symptoms, depression, obsessions and compulsions. Patients were included in a nutritional rehabilitation program. Daily caloric intake was 2000–2500 kcal and was gradually increased to 3500–4000 kcal depending on weight gain (1.0–1.5 kg per week).

Results: APE-13 levels were higher in the AN1 group than in the post-realimentation and the CG group. APE-13 levels were independent of insulin and glucose levels. Plasma ASP levels increased with increasing body weight in patients with AN, correlating with the severity of eating disorder symptoms in emaciation.

Image:

	Group M ± SD			AN1 vs. AN2		AN1 vs. CG		AN2 vs. CG	
	An1 n = 44	An2 n = 44	Control n = 29	MD (95% CI)	p	MD (95% CI)	p	MD (95% CI)	p
Age	15.50		15.00	-	-	MD (95% CI) = 0.50 (-1.00; 1.00); p = 0.995			
Height (m)	1.61		1.65	-	-	MD (95% CI) = -0.04 (-0.06; < 0.01); p = 0.024³			
Body weight (kg)	37.00	45.00	53.70	-8.10	<0.001¹	-16.70	< 0.001	-8.70	< 0.001
BMI	14.13	17.08	18.91	-3.28)	<0.001¹	-4.78	< 0.001	-1.83	0.006
ASP [ng/ml]	8.06	10.08	5.61	-2.04	0.008²	2.45	0.961	4.47	0.075
APE-13 [pg/ml]	113.56	50.93	68.08	30.99	0.037²	45.48	0.046	-17.15	0.479

Image 2:

	Group M			AN1 vs. AN2		AN1 vs. CG		AN2 vs. CG	
	An1 n = 44	An2 n = 44	Control n = 29	MD (95% CI)	p	MD (95% CI)	p	MD (95% CI)	p
BDI	13.00	11.50	5.00	3.00	0.012²	8.00	0.003	6.50	0.042
HAMD	12.00	8.00	0.00	4.50	0.050²	12.00	< 0.001	8.00	< 0.001
CYBOCS	8.00	2.00	2.00	6.00	< 0.001²	6.00	0.006	0.00	0.079
EAT-26	22.00	7.00	4.50	11.00	< 0.001³	17.50	< 0.001	2.50	0.079

Image 3:

	AN1				AN2				CG			
	ASP		APE-13		ASP		APE-13		ASP		APE-13	
	rho	p	rho	p	rho	p	rho	P	rho	p	rho	p
BDI	0.23	0.298	-0.46	0.034	0.06	0.771	0.28	0.181	-0.26	0.201	-0.09	0.736
HAMD	0.10	0.661	-0.42	0.051	0.06	0.751	0.11	0.579	-0.25	0.214	-0.31	0.242
CYBOCS	0.23	0.291	< 0.01	0.998	0.04	0.832	0.15	0.461	-0.21	0.315	-0.16	0.542
EAT-26	0.51	0.025	-0.50	0.028	-0.13	0.588	0.53	0.030	0.19	0.420	0.34	0.237

Conclusions: The presented data suggest that APE-13 and ASP may be AN's biomarkers-regulation of eating behavior by APE-13 and ASP, the close relationship between them and emotional behavior, and changes in neurohormone levels in patients with eating and affective disorders seem to support these hypotheses. Moreover, their plasma levels seem to be related to the severity of psychopathological symptoms of eating disorders.

Disclosure of Interest: None Declared

O0085

The role of dysregulated ghrelin/LEAP-2 balance in eating disorder: a translational study in anorexia nervosa

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Introduction: Anorexia nervosa (AN) is a complex psychiatric disorder characterized by a persistant decrease in food intake leading to dramatic weight loss and energy deficit. The ghrelin system is a key regulator of appetite and food intake across species. LEAP-2, a recently discovered ghrelin antagonist, appears to be up-regulated in obesity and opposes to the orexigenic drive of ghrelin. The evolution of LEAP-2 levels could be an interesting insight to reflect the regulation of appetite in eating disorders such as anorexia nervosa (AN).

Objectives: We tested this hypothesis and here provide the first study exploring the ghrelin and LEAP-2 regulation in long-term food restriction followed by refeeding in both mice and patients suffering from AN.

Methods: Using a translational strategy, we compared the regulation of ghrelin and LEAP-2 concentrations in blood during food restriction and after refeeding i/ in female mice exposed to a 14 days protocol combining quantitative food restriction and running wheel activity followed by 10 days of progressive refeeding; ii/ in an ongoing longitudinal study of patients with AN evaluated before and after refeeding (n=30) as well as 6 months after hospital discharge to evaluate if the weight gain was stable (n=7) or unstable (n=10). Plasma concentrations of ghrelin and LEAP-2 were measured with selective immunoassays.

Results: Long-term food restriction in mice was associated with increased ghrelin (p<0.001) and decreased LEAP-2 concentrations (p=0.006) compared to *ad libitum* fed controls. Refeeding led to a decrease in ghrelin (p<0.01) and increase in LEAP-2 concentrations (p<0.01). Patients with AN displayed increased ghrelin levels (p<0.01) but also higher LEAP-2 concentrations on admission than after refeeding (p=0.04). LEAP-2 decreased with refeeding. On 17 patients re-evaluated 6 months after discharge, patients with unstable weight gain exhibited a greater decrease of LEAP-2 concentrations during refeeding compared to patient with stable

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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doi: 10.1192/j.eurpsy.2023.291

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 Nightingale Health platform. Phase 1 release of these data included a random subset of 118,462 UK Biobank participants. Metabolomic age delta (MetaboAgeΔ) was defined as the difference between predicted biological age and observed chronological age. We estimated group differences in MetaboAgeΔ between individuals with and without mental disorders and examined whether polygenic scores for mental disorders predicted MetaboAgeΔ.

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 MetaboAgeΔ values than people without a mental illness. For example, MetaboAgeΔ 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 MetaboAgeΔ.

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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doi: 10.1192/j.eurpsy.2023.292

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