Results: The distribution of haplogroups was $n = 74$ HV, $n = 33$ JT, $n = 38$ UK and $n = 7$ I/X/W. The prevalence of AIM was higher in the UK haplogroup ($n = 23$ AIM+, $n = 15$ AIM-) compared to other European haplogroups (OR = 2.35, 95% CI = 1.1–5.07, $p = 0.026$). Variant analyses revealed nominal associations for m.1811A > G of mt-RNR2 (G allele; OR = 3.7, 95% CI = 1.5–9.9 $p = 0.004$) and m.1189 of mt-RNR1 (C allele, OR = 4.6, 95% CI = 1.3–21.9, $p = 0.02$); neither variant remained significant after multiple testing correction.

Conclusion: Preliminary results suggest that mtDNA variants may play a role in treatment outcomes in patients with BD, although interpretation of current findings is limited due to sample size constraints. Analyses of additional samples and treatment outcomes are ongoing.

P63 | Enrichment of AKAP11 consequential variants in bipolar disorder patients: Whole genome sequencing analysis

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Introduction: Bipolar disorder (BD) is a heritable neuropsychiatric disorder characterized by episodes of mania and episodes of depression. Numerous twin studies estimated broad heritability of BD around 67%. The implicated genes encode ion channels, neurotransmitter transporters, and synaptic and calcium signalling pathways. Latest meta-analyses led to delineation of the enrichment of rare consequential variants in patients with BD. AKAP11 emerged as the strongest candidate and a definitive risk gene. It is highly expressed in the brain and has been shown to interact with GSK3B, the hypothesized target of lithium therapy.

Method: In this study we investigated the frequency of and type of AKAP11 variants in large cohort of whole genome sequencing samples obtained from BD patients. We specifically tested the hypothesis of enrichment of rare MAF <5, pLOFs and missense variants in AKAP11 in the BD cases. The analysis consisted of 456 samples. Genetic analyses were adjusted for PCs, sex and age.

Results: We report a significant enrichment of such AKAP11 variants, specifically, we detect (alleles): 133/456 in cases versus internal controls: 654 /2845. This is a significant effect (p-value – 0.0042), OR 1.4 (CI 1.1–1.7). Altogether we report 105 carriers of at least one AKAP11 variant. The age of onset was on average 24 years old in the carriers and 26 years old in the non-carriers, with earlier onset on average at 20 years old observed in carriers of multiple variants within AKAP11.

Conclusion: This analysis is demonstrating the role for rare coding variation as a significant risk factor in BD etiology.

P64 | Changes in morbidity among bipolar I patients during the pandemic: Comparison between two seven-month periods

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Introduction: Converging evidence supports the involvement of circadian rhythm disturbances in the course and morbidity of bipolar disorder (BD). During 2020, lockdown measures were introduced worldwide to contain the health crisis caused by the COVID-19 pandemic. As a result, chronobiological rhythms were critically disrupted, leading to sleep disturbances and psychological symptoms in the general population. Within this context, a mental health crisis was thought to be approaching and it was reasonable to expect that BD-related outcomes would worsen because of these circumstances. The current study aimed to explore changes in illness severity among BD patients living under strict lockdown.

Method: Thirty-seven type I BD outpatients under naturalistic treatment conditions were followed from March to September 2020 using a mood chart technique. Different variables of illness severity, including mood instability, were assessed and compared with the clinical outcomes obtained during the same seven-month period in 2019.

Results: No significant between-period differences were observed in patients' clinical course, intensity of pharmacological treatment, or number of outpatient visits. During the pandemic, most patients (54%) did not exhibit any increase in mood instability or in the time spent with mood symptoms.

Conclusion: In line with previous longitudinal studies of BD patients, the results of this study show no worsening in clinical morbidity during the pandemic. Such a conspicuous contrast between our initial predictions and the observed findings highlights the fact that we are still far from being able to accurately predict the evolution of the disorder and the impact that specific stressors have on illness variables.

P65 | Low postural dynamics are associated with higher illness burden in bipolar disorder

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Introduction: While motor abnormalities are commonly seen during depressive or manic episodes, not much attention has been paid to postural abnormalities during euthymia and their association with illness