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The Role of Sex in Patients with Major Depressive Disorder - Findings from a Cross- Sectional European Multicenter Study

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Background/Aims

Since the impact of sex on the evolution and phenotype of major depressive disorder (MDD) was reported previously [1-3], the objectives of the present observational, non-interventional, multicenter, cross-sectional study were to identify male to female sex ratio in a large international and naturalistic sample of 1410 adult in- and outpatients with MDD as primary diagnosis, and to investigate possible differences in socio-demographic-, clinical- and treatment patterns between male- and female MDD patients [4].

Methods

The present analyses are based on the project “Clinical and biological correlates of resistant depression and related phenotypes” performed between 2011 - 2016 by the “European Group for the Study of Resistant Depression (GSRD)” across 10 sites in Austria, Italy, Belgium, Germany, Greece, France, Israel, and Switzerland [5]. Chi-squared tests, analyses of (co)variance and logistic regression analyses considering age and research center as covariates were applied to reveal potential differences between male- and female MDD patients [4].

Results

Compared to females, male MDD patients amounted to 33.1% (N = 467) of the whole sample and were associated with inpatient status, moderate to high suicidality levels, first-line

antidepressant (AD) treatment with noradrenergic- and specific serotonergic ADs, as well as higher mean daily doses of the administered first-line ADs [4]. Female MDD patients (66.9%; N = 943) were related to outpatient status, lower suicidality levels, somatic comorbidities in general and comorbid thyroid dysfunction, migraine and asthma in particular [4].

Conclusions

The aforementioned clinical divergencies may support the concept of male- and female depressive syndromes [1-3] and might further serve as predictors of their severity and course, since they represent phenomena that were repeatedly related to difficult-to-treat conditions in MDD [4, 5]. Considering sex in the diagnostic and treatment processes may, hence, support clinicians in the management of challenging clinical manifestations as suicidality and/or comorbidities, and prevention of resistance and chronicity [4].

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Statement of Ethics

The present research complies with internationally-accepted standards for research practice and reporting, and has been performed with approvals of appropriate ethics committees and with appropriate participants’ informed consent in compliance with the Helsinki Declaration.

Conflict of Interest Statement

Dr. Bartova has received travel grants and consultant/speaker honoraria from AOP Orphan, Medizin Medien Austria, Vertretungsnetz, Schwabe Austria, Janssen and Angelini. Dr. Dold has received travel grants and consultant/speaker honoraria from Janssen-Cilag. Dr. Frey has received consulting fees from Janssen-Cilag. Dr. Zohar has received grant/research support from Lundbeck, Servier, and Pfizer; he has served as a consultant or on the advisory boards for Servier, Pfizer, Solvay, and Actelion; and he has served on speakers' bureaus for Lundbeck, GlaxoSmithKline, Jazz, and Solvay. Dr. Mendlewicz is a member of the board of the Lundbeck International Neuroscience Foundation and of the advisory board of Servier. Dr. Souery has received grant/research support from GlaxoSmithKline and Lundbeck; and he has served as a consultant or on advisory boards for AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen, and Lundbeck. Dr. Montgomery has served as a consultant or on advisory boards for AstraZeneca, Bionevia, Bristol-Myers Squibb, Forest, GlaxoSmithKline, Grunenthal, Intellect Pharma, Johnson & Johnson, Lilly, Lundbeck, Merck, Merz, M's Science, Neurim, Otsuka, Pierre Fabre, Pfizer, Pharmaneuroboost, Richter, Roche, Sanofi, Sepracor, Servier, Shire, Synosis, Takeda, Theracos, Targacept, Transcept, UBC, Xytis, and Wyeth. Dr. Fabbri has been supported by Fondazione Umberto Veronesi (https://www.fondazioneveronesi.it). Dr. Serretti has served as a consultant or speaker for Abbott, Abbvie, Angelini, AstraZeneca, Clinical Data, Boheringer, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Innovapharma, Italfarmaco, Janssen, Lundbeck, Naurex, Pfizer, Polifarma, Sanofi, and Servier. Within the last three years, Dr. Kasper received grants/research support, consulting fees, and/or honoraria from Angelini, Celegne GmbH, Eli Lilly, Janssen-Cilag Pharma GmbH, KRKA-Pharma, Lundbeck A/S, Mundipharma, Neuraxpharm, Pfizer, Sanofi, Schwabe, Servier, Shire, Sumitomo Dainippon Pharma Co. Ltd., sun Pharma and Takeda. All other authors declare that they have no conflicts of interest.

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[20] Genetic Variations Associated with Treatment Response in Bipolar Depression

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Background: Several pharmacogenetic decision support tools for medication selection in psychiatric disorders based on genetic variants have been developed in the last decade [1]. The scientific evidence of the gene-drug pairs analyzed are mainly based on pharmacogenetic studies in patients with major depression or schizophrenia [2]. To date, the evidence of pharmacogenetics in bipolar disorders (BD) is scarce [3].

Objectives: The aim of this study was to evaluate the impact of individual genes, with pharmacogenetic relevance in other psychiatric conditions, in the response to treatment, the presence of adverse effects and the presence of (hypo)manic switches in patients with bipolar depression.

Methods: Observational, retrospective, epidemiological study. Included patients were adults diagnosed of BD. Patients provided a saliva sample and DNA was analyzed through the Neuropharmagen® kit, a commercial pharmacogenetic decision support tool developed by AB-Biotics SA. The test reported each individual drug assessed using a color-coding system: (1) green: expectancy of good response to therapy in terms of efficacy or tolerability; (2) white: expectancy of a “standard response”; (3) yellow: necessity of an attentive dose monitoring; (4) red: index of high-risk treatment emergent adverse events or lower efficacy [4]. The most recent index episode of major depression according to the DSM-IV-TR was identified retrospectively. The patient’s disease severity was assessed using the modified version of the Clinical Global Impression for Bipolar Disorder (CGI-BP-M) at the index episode, after the index episode, and at enrolment. Multiple linear regression analysis with a forward-selection approach (p-value=0.05) was used to identify the pharmacogenetic and clinical predictor variables with a significant contribution to each relevant clinical outcome. The study was approved by the Institutional Review Board (HCB/2015/0990). All patients provided written informed consent to participate.

Results: Seventy-six patients with BD (65.8% female; 54% BD type I) were included. The most prescribed medications for treating the index episode were lithium (n=55), quetiapine (n=47), and SSRIs (n=28). Twenty patients (26.3%) experienced mood switch. The mean of adverse effects was 0.9±1.1. The pharmacogenetic variable green-code for SNRIs correlated with lower scores in the CGI-BP-M scale for depression at follow-up (B=-0.472; p=0.026). This code corresponds to genetic variants on the ABCB1 transporter, associated with an increase of the levels of (des)venlafaxine in the brain, which could explain the association with a better treatment response. Yellow-code for SSRIs was significantly correlated with the presence of (hypo)manic switch: adjusted odds ratio (OR)=3.41; CI95%= 1.042-11.15; p=0.043, which translates to an increased probability of switch occurrence. Green-code for risperidone/paliperidone was significantly correlated with a lower number of adverse effects (B=-1.139; p=0.014). This code is associated with a 4-gene combination in the mTOR pathway associated with less adverse effects (Mas et al., 2015). Yellow-code for second generation antipsychotics other than quetiapine was significantly correlated with a higher number of adverse effects (B=0.495; p=0.018). This code is associated with reduced CYP3A4 metabolism, which could explain the increase in adverse effects.

Conclusions:

1. Pharmacogenomic testing shows promising results on treatment effectiveness, tolerability in BD, as well as on the predictive capability of (hypo)manic switches.
2. Further research on validity, reliability, clinical usefulness, and cost-effectiveness of the pharmacogenetic decision support tools in BD is needed before their implementation into clinical practice.

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Best Poster Presentations

The Impact of Job and Income Loss on Mental Health Outcomes during the COVID-19 Pandemic: Results from a Population-Based Survey

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Background

COVID-19 outbreak, which has been followed by home confinement, is expected to have profound negative impact on people's mental health. Associated factors, such as losing jobs and income, can be expected to lead to an increased risk of psychopathology such as anxiety and depression. This study aimed at determining the impact of job loss or being temporarily laid off and income loss on mental health wellbeing among the Spanish active working population during the first wave of the COVID-19 lockdown and the potential moderating role of socio-demographic variables.

Methods

A total of 3500 Spanish adults were interviewed by phone during the COVID-19 lockdown, from which 3310 corresponded to the active working population. Mental health assessment either in the last two weeks or the last month included Generalized Anxiety Disorder (GAD; measured with GAD-7), panic attacks (assessed with an item from the WMH-ICS), depression (PHQ-8 scale), Posttraumatic stress disorder (PSTD; measured with the PCL-5 questionnaire) and substance abuse (CAGE-AID). Participants also reported about their working conditions and sociodemographic variables. Unadjusted and adjusted logistic regression models were calculated, with psychological variables as the outcomes, and job loss/temporary lay-off and income loss as the main explanatory variables. Separated models were calculated for each explanatory variable. The adjusted logistic regression models included gender, age, education level and marital status as covariates.

Results

In our weighted sample (*N* = 3310), 19.63% reported having lost their job or being temporarily laid off work and 33.88% having suffered from a loss of income due to the coronavirus pandemic. In the unadjusted models, job loss and income loss were found to significantly increase the odds of suffering from current depression (Job loss: OR = 1.42, 95%CI = 1.10-1.83; income loss: OR = 1.59, 95%CI = 1.28-1.99), PTSD (Job loss: OR = 1.39, 95%CI = 1.06-1.84; income loss: OR = 1.64, 95%CI = 1.29-2.08) and the presence of panic attacks (Job loss: OR = 1.37, 95%CI = 1.04-1.79; income loss: OR = 1.74, 95%CI = 1.38-2.20). Additionally, people experiencing income loss had significantly higher odds of suffering from GAD (OR = 1.49, 95%CI = 1.19-1.87). For current substance abuse, no significant associations were found. In the adjusted models, only income loss was found to be related to a higher risk for current depression (OR = 1.30, 95%CI = 1.03-1.63) and panic attacks (OR =1.34, 95%CI =1.05-1.71).

Conclusions

Our findings show that only income loss during the COVID-19 outbreak appeared to be associated with current depression and presence of panic attacks, and these associations were beyond the presence of confounder variables. These findings suggest that, contrary to losing job, it is the prospective of losing income (and the associated financial hardship) during the COVID-19 pandemic the factor associated with an increased risk for mental health problems. This highlights the importance of implementing additional social and income policies during the COVID-19 pandemic to prevent health inequalities.

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Conflict of Interest Statement

None.

A Virtual Positive Psychology Based Intervention Model for Social Anxiety in Young Adults during the COVID 19 Pandemic

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Background

The COVID 19 pandemic has brought about huge changes to all our lives. All over the world, people have evolved and brought forward new and effective coping strategies. Priorities of individuals have changed; people are more focused on micromanaging their physical and mental health.

Aim

This paper is the result of our effort to create a virtual positive psychology based intervention model to work with the students and help them overcome the social anxiety that they experience after days of being alone and emerge with the essential coping skills for their future life as well.

Methods

An initial survey of 258 students in the age group of 18 to 23 years were conducted using the Liebowitz Social Anxiety Scale (Liebowitz,, M., 1987) and the Subjective Happiness Scale (Sonja Lyubomirsky). After the initial screening 55 students who were vulnerable to develop anxiety and depression were selected. After an informed consent, the 15 day intervention model designed by the researchers was conducted. The whole intervention had a set of exercises conveyed and followed up virtually through electronic mail, videos, Google meets and whatsapp. Daily motivational messages with small exercises were also sent to them and their responses collected for each day. After every 5 days, a feedback session was conducted with a day of break to reflect upon the intervention. So the whole intervention model took 18 days. The tests were repeated after the intervention. A follow up was conducted with the same psychological tests after a period of three months.

Results and Conclusions

The results indicated that there is a significant difference in the before, after and follow up phases in Social Anxiety levels and Happiness of the participants. This indicates that the intervention is successful in reducing the negative affect causing psychological vulnerability in the participants.

Key Words: Social Anxiety, Positive Psychology

Disclosure Statement:

The authors hereby declare that there is no conflict of interest in the present study.

Funding Sources Statement:

The authors hereby declare that no funds have been sought or received for this study.

Statement of Ethics:

The procedures followed have been assessed by the Departmental Committee and found acceptable. Also Informed Consent has been obtained from all the participants of the study.

Omega 3 Fatty Acids as an Adjuvant in the Treatment of Major Depression

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Objectives

To demonstrate that the addition of omega 3 polyunsaturated fatty acids (PUFAs) to dual antidepressant treatment improves the efficacy of the antidepressant response.

Methods

Randomized double-blind, placebo-controlled clinical trial, sample of 80 patients diagnosed according to DSM V applying Hamilton scale for depression (HAM-D) at baseline, every 2 weeks until week 12. They were distributed in2 groups of 40 patients, each group studied with mirtazapine: 30 mgs / day and PUFA omega 3: 500 mgs (300 mgs EPA and 200 mgs DHA) three times / day and placebo group with mirtazapine: 30 mgs / day and placebo.

Results

In the group treated with mirtazapine plus omega 3 fatty acids, clinical improvement was evident from the 4thweek (% AV. 56.8%) and remission to the 8th. (Average HAM-D: 5.3), a statistically significant result compared to patients with mirtazapine plus placebo, where it could be a clinical improvement from week 6 (% AV. 62.3%) and remission at 10th. (HAM-D average: 4.7).

Conclusions

The addition of Omega 3 fatty acids as an adjunct in the treatment of major depression improves symptoms significantly (p <5%) until remission.

Poster Presentations

Clinical measurement of the Time to re-orientation in electroconvulsive therapy for a depressive episode

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Background

Electroconvulsive therapy (ECT) is an important modality in the treatment of a wide range of serious neuropsychiatric disorders. Its role is irreplaceable and even life-saving.

The use of ECT used to be associated with transient cognitive impairment (TCI) (currently considered a side effect). The importance of individual current parameters (seizure threshold, seizure duration, frequency, current amplitude, duration of stimulation, and pulse width) has been taken into account by many research efforts in recent years, mainly their influence on efficacy and occurrence of side effects (SE). The time to reorientation (or time to recovery, TTR) is a very simple parameter to measure, which has predictive value for the TCI. The common clinical measurement of TTR is an example of good practice.

Methods

With a concentration on minimalizing the TCI, we use so-called ultra-brief pulses (0,3ms) in a right-unilateral setting in a depressed patient. Energy titration is a basic prerequisite for minimizing the dose of energy used to induce an adequate therapeutic seizure (measured by two-channel EEG; 20-60s of epileptiform activity).

Results

We observed 46 patients in 158 ECT sessions (of which 40,03 % were males) with a mean age of 50,74 years (median 54; SD 13,01) with various diagnoses (ICD-10) of non-psychotic depressive episodes. We excluded the titration (first) session of ECT from further statistical analysis (14 measurements). The average seizure lasted 31,14 sec (median 30; SD 17,04). The following time was measured since the press of the trigger. The average time to the first spontaneous opening of the eyes was 6,45 min (median 6; SD 2,16). The average time to full vigilance (Glasgow coma scale 4+5+6) was 9,32 min (median 9; SD 3,69). The average time to full lucidity (oriented in person, time, space, and situation) was 12,42 min (median 12; SD 4,996).

Conclusion

Time to re-orientation (defined as the time from first eyes opening till full lucidity) was 5,97 min (median 5; SD 4,13). Further research and perhaps correlation to other parameters is desirable.

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The role of the Kindling model on the prevention of mood episodes

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Introduction: Bipolar disorder is a chronic and recurrent disorder characterized by excessive variations, in amplitude and/or frequency, of mood, energy or activity. The model of sensitization and kindling helps to conceptualize processes occurring in the longitudinal course of bipolar disorder.

Objectives: To explore the concept of the Kindling model applied to bipolar disorder and assess how it can help on preventing new mood episodes.

Methods: Non-systematic literature review using the most relevant papers found on the database PubMed with the keywords “kindling effect”, “allostatic load”, “bipolar disorder” and “prevention”.

Results: The phenomenon of kindling was first discovered by Goddard in 1967 who described it in epilepsy. Later, Post applied it to the bipolar disorder, arguing that the initial episodes of both unipolar and bipolar affective disorders are often precipitated by psychosocial stressors, but after multiple recurrences, not only do precipitated episodes continue to occur, but so do spontaneous ones as well. Both stressors and mood episodes may leave residual traces and vulnerabilities to further occurrences of affective illness in individuals with bipolar disorder. A major goal of treatment of affective disorders is to generate and sustain remission. The kindling model clarifies aspects of the longitudinal course of episode development, recurrence, and progression to spontaneity, as well as further conceptual and theoretical rationales for intervention in order to prevent illness progression.

Conclusion: The value of the kindling model appears to reside in its utility for clarifying the processes involved in acute episode generation and progression and, therefore, promoting early intervention and prevention.

Predictors of MDD and GAD in patients after severe burn trauma

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Background/Objectives. Depression, along with post-traumatic stress disorder (PTSD) and generalized anxiety disorder (GAD) is one of the most common mental health problems in patients after burn trauma.

Methods: N = 292 patients after burn trauma of the Burn Center, Department of Burn Medicine 3rd Medical Faculty and University Hospital KV, were examined at the end of hospitalization in years 2016-2021. Their mean age was = 46.65, there were 70% of men, TBSA (Total Burn Surface Area) was = 9.89%, the mean length of hospital stay was = 24.54 days. All patients signed the IS and the research was approved by the local EC. The MDD and GAD module from the structured diagnostic interview of M.I.N.I. was used to detect the presence of major depressive disorder (MDD) and generalized anxiety disorder (GAD) based on the DSM-IV gold standard (Sheehan et al., 1997). Socio-demographic (age, gender, education, social status) and clinical variables (TSBA%, degree of burns, location of burns in visible places, work injury, use of anxiolytics, use of antidepressants, pain intensity/discomfort) were also determined.

Results. N = 27 patients (9.2 %) met the criteria of MDD. Based on a stepwise logistic regression to predict MDD in the group of sociodemographic variables, a significant borderline variable of the divorced/widowed social status was found (p = 0.057). No logistic regression model was created for this group of independent variables. The logistic regression model of two significant clinical variables (TBSA % and antidepressant use, R^2 = 0.26), explains 26% of MDD variability. Reducing TBSA% by one unit increases the risk of MDD by 9.1 times (OR = 0.91, 95% CI = 0.89-0.98, p = <0.0161), patients who have taken antidepressants during hospitalization have a more than 10 times higher risk of MDD (OR = 10.0, 95% CI = 3.23-31.06, p = <0.0001). N = 10 patients (3.4 %) met the GAD criteria. Based on a stepwise logistic regression to predict GAD in the group of sociodemographic variables, only to be unemployed (p = 0.0079) was found as significant variable, together with bordeline marital status divorced (p = 0.066). No logistic regression model was created for the group of socio-demographic independent variables. The following two independent variables were selected from a group of clinical variables by logistic regression analysis: the location of burns in visible places and the use of antidepressants (R^2 = 0.30). This model explains 30% of the GAD variability. Patients with burns located outside visible areas (head, neck, upper limbs) have an 88% increased risk of GAD (OR = 0.12, 95% CI = 0.02-0.57, p = <0.0081), patients who have taken antidepressants during hospitalization have more than 32 times higher risk of GAD (OR = 0.32, 95% CI = 6.85-142.02, p = <0.0001).

Conclusions. Early and correct diagnosis of depression is the basis for its successful treatment, because the chronification of depressive disorders is demonstrably related to a reduced ability to regenerate burn trauma.

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Indirect comparison estimating the benefit of esketamine compared to real-world treatment of treatment resistant depression in general psychiatry: preliminary analysis

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INTRODUCTION

Most patients with treatment resistant depression (TRD) do not respond to treatment in real-world clinical practice [1], demonstrating the need for novel options with improved efficacy. Recently, esketamine nasal spray (NS), in combination with a selective serotonin reuptake inhibitor or serotonin-norepinephrine reuptake inhibitor, was approved for treatment of TRD [2]. Comparisons of esketamine with real-world treatment strategies for TRD are needed.

AIMS

To compare esketamine NS efficacy data with real-world treatment outcomes for TRD.

METHODS

An indirect treatment comparison (ITC) of data from two studies was performed. The European Observational TRD cohort (EOTC) was a prospective, non-interventional, multicentre study in patients starting a new, routine treatment for TRD. SUSTAIN-2 was a long-term, open-label study of the safety and efficacy of esketamine NS plus a newly-initiated antidepressant for TRD, including European patients. Both studies defined TRD as failure of ≥2 treatments given at adequate dose and duration in the current episode and were selected to ensure similar recruitment conditions and follow-up time. Response to treatment (≥50% improvement in total Montgomery Åsberg Depression Rating Scale [MADRS] score) and remission (total MADRS score ≤10) at 6 months were compared. Multivariable logistic regression was used to estimate treatment differences while adjusting for 17 covariates (socio-demographics, clinical/psychometric/disease/treatment history). Treatment differences were also estimated by reweighting observations in EOTC (inverse probability weighting using propensity scores estimated with the 17 covariates) using SUSTAIN-2 as reference, resulting in an estimate of stabilized average treatment effect among treated (sATT).

RESULTS

Baseline characteristics were similar between the two studies (Table). Compared with patients receiving real-world treatment, patients receiving esketamine NS had an adjusted odds ratio (OR) for remission of 3.34 (95% confidence interval [CI]: 2.31–4.83; p<0.0001), with a relative risk (RR) of 2.64 (95% CI: 2.01–3.38) and risk difference (RD) of 0.18 (95% CI: 0.11–0.27). Regarding response, the adjusted OR was 4.38 (95% CI: 3.16–6.09; p<0.0001), with a RR of 2.80 (95% CI: 2.32–3.29) and RD of 0.30 (95% CI: 0.22–0.38). The estimated probability of remission was 0.32 (95% CI: 0.28–0.35) for patients receiving esketamine NS and 0.12 (95% CI: 0.09–0.16) for real-world treatment, while for response, it was 0.47 (95% CI: 0.43–0.51) and 0.17 (95% CI: 0.13–0.21), respectively (sATT estimate). Results were similar for 27 different sensitivity analyses, using alternative adjustment approaches and automatic variable selection methods.

CONCLUSIONS

While interpretation of these preliminary analyses must consider limitations resulting from pooling data from separate sources, the two study populations are similar. This ITC suggests esketamine NS is beneficial over real-world treatment for TRD patients. Consistent results following adjustment for multiple covariates and several sensitivity analyses supports robustness of the comparison.

Table. Baseline characteristics

Mean (SD), unless otherwise stated	EOTC (N=335)	SUSTAIN-2 (N=689)
Age, years	51.3 (10.6)	49.4 (12.6)
Female, n (%)	210 (62.7)	437 (63.4)
Total MADRS score	32.0 (6.0)	31.2 (5.0)
Prior failed treatments	2.7 (0.9)	2.7 (1.1)

EOTC: European Observational TRD cohort; MADRS: Montgomery Åsberg Depression Rating Scale; TRD: treatment resistant depression.

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Indirect comparison estimating the benefit of esketamine compared to distinct real-world treatment strategies for treatment resistant depression in general psychiatry: preliminary analysis

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BACKGROUND

Most patients with treatment resistant depression (TRD) do not respond to treatment in real-world clinical practice [1]. Recently, esketamine nasal spray (NS), in combination with a selective serotonin reuptake inhibitor/serotonin-norepinephrine reuptake inhibitor, was approved for TRD [2]. It is thus necessary to compare esketamine with other treatment strategies in real-world clinical practice.

AIMS

To compare esketamine NS efficacy data with outcomes for distinct real-world treatment strategies for TRD.

METHODS

An indirect treatment comparison (ITC) was performed with data from two studies of TRD, defined as failure of ≥2 treatments in the current episode: the European Observational TRD cohort (EOTC; a prospective, non-interventional study in real-world clinical practice) and SUSTAIN-2 (an open-label study of esketamine NS plus new oral antidepressant). These studies were selected to ensure similar recruitment conditions and follow-up time. Patients' response (≥50% improvement in total Montgomery Åsberg Depression Rating Scale [MADRS] score) and remission (total MADRS score ≤10) at 6 months was compared. Real-world treatment in the EOTC (physicians' choice) was classified as monotherapy (1 antidepressant), combination therapy (≥2 antidepressants) and augmentation therapy (≥1 augmentation medication plus ≥1 antidepressant). Treatment differences were estimated by reweighting observations in the EOTC (inverse probability weighting) using propensity scores estimated with 17 covariates (socio-demographics, clinical/psychometric/disease/treatment history) using SUSTAIN-2 as reference, in stabilized average treatment effect among treated (sATT) models, versus all patients as well as each of the three comparator treatment strategies.

RESULTS

At baseline, patients had similar mean age, total MADRS score and number of prior treatment failures, and similar sex ratios in both studies. Raw and reweighted probabilities, as well as adjusted odds ratios (OR), for both response and remission were consistently superior for esketamine versus real-world treatment, irrespective of comparator treatment strategy (Table). Results were equivalent for sensitivity analyses conducted using alternative adjustment approaches and automatic variable selection methods.

CONCLUSIONS

While preliminary, this ITC suggests esketamine NS is beneficial over real-world treatment for TRD patients, irrespective of treatment strategy. Consistent results following adjustment for multiple covariates demonstrates analytical robustness. However, interpretation of these analyses must consider limitations of comparing data from separate sources.

Table. ITC of esketamine NS plus oral antidepressant versus real-world treatment (sATT)

Comparator	Raw Probability (CI)[a]	Reweighted Probability (CI)[a]	Adjusted OR (CI)[a]
Response			
Esketamine NS	0.47 (0.43–0.51)	0.47 (0.43–0.51)	
All treatments	0.16 (0.13–0.21)	0.17 (0.13–0.21)	4.38 (3.16–6.09)**
Monotherapy	0.21 (0.14–0.30)	0.10 (0.05–0.18)	8.26 (4.04–16.88)**
Combination	0.17 (0.12–0.23)	0.18 (0.13–0.24)	4.08 (2.65–6.27)**
Augmentation	0.11 (0.07–0.18)	0.19 (0.13–0.26)	3.83 (2.41–6.08)**
Remission			
Esketamine NS	0.32 (0.28–0.35)	0.32 (0.28–0.35)	
All treatments	0.11 (0.08–0.15)	0.12 (0.09–0.16)	3.34 (2.31–4.83)**
Monotherapy	0.14 (0.08–0.23)	0.07 (0.03–0.14)	6.47 (2.79–15.00)**
Combination	0.12 (0.07–0.17)	0.15 (0.10–0.21)	2.67 (1.68–4.25)**
Augmentation	0.07 (0.04–0.12)	0.15 (0.10–0.22)	2.55 (1.55–4.21)*

[a]95% CI. *p<0.005; **p<0.0001. CI: confidence interval; ITC: indirect treatment comparison; NS: nasal spray; OR: odds ratio; sATT: stabilized average treatment effect among treated.

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Early Risk Factors of Anxiety Disorders: The Moderator Role Of Gender In The Relationship Between Behavioral Inhibition And Parental Behaviour In Preschool Children

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Background/Aims Preschool Behavioural Inhibition (BI) was found to be a temperamental risk factor of anxiety disorders in later life; especially in women. Similarly, previous research revealed that parental behaviour plays a major role in the development and maintenance of anxiety disorders. Gender differences in parental responses to child's temperament may contribute to the stronger association between BI and anxiety disorders in females. We aimed to examine the moderating effect of child's gender in the association between child's BI and parenting behaviour in a non-clinical sample of parents of preschool children.

Methods A cross-sectional sample of parents (N=94) of preschool children (girls 47.4%) filled out the Behavioural Inhibition Questionnaire (BIQ) and the Multidimensional Assessment of Parenting Scale (MAPS).

Results Child's gender was found to moderate the relationships between BIQ scores and MAPS Supportive Parenting ($F(3,90)=4.350$, $p=.007$, $R^2=.127$), as well as Harsh Parenting ($F(3,89)=3.478$, $p=.019$, $R^2=.105$). In boys, higher BIQ scores were associated with higher levels of Supporting Parenting ($b=.005$, $p=.027$), while in girls, higher BIQ scores were related to lower levels of Supported Parenting ($b=-.004$, $p=.037$). Furthermore, in boys, no association was found between BIQ scores and Harsh Parenting ($b=.005$, $p=.835$); however, higher BIQ scores were related to higher levels of Harsh Parenting in girls ($b=.067$, $p<.001$).

Discussion/Conclusions Our results suggest that parental responses to their preschool child's Behavioural Inhibition may vary as a function of child's gender. This may lead to gender differences in developmental pathways to anxiety disorders.

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