S of 5.1.

Results: All patients reached the week 24 visit of their evaluation, and the overall tolerability of the antipsychotic treatment was good. All patients had lower PANSS scores at week 24 (the mean decrease was -25.6 points compared to baseline), higher GAF scores (+27.7 points), and lower CGI-S (-2.5 points). CSSRS did not change significantly during the 6 months, the score remained at minimum value, and the CDS scores also remained constantly under 3. ESRS recorded transient increments, but at week 12 they were not significantly increased reported at the baseline values, and no corrective medication was recommended throughout the 6 months for extrapyramidal symptoms. MSSS mean score did not change significantly at week 12 compared to its baseline values.

Discussion: Atypical antipsychotics are efficient and well tolerated in patients with schizophrenia and multiple sclerosis dual diagnosis. The positive effects of atypical antipsychotics maintained during the 6 months of monitoring and they had no significant impact over the multiple sclerosis symptoms.

References
1. Arneth BM. Multiple sclerosis and schizophrenia. Int J Mol Sci 2017;18(8):1760.
2. Andreassen OA, Harbo HF, Wang Y, et al. Genetic pleiotropy between multiple sclerosis and schizophrenia but not bipolar disorder: differential involvement of immune-related gene loci. Mol Psychiatry 2015;20(2):207–14.
3. Kroken RA, Sommer IE, Steen VM, et al. Constructing the immune signature for schizophrenia for clinical use and research; an integrative review translating descriptives into diagnostics. Front Psychiatry 2018;9:753.
a challenge for their treating physicians and although many augmentation strategies have been tried, including other agents with antipsychotic properties, mood-stabilizers, antidepressants, glutamatergic agents and neuromodulation techniques.

Methods: A literature review was conducted in the main electronic databases (PubMed, Cochrane, EMBASE, CINAHL), and papers published between January 2000 and August 2019 were included. The search paradigm was “ultra-resistant schizophrenia” or “clozapine-resistant schizophrenia” or “add-on to schizophrenia” and non-proprietary names of currently marketed antipsychotics, mood stabilizers, anxiolytics, antipsychotics, nootropics, “neuromodulation techniques” and “psychotropics”.

Results: A number of 197 papers resulted from the primary search, and 45 papers remained after de-duplication and application of inclusion and exclusion criteria. Electroconvulsive therapy seems to be efficient and the response rate ranges from 37.5 to 100% in cases of ultra-resistant schizophrenia [1]. Transcranial direct-current stimulation (tDCS) lead to meaningful improvement in positive symptoms and overall symptomatology when compared to no standard treatment of the control group, in a 4 weeks trial [2]. A 21-week pragmatic trial did not find any significant lasting effect of the cognitive-behavioral therapy (CBT) on total symptoms of schizophrenia compared to treatment as usual, although improvements were detected [3]. Pharmacological augmentation of clozapine included amisulpride (results were not significant), mexiteline (positive effects, but the trial included a small number of patients), reboxetine (uncertain efficacy), ziprasidone (possible effective on negative and cognitive symptoms), aripiprazole (uncertain effect based on multiple trials), lamotrigine (not efficient), pimozide (not efficient),sertindole (no benefits detected, possible worsen psychosis in several cases), tetrabenazine (not effective), duloxetine (possible efficacy on negative and general psychopathology, but not on the executive cognitive functions), topiramate (no efficacy), valproic acid (possible efficacy, larger trials needed), risperidone (not efficient), donepezil (not efficient), mirtazapine (possible efficacy), sulpiride (possible efficacy in a subgroup of schizophrenia patients).

Discussion: Until now no single pharmacological augmentation strategy to clozapine has been proven superior to other in double-blind randomized, large-scale placebo-controlled data. Electroconvulsive therapy seems to be the only non-pharmacological technique with enough data to support its efficacy in ultra-resistant cases of schizophrenia. Other neuromodulatory techniques, like tDCS, are still in early enough data to support its efficacy in ultra-resistant cases of schizophrenia. Though each patient benefitted from clozapine alone, negative symptoms persisted. Patients, their families, and treatment program staff all observed a significant reduction in the patients’ anxiety and ability to participate in social roles and activities.

References
1. Grover S, Hazari N, Kate N. Combined use of clozapine and ECT: a review. Acta Neuropsychiatr 2015;27(3):131–142.
2. Lindenmayer JP, Kulsa MKC, Sultana T, et al. Transcranial direct-current stimulation in ultra-resistant schizophrenia. Brain Stimul 2019;12(4):54–61.
3. Morrison AP, Pyle M, Gumley A, et al. Cognitive behavioural therapy in clozapine-resistant schizophrenia (FOCUS): an assessor-blinded, randomised controlled trial. Lancet Psychiatry 2018;5(8):633–643.

T198. CAN AUGMENTED SUBLINGUAL OXYTOCIN DECREASE NEGATIVE SYMPTOMS WITHIN TREATMENT RESISTANT SCHIZOPHRENIC POPULATIONS: A PILOT STUDY

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Background: The prevalence of schizophrenia in the United States ranges between 0.5% and 1%. This difficult-to-treat disorder is marked by the presentation of symptoms that are both positive (i.e. hallucinations) and negative (i.e. blunted affect), as well as disturbances in cognition and affect. Several second-generation antipsychotics (i.e. olanzapine, risperidone) have been utilized for their varying effects on the symptoms of schizophrenia, yet 20% to 60% of patients with schizophrenia are considered treatment-resistant. While clozapine is shown to be the most effective antipsychotic, negative symptoms commonly persist in clozapine-treated patients. Research shows that oxytocin has neuromodulatory effects on social perception and enhances empathy and attentional engagement in individuals with schizophrenia, suggesting it may have therapeutic effects on negative symptoms. The present study presents a pilot prospective research study evaluating the efficacy of combining clozapine and sublingual oxytocin for the reduction of positive and negative symptoms.

Methods: Prospective research study evaluated 25 treatment resistant schizophrenic patients who were admitted to the persistent psychotic disorder unit at a private hospital, with an average treatment duration of 2.9 months with a range between 1 and 9 months. All have been followed as outpatient for up to 30 months after discharge. All patients were 18 years or older and met the DSM-5 criteria for schizophrenia. The Positive and Negative Syndrome Scale (PANSS) was used to assess the efficacy of the combination treatment. Clozapine was prescribed to all patients after they had failed to improve in three different trials of other antipsychotic medications.

Results: A time-series analysis demonstrated a significant decrease in PANSS scores across admission, stabilization of clozapine and stabilization of oxytocin (p <.02) with the overall average PANSS score on admission was 102; after stabilization on clozapine, the average score decreased to 68. After administration oxytocin (8 weeks) the average score decreased further to 47 and improved PANSS score were not related to serum clozapine levels. Clinical and family notes indicated clinically meaningful improvements in affect, eye contact, and ability to socialize. These gains have been sustained over the full range of our observations. Families self-reported an increased ability to participate in social roles and activities.

Discussion: The combined effect extends the current research of augmenting sublingual oxytocin and clozapine for individuals with previously treatment-resistant symptoms. Though each patient benefited from clozapine alone, negative symptoms persisted. Patients, their families, and treatment program staff all observed a significant reduction in the patients’ anxiety and an improvement in the patients’ relatedness. While this case series cannot establish that oxytocin is responsible for the clinical improvements seen here, it does suggest that it may improve negative symptoms and social functioning in patients with treatment-resistant schizophrenia showing incomplete improvement with clozapine alone. The present study suggests the need for future research to explore the possibility that oxytocin can mitigate the negative symptoms of schizophrenia.

T199. 7% WEIGHT CHANGE ASSOCIATED WITH ANTIPSYCHOTICS: A META-ANALYSIS

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Background: In recent years, antipsychotic-induced weight gain (AIWG) has gained more attention in research. Although interventions to prevent weight gain are currently being investigated, AIWG remains a major problem for both patients and clinicians and often results in poor treatment adherence, a decrease in quality of life. Furthermore, schizophrenia is associated with higher mortality rates and a decreased life expectancy. Recently, some new antipsychotic drugs have been introduced that are hypothesized to entail no or low incidences of clinically relevant weight gain (CRWG), and high incidences of clinically relevant weight loss (CRWL). Here ‘clinically relevant’ is defined as >7% weight change. In this meta-analysis, we