nervous system activity and lowered parasympathetic nervous system activity to the audiovisual stimulation. These results suggested that schizophrenic patients would show higher negative affect, less adaptive autonomic nervous system and hypersensitive or sharp to audiovisual stimulation, and decreased relaxation ability after stimulation. Audiovisual stimulation in integrative arts therapy program for schizophrenia might have avoid overactive sympathetic stimulation and recommend activate parasympathetic stimulation. Integrative art therapy for schizophrenia must be sufficiently relaxed, empathetic, and promote positive affect during therapeutic process.

F224. UTILITY OF SALIVA FOR MONITORING OF CLOZAPINE LEVELS

Jimmy Lee*[,1], Jie Yin Yee[1], Yuen Mei See[1], Charmaine Tang[1], Boon Tat Ng[1], Gary Remington[2], Balram Chowbay[3]
[1]Institute of Mental Health, Singapore; [2]Centre for Addiction and Mental Health (CAMH), University of Toronto; [3]National Cancer Centre, Singapore

Background: Clozapine has specific indication for use in Treatment Resistant Schizophrenia (TRS) with guidelines for therapeutic drug monitoring. Though a plasma level > 350 ng/ml has been cited as the therapeutic threshold, many other studies have shown poor or inconsistent associations between blood levels of clozapine and side effects. Clozapine is about 95% bound to plasma proteins with a small biologically active fraction. Saliva presents as a promising alternative for therapeutic drug monitoring where clozapine levels would be at equilibrium with free unbound clozapine in the plasma. This provides the added advantage of a potentially stronger relationship with efficacy and adverse effects when compared to plasma levels because of saliva's closer representation of biologically-active clozapine. Salivary collection is also non-invasive and can be sampled serially for more precise evaluation of intra-individual variations. In the present investigation, we set out to evaluate the agreement and comparative clinical utility between plasma and salivary clozapine levels.
Methods: 53 participants with schizophrenia and on stable doses of clozapine for at least 2 weeks were recruited for the study. Participants had to undergo a clinical interview and the SCID, PANSS, plus side effect scales were administered. Symptomatic remission status was defined using the symptom criteria proposed by Andreasen et al (2005). A fasting sample of venous blood and salivary sample were collected at the same time. Assays for clozapine and norclozapine were performed using high performance liquid chromatography. A total of 106 saliva and plasma samples have been analysed.
Results: Our results showed strong correlations between plasma and salivary levels of clozapine ($r=0.61$, $P<0.05$) and norclozapine ($r=0.63$, $P<0.05$). Twenty (37.7%) participants achieved symptomatic remission at the time of recruitment. Non-remitters had a significantly higher level of plasma clozapine. Thirty-one (93.9%) participants in the non-remitter group have plasma clozapine levels greater than 350ng/ml.
Discussion: Our study shows potential for salivary samples to be an alternate non-invasive source for therapeutic drug monitoring of clozapine. This will be useful in serial monitoring of clozapine levels to evaluate treatment adherence and fluctuating pharmacokinetic profiles. There is a significant proportion of patients who do not achieve symptomatic remission on clozapine, which highlights a pressing need to identify new pharmacological agents or modalities of treatment.

F225. LEVODOPA AUGMENTATION OF ANTIPSYCHOTICS FOR THE TREATMENT OF NEGATIVE SYMPTOMS IN SCHIZOPHRENIA

George Foussias*[,1], Naren Rao[2], Gagan Fervaha[1], Carol Borlido[1], Lillian Haber[1], Hiroyoshi Takeuchi[3], Romina Mizrahi[1], Gary Remington[4]
[1]Centre for Addiction and Mental Health; [2]National Institute of Mental Health and Neurosciences, Bangalore [3]Keio University, School of Medicine; [4]Centre for Addiction and Mental Health, University of Toronto

Background: Negative symptoms (i.e., motivation deficits and diminished emotional expression) are prevalent in schizophrenia and consistently linked with functional impairment for affected individuals. Despite advances in psychopharmacology for schizophrenia, there remain no effective treatments for these negative symptoms. Older literature, however, suggests that levodopa in conjunction with antipsychotic treatment can have beneficial effects for patients with schizophrenia. While supporting the safety and potential efficacy of dopamine augmentation, these studies did not evaluate effects within specific symptom domains, particularly negative symptoms. This open-label pilot study was conducted to evaluate the preliminary efficacy and safety of levodopa augmentation of antipsychotics for the treatment of negative symptoms.
Methods: Ten stable outpatients with schizophrenia between the ages of 18 and 60 were enrolled. All were treated with stable atypical antipsychotic monotherapy for at least eight weeks, and had a minimum total score of 30 on the Scale for the Assessment of Negative Symptoms (SANS). Participants were treated with adjunctive open-label levodopa/carbidopa, with dose titration to levodopa 300mg TID over 38 days as tolerated, and dose maintenance for the remainder of the eight-week trial. Baseline assessments consisted of the SANS, Scale for the Assessment of Positive Symptoms (SAPS), Brief Psychiatric Rating Scale (BPRS), Clinical Global Impression (CGI), Calgary Depression Scale for Schizophrenia (CDSS), MATRICS Consensus Cognitive Battery (MCCB), and Quality of Life Scale (QLS) for community functioning. Treatment side effects were evaluated with the Simpson Angus Scale (SAS), Barnes Akathisia Rating Scale (BARS), Abnormal Involuntary Movement Scale (AIMS), UKU side effect rating scale (UKU), Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS), Yale-Brown Obsessive Compulsive Scale (YBOCS), and Barratt Impulsiveness Scale (BIS). Participants were reassessed on measures of psychosis and side effects weekly for the first four weeks, and every two weeks thereafter. The SANS and CGI were repeated at weeks 4 and 8, with the MCCB and QLS re-administered at week 8. Statistical analyses included the intent-to-treat sample (i.e., participants who received at least one dose of study medication) and consisted of linear mixed models for change in SANS total score (our primary outcome), and change in other clinical and side effects measures as a result of treatment.
Results: Enrolled participants (eight male and two female) had a mean age of 37.2 years. Seven participants completed the study, with three participants dropping out. The mean final dose of levodopa for study completers was 835.7 mg (SD 170.1). Levodopa augmentation resulted in a significant improvement in negative symptoms, with a mean SANS reduction for study completers of 15.3 (SD 5.7). This equated to a mean SANS improvement of 25.5% (range 17% to 57%), with 43% of study completers experiencing > 20% improvement in SANS score. Notably, significant improvement in negative symptoms emerged after the first four weeks of treatment. There was no significant change in positive symptoms, nor other clinical outcomes or side effect measures.
Discussion: Our findings suggest that levodopa augmentation of antipsychotics may be an effective and well-tolerated treatment for negative symptoms in schizophrenia. These findings, however, need replication in larger randomized controlled trials. With the dearth of available treatments for negative symptoms, levodopa augmentation may represent a novel pharmacologic strategy to address this critical unmet therapeutic need for schizophrenia.

F226. CLINICAL FACTORS ASSOCIATED WITH CONTINUATION OF LONG-ACTING INJECTABLE ANTIPSYCHOTIC MEDICATION: RETROSPECTIVE CHART REVIEW

Shi Hyun Kang*[,1], Jong Il Lee[1]
[1]Seoul National Hospital