Adverse effects were mentioned at the higher dose (10mg) with negative reaction times, sedation and confusion.
Conclusion. There is a potential favourable effect of prescribing melatonin for mild to moderate AD, but there is limited evidence for prescribing it for moderate to severe AD. Furthermore, there is emerging evidence on melatonin's neuroprotective effect and potential treatment options for mild to moderate AD; further research is required for both sleep and neuroprotection in AD.

Choices Today, Behaviours Tomorrow: Longitudinal Associations Between Childhood Risky Decision-making and Adolescent Conduct Disorder Behaviours – a Nationally Representative Prospective Cohort Study in the United Kingdom

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Aims. Conduct disorder carries significant individual and societal repercussions. Despite heightened risk-taking and challenges in adapting to changing probabilities of choice outcomes being linked to maladaptive behaviours such as conduct disorder, no study to date has examined the association behind childhood decision-making and adolescent conduct disorder. This study seeks to address this gap by exploring the longitudinal association between these two variables. Understanding the mechanisms underlying conduct disorder could help with developing new preventive interventions.
Methods. We used data from the Millennium Cohort Study, a nationally representative UK cohort; participants included those with complete data on exposure, outcome and confounding variables (n = 7,237). The exposure, childhood decision-making at 11 years was measured using the Cambridge Gambling Task risk-taking and risk-adjustment measures. The outcome, a binary measure of adolescent conduct disorder was created using items from the risky and antisocial behaviour interview sections at age 17. We used logistic regression to examine the association between childhood decision-making and adolescent conduct disorder and adjusted for relevant confounders.
Results. The univariable model showed that at age 11, each 20-point increase in risk-taking score increased the odds of conduct disorder behaviour at age 17 by 32% (OR = 1.32, 95% CI 1.18–1.44, p < 0.0001). In the multivariable model, there was strong evidence that a 20-point increase in risk-taking at 11 years was associated with 18% higher odds of conduct disorder behaviour at 17 years (OR = 1.18, 95% CI 1.05–1.33, p = 0.005). There was no evidence that this association differed by sex. Risk adjustment at 11 years showed no association with conduct disorder behaviours at age 17 both in the univariable model (OR = 0.96, 95% CI 0.88–1.06, p = 0.440) and the multivariable model (OR = 0.96, 95% CI 0.88–1.06, p = 0.433).
Conclusion. We found that risk-taking at 11 years was associated with conduct disorder behaviour at 17 years. If causal, our findings suggest that risk-taking might be a potential mechanism underlying adolescent conduct disorder behaviours. This may be useful in informing the design of preventive strategies, such as encouraging positive risk-taking in children and discouraging negative risk-taking behaviours.

BMAL1 Genetic Variation in Metabolic and Mental Health

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Aims. Epidemiological studies have previously shown a link between cardiometabolic disease and severe mental illness. The extent and mechanisms behind this link are poorly understood currently but links to impairments in the stress response and cortisol regulation have been thought to play a significant role. *BMAL1* is a circadian rhythm regulation gene found on chromosome 11 which has been associated with a variety of pro-inflammatory states as well as conditions such as depression, schizophrenia, type 2 diabetes mellitus and myocardial infarction. Our study aimed to investigate the genetic structure of the *BMAL1* gene locus and its associations with both cardiometabolic and psychiatric traits and conditions.
Methods. We used genetic data from the UK Biobank which recruited ~500,000 participants. Of these we used a population of ~430,000 self-reported white British participants and data from a variety of questionnaires and investigations looking at severe mental illness and cardiometabolic traits. We performed association analyses using Plink 1.07 with Bonferroni correction being performed for multiple testing using a number of genetic variants. Our threshold for significance was defined as a p-value $< 5.35 \times 10^{-5}$. Conditional analysis was then performed to identify if there were multiple independent signals for each phenotype.
Results. *BMAL1* variants were associated with BMI, diastolic, systolic blood pressure, waist-hip ratio and neuroticism score, and risk of anhedonia, major depressive disorder and risk-taking behaviour. Multiple significant independent signals were identified for BMI and waist-hip ratio. Linkage disequilibrium (LD) analysis showed significant coinheritance of specific traits which could suggest a role for *BMAL1* and the encoded protein as a link between cardiometabolic and mental health traits.
Conclusion. This is the first study that systematically investigated associations between the *BMAL1* locus across a variety of different mental and cardiometabolic phenotypes in a population-level cohort. Our study has shown that there is a link between the *BMAL1* locus and both cardiometabolic and mental health phenotypes. Further research is required to investigate the exact biological mechanism by which *BMAL1* connects severe mental illness and cardiometabolic disease.

The Association Between Severe Mental Illness and Receipt of Acute Cardiac Care for Myocardial Infarction, and the Impact of the COVID-19 Pandemic

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Aims. To compare receipt of acute cardiac care in people with versus without severe mental illness (SMI) and investigate the impact of the COVID-19 pandemic on any differences in care. We hypothesised that, compared with those without SMI, patients with an SMI are less likely to receive guideline recommended acute cardiac care and that disparities worsened as a result of the pandemic.
Methods. We conducted a cohort study using data from the CVD-COVID-UK resource, which links electronic health data from multiple sources. Our cohort included 95,125 adults with a non-ST-elevation MI (NSTEMI) recorded in the Myocardial Infarction National Audit Programme (MINAP) dataset between 1 November 2019 and 31 March 2022. We defined SMI as schizophrenia, schizoaffective disorders or bipolar disorder (BD), ascertained through recorded diagnosis in primary care or hospital admission records. We examined receipt of cardiac care standards for NSTEMI, including: admission to a cardiac ward; angiogram eligibility; receipt of angiogram (in those eligible); angiogram within 72 hours; secondary prevention medication prescribing at discharge, and arrangement of post-discharge cardiac rehabilitation. We used logistic regression to obtain odds ratios (ORs) for the association between SMI and receipt of each care indicator, adjusting for age, sex and time period. We tested for an interaction between SMI and time period in order to determine if any disparities had changed since the start of the COVID-19 pandemic.
Results. Within our cohort, 620 patients (0.6%) had schizophrenia and 575 (0.6%) had BD. Compared with people without SMI and after adjusting for age, sex and period, patients with an SMI were less likely to receive each of the cardiac care standards. For example, compared with those without SMI, those with SMI were less likely to: be admitted to a cardiac ward (schizophrenia: OR 0.72, 95% CI 0.61–0.85; BD: 0.74, 95% CI 0.63–0.88); be eligible for an angiogram (schizophrenia: 0.37, 95% CI 0.29–0.47; BD: 0.52, 95% CI 0.40–0.68); receive an angiogram (schizophrenia: 0.22, 95% CI 0.18–0.28; BD: 0.51, 95% CI 0.39–0.66); and receive an angiogram within 72 hours (schizophrenia: 0.71, 95% CI 0.56–0.90); BD: 0.80, 95% CI 0.64–1.00). We generally found no evidence that disparities had changed since the start of the COVID-19 pandemic.
Conclusion. We identified marked SMI disparities in receipt of acute cardiac care among people treated in hospital for a NSTEMI. Further research should seek to identify reasons for, and inform interventions to, address these disparities.

Pre-operative Mental Health and Adverse Outcomes Following Total Knee Replacement: A Prospective Cohort Study

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Aims. Total knee replacements (TKRs) are effective procedures for severe osteoarthritis. Some studies suggest that people with common pre-operative mental health problems are more likely to experience complications following joint replacement. This study aimed to determine whether people who described pre-operative anxiety or depression were more likely to report an adverse event, or outcome, following a TKR.
Methods. A prospective cohort of people undergoing TKR at a surgical centre in England between 2012–2013 as part of service evaluation were studied. Following informed consent, participants completed pre-operative sociodemographic questionnaires alongside several patient-reported outcome measures (PROMs): the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), EuroQoL Five-dimensions Descriptive System (EQ-5D-3L), and the Self-Administered Patient Satisfaction Scale for Primary Knee Arthroplasty. Participants were classified as exposed if they described moderate or extreme problems with anxiety or depression in the mental health subset of the EQ-5D-3L. The primary outcome was the presence of a patient-reported adverse event (bleeding, infection or fracture) at 3 months post-surgery measured through a short postal questionnaire. Repeat PROMs were assessed at 3- and 12-months post-surgery. Logistic regression was used to model the association between pre-operative mental health status and probability of an adverse event, or outcome, occurring following adjustment for age, sex and body mass index.
Results. Of the 206 individuals studied, over a third (n 72/206, 35%) had reported problems with anxiety or depression before surgery. Among those returning completed follow-up questionnaires, 20% (n 34/168) described an adverse event at 3 months. Pre-operative anxiety or depression was not associated with an increased odds of reporting an adverse event (aOR 0.85, 95% CI 0.35–2.05) at 3 months post-surgery. People who described problems with anxiety or depression were more likely to have a greater degree of pre-operative functional impairment. Even after adjusting for a higher pre-operative symptom burden, exposed participants were more likely to report problems with activities of daily living (aOR 2.32, 95% CI 1.09–4.94) and pain or discomfort (aOR 5.58, 95% CI 1.77–17.60) at 3 months post-surgery. However, they did not have an increased odds of describing worse function, reduced health-related quality of life, or being dissatisfied with their TKR at 12 months post-surgery.
Conclusion. Despite having a higher burden of morbidity prior to undergoing surgery, pre-operatively anxious or depressed participants did not have an increased odds of reporting an adverse event at 3 months and went on to experience comparable improvements in PROMs at 12 months post-surgery.

Modafinil in Post-Traumatic Brain Injury Apathy: A Sleeping Giant?

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