34 points in the Montgomery-Asberg-Depression Rating Scale (MADRS). Randomised patients took 80 mg Silexan, 50 mg Sertraline, or placebo once daily over 8 weeks. Primary efficacy endpoint was the change of the MADRS total score between baseline and week 8. Response (a reduction of the MADRS total score ≥50%), remission (MADRS total score <10 at the end of the treatment), the Patient Health Questionnaire PHQ-9, the Beck Depression Inventory, the Clinical Global Impressions, and the Sheehan Disability scale served as secondary endpoints.
Results: The full analysis set consisted of 498 patients. Between the start and end of treatment, the MADRS total score decreased by 12.1 (13.3, 11.0) points (adjusted mean, 95% confidence interval) in patients treated with Silexan, by 12.6 (13.7, 11.5) points in patients treated with Sertraline, and by 9.95 (11.1, 8.77) points under placebo. The confirmatory analysis proved that Silexan was significantly superior to placebo ($p<0.01$, ANCOVA). Internal validity could be shown since the treatment effects of the active comparator Sertraline were also more pronounced compared to placebo ($p<0.01$). There were no relevant differences between Silexan and Sertraline. Response was achieved by 53.5% of the patients in the Silexan group, by 54.0% of the patients in the Sertraline group, and by 41.5% of the patients in the placebo group. 44.4% of the patients treated with Silexan were remitter, compared to 45.2% under Sertraline and 32.6% under placebo. In both active treatment groups responder and remission rates were higher than in the placebo group ($p < 0.05$). Results of the secondary endpoints were in line with the results of the primary endpoint.
Conclusions: In a large phase III clinical trial, Silexan was more effective than placebo and not different to Sertraline in patients with a major depressive episode. Treatment effects were clinically relevant.

Disclosure of Interest: S. Kasper Consultant of: In the past 3 years Dr Kasper served as a consultant or on advisory boards for Angelini, Biogen, Boehringer, Esai, Janssen, IQVIA, Mylan, Recordati, Rovi, Sage and Schwabe; and he has served on speakers bureaus for Angelini, Aspen Farmaceutica S.A., Biogen, Janssen, Recordati, Schwabe, Servier, Sothema, and Sun Pharma., Speakers bureau of: In the past 3 years Dr Kasper served as a consultant or on advisory boards for Angelini, Biogen, Boehringer, Esai, Janssen, IQVIA, Mylan, Recordati, Rovi, Sage and Schwabe; and he has served on speakers bureaus for Angelini, Aspen Farmaceutica S.A., Biogen, Janssen, Recordati, Schwabe, Servier, Sothema, and Sun Pharma., E. Seifritz Consultant of: Schwabe, Janssen, Speakers bureau of: Schwabe, Janssen, H.-P. Volz Consultant of: Schwabe, Janssen, Speakers bureau of: Schwabe, Janssen

EPP0301

Ketamine enhanced ECT in refractory recurrent depression.

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doi: 10.1192/j.eurpsy.2024.480

Introduction: Recurrent Depressive Disorder is a chronic condition that significantly impacts the quality of life. Despite various treatment options, some patients face severe and treatment-resistant relapses. This case is related to research on ketamine in Electroconvulsive Therapy (ECT) for RDD. One study highlighted the efficacy and safety of ketamine compared to other anaesthetic agents in ECT for major depression. Additionally, another study explored subanesthetic doses of ketamine before each ECT session to improve therapeutic outcomes and sleep quality in patients with major depressive disorder.
Objectives: To present a clinical case of a patient with Recurrent Depressive Disorder (RDD) who improved following a change in the Electroconvulsive Therapy (ECT) protocol using ketamine as an anaesthetic inducer.
Methods: We examined the patient's medical records, including her medical history, previous treatments, and therapeutic responses.
Results: A 65-year-old childless woman with a history of stroke, bilateral carotid atheromatosis, and hypothyroidism suffered from RDD. Despite multiple prior treatments and ECT, she experienced a severe depressive relapse. Eight intensive ECT sessions were administered, with observed memory lapses. Due to the lack of response, the anaesthetic inducer etomidate was replaced with ketamine, resulting in a positive response. The patient continued pharmacological treatment with improved mood, but recent and evident memory alterations persisted, possibly related to anterograde amnesia.
Conclusions: This case highlights the complexity of RDD in patients with comorbidities and treatment-resistant relapses. The change in the ECT protocol using ketamine was effective, emphasizing the importance of alternative therapeutic approaches in refractory cases. The successful treatment of RDD in this patient using ketamine in ECT underscores the need for personalized therapeutic options in treatment-resistant patients. These scientific resources reinforce the relevance of exploring therapeutic alternatives in contemporary clinical practice. We need more research to understand the underlying mechanisms and how this approach could be enhanced in similar cases.

Disclosure of Interest: None Declared

EPP0302

Revealing complexity: beyond the whole—segmentation of hippocampal subfields in adolescents with depression and its relationships with cognition

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doi: 10.1192/j.eurpsy.2024.481

Introduction: The occurrence of depression in adolescence, a critical period of brain development, linked with neuroanatomical and cognitive abnormalities. Neuroimaging studies have identified hippocampal abnormalities in those of adolescent patients. However, few studies have investigated the atypically developmental trends in hippocampal subfields in adolescents with depression and their relationships with cognitive dysfunctions.
Objectives: To explore the structural abnormalities of hippocampal subfields in patients with youth depression and examine how these abnormalities associated with cognitive deficits.
Methods: We included a sample of 79 first-episode depressive patients (17 males, age = 15.54±1.83) and 71 healthy controls

(23 males, age = 16.18±2.85). The severity of these adolescent patients was assessed by depression scale, suicidal risk and self-harm behavior. Nine cognitive tasks were used to evaluate memory, cognitive control and attention abilities for all participants. Bilateral hippocampus were segmented into 12 subfields with T1 and T2 weighted images using Freesurfer v6.0. A mixed analysis of variance was performed to assess the differences in subfields volumes between all patients and controls, and between patients with mild and severe depression. Finally, LASSO regression was conducted to explore the associations between hippocampal subfields and cognitive abnormalities in patients.

Results: We found significant subfields atrophy in the CA1, CA2/3, CA4, dentate gyrus, hippocampal fissure, hippocampal tail and molecular layer subfields in patients. For those patients with severe depression, hippocampal subfields showed greater extensive atrophy than those in mild, particularly in CA1-4 subfields extending towards the subiculum. These results were similar across various severity assessments. Regression indicated that hippocampal subfields abnormalities had the strongest associations with memory dysfunction, and relatively week associations with cognitive control and attention. Notably, CA4 and dentate gyrus had the highest weights in the regression model.

Conclusions: As depressive severity increases, hippocampal subfield atrophy tends to spread from CA regions to surrounding areas, and primarily affects memory function in patients with youth depression. These results suggest hippocampus might be markers in progression of adolescent depression, offering new directions for early clinical intervention.

Disclosure of Interest: None Declared

EPP0303

Interventions to promote social connection and their effect on depression: An umbrella review

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doi: 10.1192/j.eurpsy.2024.482

Introduction: Social connection (SC) is a multi-dimensional concept capturing both the structural–quantitative (e.g., number of social relations, social contact frequency, network structure) and the functional–qualitative dimension (e.g., social support) of social relationships. Although empirical evidence of the association between SC measures and depression has increased significantly in recent years (De Risio et al, *J Affect Disord* 2024; 345 358–368), very little is known about the extent to which interventions that build SC are effective in improving depressive symptoms.

Objectives: This umbrella review of systematic reviews/meta-analyses aims to synthesize evidence regarding the effectiveness of SC interventions on depression. Our primary focus is on interventions directly acting upon the natural social network, while indirect interventions that aim to improve social skills, or those that provide professional (formal) or semi-professional support through health services, were excluded.

Methods: We provide a synthesis of the consistency and magnitude of the effectiveness of SC interventions on depression. We searched PubMed, PsycINFO, Cochrane Library, and EMBASE and 16 reviews/meta-analyses were included. Information on the effectiveness of SC interventions on depression were compared among different populations. The quality/certainty of evidence was assessed using AMSTAR-2 and GRADE tools.

Results: Included interventions were categorized into the following domains: social support (interventions increasing both perceived and enacted social support from family, friends, and others); social engagement (interventions aimed at strengthening social networks and contrasting social isolation); social inclusion (interventions promoting social integration and access to social capital); social identification (interventions enhancing participants' identification with a group). Overall, the evidence is rather mixed with some SC interventions resulting in little to no difference in depressive symptoms compared to usual care/other interventions. The most promising interventions appear to be those contrasting social disengagement and reducing social isolation in older individuals and in patients with depression, as well as social inclusion interventions for adolescents and young adults.

Conclusions: The broader implications of SC as a key determinant of depression call for a deep examination of the impact of interventions/preventive programs on the evolving psychopathology of depressive trajectories and inform on which targeted interventions are more effective, thus guiding public health policies.

Disclosure of Interest: None Declared

EPP0304

Identifying Depression Subtypes and Investigating their Consistency and Transitions in a 1-Year Cohort Analysis

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doi: 10.1192/j.eurpsy.2024.483

Introduction: Major Depressive Disorder (MDD) is a complex mental health condition characterized by a wide spectrum of symptoms. According to the Diagnostic Statistical Manual 5 (DSM-5) criteria, patients can present with up to 1,497 different symptom combinations, yet all receive the same MDD diagnosis. This diversity in symptom presentation poses a significant challenge to understanding the disorder in the wider population. Subtyping offers a way to unpick this phenotypic diversity and enable improved characterization of the disorder. According to reviews, MDD subtyping work to date has lacked consistency in results due to inadequate