weight gain (p=0.02). Decreasing LEAP-2 concentrations was able to predict a negative outcome (i.e. unstable weight gain) in 80% of the cases.

**Conclusions:** We provide evidence that the ghrelin/LEAP-2 system is not regulated according to the nutritional status in AN as it is in the case of a physiological adaptation to food restriction. Results from an ongoing longitudinal study exploring remission in AN suggest that the evolution of LEAP-2 concentrations during refeeding is opposed to data from preclinical model and could give new insights on the outcome of weight gain in AN.

Disclosure of Interest: None Declared

## **O0086**

## Estimating accelerated biological ageing using machine learning and metabolomics data in people with mental disorders

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**Introduction:** Accelerated biological ageing might contribute to the higher prevalence of age-related diseases and excess mortality amongst individuals with mental disorders. Recent advances in machine learning and the collection of high-dimensional molecular "omics" data allow for the quantification of biological age.

**Objectives:** The aim of this study was to use machine learning methods to predict biological age from nuclear magnetic resonance spectroscopy metabolomics data and to identify psychiatric traits associated with accelerated biological ageing.

**Methods:** The UK Biobank is a multicentre community-based observational study that recruited >500,000 middle-aged and older adults. 168 metabolomic measures were quantified using the Night-ingale Health platform. Phase 1 release of these data included a random subset of 118,462 UK Biobank participants. Metabolomic age delta (MetaboAge $\Delta$ ) was defined as the difference between predicted biological age and observed chronological age. We estimated group differences in MetaboAge $\Delta$  between individuals with and without mental disorders and examined whether polygenic scores for mental disorders predicted MetaboAge $\Delta$ .

**Results:** Up to 110,780 participants with complete data on all metabolomic measures were included in the analysis. Individuals with a history of mental disorders had higher MetaboAge $\Delta$  values than people without a mental illness. For example, MetaboAge $\Delta$  suggested that the difference between predicted biological age and observed chronological age was about two-years greater amongst individuals with bipolar disorder than amongst people without mental illness. Polygenic scores for mental disorders were positively correlated with MetaboAge $\Delta$ .

**Conclusions:** These findings suggest that individuals with a history of mental disorders or with higher polygenic scores for mental disorders were biologically older than their chronological age.

Disclosure of Interest: None Declared

## **O0087**

## High genetic diagnostic yield in children and adolescents with psychiatric disorders

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**Introduction:** Psychiatric disorders are more prevalent in children with mild (MID) to borderline intellectual functioning (BIF). Rare pathogenic variants in neurodevelopmental genes increase the risk for psychiatric disorders and may explain the comorbidity. Despite these patients represent up to 35% of those attended at mental health services, genetic diagnosis is usually not offered. The identification of mentioned variants could lead to improved clinical care.

**Objectives:** To identify pathogenic variants responsible of the psychiatric disorders in mild and borderline intellectual functioning.

To correlate phenotypic and genetic profiles to personalize diagnostic, clinical care and support to clinicians and families.

**Methods:** Whole exome sequencing (WES) was performed on 99 enrolled children/adolescent (6-18 yo) affected by a psychiatric condition diagnosed following DSM-5 criteria, and either MID (IQ 55-69) or BIF (IQ 70-85). Severity and interference of IQ and psychiatric comorbidity was evaluated using several psychometric tests (Conners, CDI, STAIC, CAARMS, CBCL and hONOSCA). Inheritance pattern was assessed through Sanger sequencing. ACMG/AMP guidelines were used for variant classification.

**Results:** In our cohort, 64% patients presented BIF and 36% MID. 45% of the patients had 2 or more psychiatric diagnoses, the most prevalent (87%) being attention deficit hyperactivity disorder and, in second place, autism spectrum disorder (51%).

WES identified pathogenic/likely pathogenic variants in 30% of analyzed patients (30/99), 80% of the variants were de novo. There is no significant difference in patient severity between those with a genetic diagnosis and those without.

**Conclusions:** Rare deleterious and *de novo* variants in neurodevelopmental genes are responsible for the comorbidity that exists between psychiatric disorders and mild/borderline intellectual disability.

The high diagnostic yield obtained from our exome sequencing approach demonstrates the need to offer genetic testing in children with psychiatric disorders and comorbid mild to borderline intellectual functioning.

Finally, patients being identified with a genetic diagnosis are subsequently attended in a specialised unit for rare disorders to receive personalised clinical management.

Disclosure of Interest: None Declared