

**Introduction:** Depression is a severe mental disorder with an estimated 3.8% of the population affected, representing a leading cause of disability worldwide. Being linked to reduced quality of life and individual functioning, medical morbidity and mortality, depression has a huge social and economic impact. A wide range of potentially modifiable factors for depression has been identified. Among these, social factors (e.g. support/engagement) appear to play a major role in the emergence and severity of depression.

**Objectives:** We aimed at providing a quantitative synthesis of the consistency and magnitude of the association between measures of social connection and depression. Social connection included both quantitative (i.e. existence/absence of social relationships) and functional (i.e. support provided) measures of social relationships, as well as measures focusing on social inequalities related to participation in community spaces/activities (i.e. social discrimination).

**Methods:** We searched PubMed, PsycINFO, Cochrane Library and EMBASE. The strength of the association between exposure factors (social measures) and depression was extracted and equivalent odds ratios were computed to compare the strength of the effect sizes among meta-analyses. The quality of each review was assessed using AMSTAR-2.

**Results:** As a result of the selection process 47 studies were included in the umbrella review. Social support was found to have a protective role on depression, with an observed moderate/strong effect in peripartum population and a weaker effect in clinical populations (e.g. AIDS/HIV patients). A moderate association between stigma/discrimination and depression emerged in clinical populations (e.g. epilepsy, mental illness, post-stroke), while a weaker effect was found in (ethnic) minorities. There are still few studies quantitatively investigating the link between depression and other social measures (e.g. community connectedness).

**Conclusions:** Our findings align with the literature on social connection and mental health, confirming the role of social determinants in the emergence and severity of depression, particularly in the case of vulnerable populations. Social factors emerge as important modifiable targets in the context of depression prevention. Efforts to counteract disconnection at the societal and individual levels and to reduce stigma should be central to an effective depression prevention agenda.

**Disclosure of Interest:** None Declared

## EPP0598

### Repetitive Transcranial Magnetic Stimulation with and without Internet-Delivered Cognitive Behavior Therapy for the Treatment of Resistant Depression: Patient-centered Randomized Controlled Pilot Trial

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**Introduction: Background:** Treatment-resistant depression (TRD) is considered one of the major clinical challenges in the field of psychiatry. At least 15% of all patients with MDD remain

refractory to any treatment intervention. Repetitive transcranial magnetic stimulation (rTMS) is considered a treatment option for patients with TRD. Additionally, iCBT is an evidence-based psychotherapy for the management of TRD.

**Objectives:** This study aims to evaluate the clinical effectiveness of adding iCBT to rTMS treatment as an innovative combined intervention, exploring the short and long-term outcomes on patients with TRD

**Methods:** This study is a randomized controlled trial. Participants diagnosed with TRD were randomized to one of two interventions: rTMS alone and rTMS+iCBT. Each group completed evaluation measures at baseline, discharge (6 weeks), and one & three months after discharge. The primary outcome measure was the mean change in the Hamilton depression rating scale (HAM-D-17) from baseline to three months.

**Results:** Preliminary results for the early outcome of the study showed that after adjusting for the baseline scores, there was no significant difference in the mean score of HAM-D-17 from baseline to six weeks between the participants of the two groups, ( $F(1, 53) = 0.15, p = 0.70, \text{partial } \eta^2 = 0.003$ ). The result of the long-term effectiveness is underway, forecasting the potential synergism of the two interventions.

**Conclusions:** This study found the combined treatment of rTMS + iCBT not to be superior to treatment with rTMS alone, in the short term. We hope the long-term results would thoroughly address the effectiveness of the combined therapy in this randomized controlled trial.

**Disclosure of Interest:** None Declared

## EPP0599

### Systematic Review on the Mechanisms of Action of Psilocybin in the Treatment of Depression

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**Introduction:** Despite emerging evidence suggesting the efficacy of psilocybin in the treatment of mood disorders such as depression, the exact mechanisms by which psilocybin is able to elicit these antidepressant effects remains unknown.

**Objectives:** As the use of psilocybin as a treatment modality for depression has garnered increasing interest, this study aims to summarize the existing evidence of the mechanism of action with which psilocybin alleviates depressive symptoms, focusing specifically on the neurobiological effects of psilocybin in human subjects.

**Methods:** Four databases (Ovid MEDLINE, EMBASE, psychINFO, and Web of Science) were searched using a combination of MeSH terms and free text keywords in September 2021. The original search included both human and animal studies and must have included testing of the mechanism of action of psilocybin. Only antidepressant effects were considered, with no other mood disorders or psychiatric diagnoses included. Two independent

researchers screened at every stage of the review, with a third researcher resolving any conflicts. Though a full systematic review outlining the current literature on the complete mechanisms of action of psilocybin on depression was conducted, this abstract will focus specifically on the nine papers that included human subjects, disregarding the five animal models. PROSPERO registration number: 282710.

**Results:** After removing duplicates, the search identified 2193 papers and forty-nine were selected for full text review. Out of nine papers outlining the mechanisms of action of psilocybin use in human subjects, three papers investigated psilocybin's effect on serotonin or glutamate receptor activity, two found an increase in synaptogenesis in regions such as the medial frontal cortex and hippocampus. Four found variation in blood flow to the amygdala, two found altered blood flow to the prefrontal cortex, and one found a reduction in delta power during sleep. Four papers found changes in functional connectivity or neurotransmission, most commonly in the hippocampus or prefrontal cortex.

**Conclusions:** Overall, the exact mechanism of psilocybin's potential antidepressant effect remains unclear. Multiple pathways may be involved, including alterations in serotonin and glutamate receptor activity, as well as shifts in amygdala activity, neurogenesis, and functional connectivity in various brain regions. The relative lack of studies, and the variety of neurobiological modalities and endpoints used challenged the consolidation of data into consensus findings. Further studies are needed to better characterize psilocybin's mechanism of action and to better understand the clinical effects of the use of psilocybin in the treatment of depression.

**Disclosure of Interest:** None Declared

## EPP0600

### Is the most really the best: a review for the most selective SSRI concept three decades later

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**Introduction:** Pharmaceutical slogans presuming a particular antidepressant molecule being the best solely based on a core concept could be proved "not accurate" especially following patients' actual exposure to the antidepressant for longer than the usual six or twelve weeks' trials

**Objectives:** Reviewing the current situations of **SSRI induced anhedonia** recognition and its management. Distinguishing anhedonia as a core symptoms of depression from SSRI induced anhedonia and the combination of both.

**Methods:** Review of literatures including theses related to the same topic

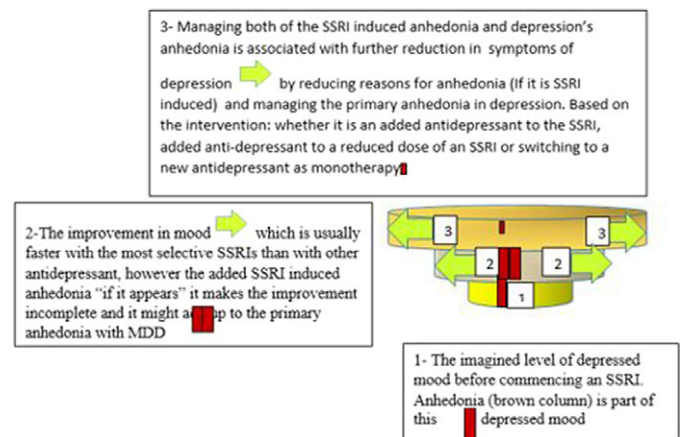
**Results:** Research suggests that, SSRIs might be more effective at treating some symptoms than others. More specifically, it has been suggested that, SSRIs might be more effective at improving symptoms such as low mood and anxiety but not anhedonia (Argyropoulos et al. *psych.pharmacology*, 2013; 27(10), 869-877). It has been proposed that, catecholaminergic antidepressants might be more effective treatments for anhedonia and emotional blunting in MDD

than SSRIs (McCabe et al. *Biological psychiatry*, 2010; 67(5), 439-445). The primary effect of SSRIs is reduced processing of negative stimuli rather than increased positive stimuli. Emotional blunting is related to SSRI dose and possibly serotonergic effects on the frontal lobes and/or serotonergic modulation of midbrain dopaminergic systems projecting to the prefrontal cortex (PFC). By enhancing serotonergic transmission, SSRIs can activate the inhibitory Gamma Aminobutyric Acid (GABA) interneurons, thereby dampening the noradrenergic and dopaminergic input (Blier. *Int J Neuropsychopharmacol.*, 2014; 17:997-1008).

Management of SSRI induced anhedonia includes lowering the current SSRI dose. Adding non SSRI antidepressant to the current SSRI dose or to a lowered SSRI dose. Gradual discontinuation of the SSRI and switching to another antidepressant with a different profile (SNRI) that might improve the patient's emotional response (Koenigs. *Behav Brain Res.*, 2009;201:239-43).

Bupropion is an antidepressant with less possibility to give rise to **emotional blunting**. (Tomoko et al. *Neuroscience Letters.*, 2021; 749, 135716. agomelatine (Thome et al. *Journal of neural transmission.*, 2015; 122(1), 3-7. Vortioxetine and others (Bing et al. *frontiers in psychiatry.*, Jan, 2019; 10-17. are of interest in this regard.

#### Image 2:



**Figure (1)** The depressed mood at base line then managed by an SSRI and managing the SSRI induced anhedonia successfully.

This figure is made fully by Dr Mohammed Allam, – however It can be cited without prior consent from Mohammed Allam.

**Conclusions:** The **most selective SSRI** concept assumes that most selective means less affinity to other receptors or secondary binding sites which might suggest less side effects and perhaps being the most efficacious. Not only serotonin but multiple neurotransmitters are in action at the downstream part of a cascade of events underpinning the etiology of MDD. MDD has heterogeneous etiology and this explains why patients respond differently. **SSRI induced anhedonia** could be tackled and we need to explore how many patients would benefit from that now and have not yet.

**Disclosure of Interest:** None Declared