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Background: Population-based and family studies have shown a substantial heritability of suicide behavior, with estimates from 30 to 55% (Voracek, 2007; Sokolowski, 2014). Recently the results of the largest genome-wide association study (GWAS) on suicide attempt, using cohorts of individuals with major depressive disorder (MDD), bipolar disorder (BD), and schizophrenia (SCZ) from the Psychiatric Genomics Consortium (PGC), were published (Niamh, 2019). Here we leverage summary data of the GWAS on suicide attempt to generate polygenic risk scores (PRS) for suicide attempt in independent samples. Also, a genetic correlation between suicide attempt and several psychiatric/personality traits has recently been reported (Ruderfer, 2019). In addition to calculating PRS for suicide attempt, we generate PRS for psychiatric disorders and personality traits based on the latest results of GWAS in independent samples. Subsequently we analyze the association of these PRS with the suicide-related information available in our sample.

Methods: The sample under analysis consists of 729 to 764 patients, depending on the suicide-related variables analysed, with BD of European origin, which was collected by the International Consortium on Lithium Genetics (ConLiGen). PRS for suicide attempt, neuroticism, and MDD were calculated for each sample in ConLiGen. PLINK 1.90 (Chang, 2015) and R were used for PRS calculation and data manipulation/analysis. The most recent GWAS for SCZ, BD, MDD, suicide and neuroticism were used as discovery samples for these calculations (Niamh, 2019; Pardillos, 2018; Stahl, 2019; Wray, 2018; Luciano, 2018). Subsequently the association of PRS with relevant clinical variables (suicidal ideation, suicide attempt, number of suicide attempts) was studied using linear/logistic models and correcting for relevant covariates.

PsyCourse, a German cohort of psychiatric patients (SCZ, BD, MDD) and healthy controls was used as independent transdiagnostic replication sample. This sample included in this study ranges from 996 to 1338 patients, depending on the suicide-related variables analysed. The same analyses as mentioned above were performed on this sample as well.

Results: Our preliminary analyses show that suicidal behavior is significantly influenced by PRS for suicide attempt in the ConLiGen sample (suicidal ideation: FDR=5.0e-10, R2=5.2%; suicide attempt: FDR=2.8e-15, R2=9.4%; number of suicide attempts: FDR=1.2e-8, R2=5.0%). PRS for neuroticism is significantly associated with suicidal ideation (FDR=0.040, R2=0.7%) and suicide attempt (FDR=0.0012, R2=1.8%). PRS for MDD is also associated with number of suicide attempts (P=0.023, R2=0.62%) but not significant after multiple test correction.

Some of these associations were replicated in the PsyCourse cohort. PRS for neuroticism are significantly associated with suicide attempt (FDR=0.038, R2=0.058%) and number of suicide attempts (FDR=0.012, R2=0.62%). There are no consistent significant associations between MDD PRS and suicidal ideation, suicide attempt or number of suicide attempts.

Discussion: Our results suggest that suicidal behavior might be influenced by polygenic burden not only for suicide attempt but also for personality traits like neuroticism and to a lesser extent psychiatric disorders like MDD. Further investigation of these overlapping risks for suicide attempt may provide biological insights into the transdiagnostic biological factors that increase suicide risk.

Disclosure: Nothing to disclose.

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ASSESSING CLINICAL, DEMOGRAPHIC AND GENETIC RISK FACTORS FOR TREATMENT ATTRIBUTED SUICIDALITY IN >20,000 AUSTRALIAN ADULTS ON ANTIDEPRESSANTS

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Background: Antidepressants have been shown to be effective at treating clinical depression. Nonetheless, some individuals might experience side effects, including treatment-related emergence or worsening of suicidality. Previous research suggests that demographic, clinical and genetic factors might explain its risk, but this has not been studied thoroughly.

Methods: Individuals who have been prescribed antidepressants were recruited as part of the Australian Genetics of Depression Study (N~20,000). Participants completed online questionnaires about lifestyle, depressive symptoms, comorbidities, treatment response and side-effects, including treatment-attributed suicide ideation (TASI) and attempt. A subset (N~15,000) were genotyped. We researched the associations of TASI with clinical and demographic factors. Furthermore, we assessed whether the liabilities to depression, schizophrenia, or bipolar disorder, as determined by polygenic risk scoring (PRS), are associated with TASI. Finally, we implemented machine learning Methods: to create classifier models and tested the predictive power of the associated variables.

Results: The mean prevalence of TASI was ~12%, which was similar across the 10 different antidepressants under analysis (range [10%-14%]). Significant associations were found for age (OR=0.97 [0.971-0.977] per year increase) and comorbid conditions such as bipolar (OR=2.2 [2.0-2.5]), posttraumatic stress (OR=2.3 [2.1-2.6]) and personality (OR=3.5 [3.0-4.0]) disorders. Past episode depressive symptoms that associated with TASI included feelings of guilt (OR=1.4 [1.07-1.83]) and thoughts of death (OR=2.62
Then, liability to depression was significantly associated with TASI (OR = 1.1 [1.06-1.13]; maximum variance explained 3.3%). However, the association with the liabilities to bipolar disorder and schizophrenia did not reach statistical significance (ORbp = 0.99 [0.98-1.01]; ORscz = 1.04 [0.99-1.08]). Machine learning classifiers (such as Ada-boost, random forests and logistic regression) distinguished TASI from non-TASI participants (AU-ROC > 0.760). TASI probability derived from these models was higher for individuals with treatment-attributed suicide attempt.

**Discussion:** This study sheds light on crucial aspects of treatment attributed suicidality. TASI prevalence was moderate, and independent of the type of antidepressant studied. This could imply either a set of common pathways being targeted by the antidepressants studied, or common genetic factors that predispose to TASI regardless of antidepressant mode of action. Interestingly, liability to depression was associated with TASI. This result is consistent with depression severity predicting treatment emergent and worsening of suicidality. Finally, the fact that TASI probabilities were higher for subjects with an actual attempt would suggest treatment-attributed suicidality to be part of a continuum. This study provides evidence of clinical, demographic and genetic risk factors associated with TASI enabling its prediction. Clinical trials could leverage these Results: to stratify subjects. Future studies should focus on assessing the heritability and SNP effects associated with TASI and testing whether common genetic factors predispose to TASI across different antidepressant classes.

**Disclosure:** Nothing to disclose.

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**72 EXPLORATORY ANALYSIS OF SEX DIFFERENCES IN BRAIN GENE EXPRESSION IN SUICIDES**

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**Background:** Suicide rates vary substantially by sex. The last suicide rate reported, in 2016, was 15.0 male suicides and 8.0 female suicides per 100 000 people. Except for some few exceptions, male-female suicide ratio is higher than one in almost all countries around the world. Plausible explanations for this phenomenon rely on community and social factors. However, biological differences between both sexes have not been fully explored in the suicidal brain as they have been limited to candidate pathways.

**Methods:** Brain tissue samples from 79 individuals were collected. Consensus diagnosis was performed according to DSM-5 criteria by a pathologist, a psychiatrist and a psychologist with information obtained from legal medical records. Then, gene expression profiles were evaluated by microarrays. We considered the following groups: i) male suicides (n=38), ii) female suicides (n=10), iii) male non-suicides (n=20), and iv) female non-suicides (n=7).

Microarray data quality control was performed. Then, microarray data were Background: corrected and quantile normalized. Differentially expressed genes among the conditions were identified by a linear model implemented in limma package.

**Results:** When comparing the gene expression profile of female suicides and female non-suicides, we identified 2512 differentially expressed genes. Functional annotation of differentially expressed genes indicated enrichment mainly in cellular component organization, vesicle and mitochondrion, immune response, and response to hormones. In males, 2274 genes were identified as differentially expressed between suicides and non-suicides. Differentially expressed genes were enriched in vesicle, mitochondrion, ribonucleoprotein complex, cellular macromolecular organization, and adhesens junction.

**Discussion:** Genetic variations with gender-specific effect have been identified in subjects with suicidal behavior previously. Regarding gene expression, sex differences have been reported in X-linked genes and glutamatergic receptors. Our study extended previous findings by evaluating sex-specific gene expression patterns at a transcriptome level, which allowed the identification of unexplored sex differences in the brain of suicide completers.

**Disclosure:** Nothing to disclose.

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**Wednesday, October 30, 2019**

**Oral Session: ADHD**

2:30 p.m. - 4:00 p.m.

**73 NEW ADHD RISK LOCI IDENTIFIED IN A GWAS META-ANALYSIS OF 126,000 ADHD CASES AND 900,000 CONTROLS**

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1 Aarhus University; 2 https://www.med.unc.edu/pgc/pgc-workgroups/attention-deficit-hyperactivity-disorder/; 3 23andMe, Inc

**Background:** Attention-deficit hyperactivity disorder (ADHD) is a highly heritable childhood psychiatric disorder affecting 5% of school-age children and 2.5% of adults. In our recent genome-wide association study (GWAS) meta-analysis of 20,183 ADHD cases and 35,191 controls we identified 12 genome-wide significant risk loci for ADHD, which revealed new and exciting information about the biology of the disorder. For ADHD we might have reached the inflection point, where the number of significant as-