36 depression-relevant abstracts
july 17 newsletter


Background Except for dementia and depression, little is known about common mental disorders in elderly people. Aims To estimate current, 12-month and lifetime prevalence rates of mental disorders in different European and associated countries using a standardised diagnostic interview adapted to measure the cognitive needs of elderly people. Method The MentDis_ICF65+ study is based on an age-stratified, random sample of 3142 older men and women (65–84 years) living in selected catchment community areas of participating countries. Results One in two individuals had experienced a mental disorder in their lifetime, one in three within the past year and nearly one in four currently had a mental disorder. The most prevalent disorders were anxiety disorders, followed by affective and substance-related disorders. Conclusions Compared with previous studies we found substantially higher prevalence rates for most mental disorders. These findings underscore the need for improving diagnostic assessments adapted to the cognitive capacity of elderly people. There is a need to raise awareness of psychosocial problems in elderly people and to deliver high-quality mental health services to these individuals.


Background Lithium and quetiapine are considered standard maintenance agents for bipolar disorder yet it is unclear how they compare in the context of early bipolar episodes. Aims To evaluate the differential effect of lithium and quetiapine on symptoms of depression, mania, general functioning, global illness severity and quality of life in patients with recently stabilised first-episode mania. Method Maintenance trial of patients with first-episode mania stabilised on a combination of lithium and quetiapine, subsequently randomised to lithium or quetiapine monotherapy (up to 800 mg/day) and followed up for 1 year. (Trial registration: Australian and New Zealand Clinical Trials Registry – ACTRN12607000639426.) Results In total, 61 individuals were randomised. Within mixed-model repeated measures analyses, significant omnibus treatment x visit interactions were observed for measures of overall psychopathology, psychotic symptoms and functioning. Planned and post hoc comparisons demonstrated an advantage of lithium over quetiapine. Conclusions In people with first-episode mania treated with a combination of lithium and quetiapine, continuation treatment with lithium rather than quetiapine is superior in terms of mean levels of symptoms during a 1-year evolution.


Importance Previous observations of a higher risk of child autism spectrum disorder with serotonergic antidepressant exposure during pregnancy may not be causal. Methods To evaluate the association between maternal prescription for a selective serotonin or serotonin-norepinephrine reuptake inhibitor between conception and delivery. Main Outcomes and Measures Child autism spectrum disorder identified after the age of 2 years. Exposure group differences were addressed by inverse probability of treatment weighting based on derived high-dimensional propensity scores (computerized algorithm used to select a large number of potential confounders) and by comparing exposed children with unexposed siblings. Results There were 35 906 singleton births at a mean gestational age of 38.7 weeks (50.4% were male, mean maternal age was 26.7 years, and mean duration of follow-up was 4.95 years). In the 2837 pregnancies (7.9%) exposed to antidepressants, 2.0% (95% CI, 1.6%-2.6%) of children were diagnosed with autism spectrum disorder. The incidence of autism spectrum disorder was 4.51 per 1000 person-years among children exposed to antidepressants vs 4.20 per 1000 person-years among unexposed children (between-group difference, 2.59 [95% CI, 2.33-2.86]; adjusted HR, 1.59 [95% CI, 1.37-2.02]). After inverse probability of treatment weighting based on the high-dimensional propensity score, the association was not significant (HR, 1.61 [95% CI, 0.95-2.97]). Conclusions and Relevance In children born to mothers receiving public drug coverage in Ontario, Canada, in utero serotonergic antidepressant exposure compared with no exposure was not associated with autism spectrum disorder in the child. Although a causal relationship cannot be ruled out, the previously observed association may be explained by other factors.


(available in free full text) Background Primary care is an important context for addressing health-related behaviours, and may provide a setting for identification of gambling problems. Aim To indicate the extent of gambling problems among patients attending general practices, and explore settings or patient groups that experience heightened vulnerability. Design and setting Cross-sectional study of 11 general practices in Bristol, South West England. Method Adult patients (n = 1058) were recruited from waiting rooms of practices that were sampled on the basis of population characteristics. Patients completed anonymous questionnaires comprising measures of mental health problems (for example, depression) and addictive behaviours (for example, risky alcohol use). The Problem Gambling Severity Index (PGSI) measured gambling problems, along with a single-item measure of gambling problems among family members. Estimates of extent and variability...
according to practice and patient characteristics were produced. Results There were 0.9% of all patients exhibiting problem gambling (PGSI ≥5), and 4.3% reporting problems that were low to moderate in severity (PGSI 1–4). Around 7% of patients reported gambling problems among family members. Further analyses indicated that rates of any gambling problems (PGSI ≥1) were higher among males and young adults, and more tentatively, within a student healthcare setting. They were also elevated among patients exhibiting drug use, risky alcohol use, and depression. Conclusion There is need for improved understanding of the burden of, and responses to, patients with gambling problems in general practices, and new strategies to increase identification to facilitate improved care and early intervention.


The brain and the immune system are not fully formed at birth, but rather continue to mature in response to the postnatal environment. The two-way interaction between the brain and the immune system makes it possible for childhood psychosocial stressors to affect immune system development, which in turn can affect brain development and its long-term functioning. Drawing from experimental animal models and observational human studies, we propose that the psychoneuroimmunology of early-life stress can offer an innovative framework to understand and treat psychopathology linked to childhood trauma. Early-life stress predicts later inflammation, and there are striking analogies between the neurobiological correlates of early-life stress and of inflammation. Furthermore, there are overlapping trans-diagnostic patterns of association of childhood trauma and inflammation with clinical outcomes. These findings suggest new strategies to remediate the effect of childhood trauma before the onset of clinical symptoms, such as anti-inflammatory interventions and potentiation of adaptive immunity. Similar strategies might be used to ameliorate the unfavorable treatment response described in psychiatric patients with a history of childhood trauma.


Abstract Background Major depressive disorder is an emotional disorder. It is important to improve our understanding of the role of affect in relapse/recurrence of depression. Thus, in this study examines whether affect plays a role in prospectively predicting depressive symptomatology and if there are indications for emotional scarring as a consequence of undergoing depressive episodes. Methods In 107 patients remitted from recent depressive affect was examined in predicting depressive symptomatology as measured with the Inventory of Depressive Symptomatology – Self Report. Affect was measured with the Positive and Negative Affect Schedule and with a one item Visual Analogue Mood Scale. Indication of emotional scarring was examined by comparing previous depressive episodes to levels of affect. Results Less positive affect as assessed after remission predicted increased depressive symptomatology six months later, even after we controlled for baseline depressive symptomatology. Negative affect also predicted depressive symptomatology six months later, but not after controlling for baseline depressive symptomatology. No relationship was found between affect and number of previous episodes. Limitations All participants in this study had two or more previous depressive episodes and received CBT during the acute phase of their depression. The instruments that measured mood and affect were administered within 4 weeks of each other. Conclusions Positive affect and negative affect as assessed after remission in recurrent depression can predict depressive symptomatology. Especially positive affect seems to play an independent role in predicting depressive symptomatology. Directly targeting positive affect in relapse prevention during remission might be a way to enhance treatment effects.


Objective: Conventional antidepressant treatments result in symptom remission in 30% of those treated for major depressive disorder, raising the need for effective adjunctive therapies. Inflammation has an established role in the pathophysiology of major depressive disorder, and minocycline has been shown to modify the immune-inflammatory processes and also play a role in stress and place neuroplasticity. A double-blind, randomised, placebo-controlled trial examined adjunctive minocycline (200 mg/day, in addition to treatment as usual) for major depressive disorder. This double-blind, randomised, placebo-controlled trial investigated 200 mg/day adjunctive minocycline (in addition to treatment as usual) for major depressive disorder. Methods: A total of 71 adults with major depressive disorder (Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition) were randomised to this 12-week trial. Outcome measures included the Montgomery–Asberg Depression Rating Scale (primary outcome), Clinical Global Impression–Improvement and Clinical Global Impression–Severity, Hamilton Anxiety Rating Scale, Quality of Life Enjoyment and Satisfaction Questionnaire, Social and Occupational Functioning Scale and the Range of Impaired Functioning Tool. The study was registered on the Australian and New Zealand Clinical Trials Register: www.anzctr.org.au, #ACTRN12612000283875. Results: Based on mixed-methods repeated measures analysis of variance at week 12, there was no significant difference in Montgomery–Asberg Depression Rating Scale scores between groups. However, there were significant differences, favouring the minocycline group at week 12 for Clinical Global Impression–Improvement score – effect size (95% confidence interval) = −0.62 [−1.8, −0.3], p = 0.02; Quality of Life Enjoyment and Satisfaction Questionnaire score – effect size (confidence interval) = −0.12 [0.0, 0.2], p < 0.001; and Social and Occupational Functioning Scale and the Range of Impaired Functioning Tool score −0.79 [−4.5, −1.4], p < 0.001. These effects remained at follow-up. Conclusion: While the primary outcome was not significant, the improvements in other more comprehensive clinical measures suggest that minocycline may be a useful adjunct to improve global experience, functioning and quality of life in people with major depressive disorder. Further studies in people with major depressive disorder are warranted to confirm the potential of this accessible agent to optimise treatment outcomes.


Abstract Aim Increasing literature has shown the usefulness of a dimensional approach to autism. The present study aimed to determine the psychometric properties of the Adult Autism Subthreshold Spectrum (AdAS Spectrum), a new questionnaire specifically tailored to assess subthreshold forms of autism spectrum disorder (ASD) in adulthood. Methods 102 adults endorsing at least one DSM-5 symptom criterion for ASD (ASDs), 143 adults diagnosed with a feeding and eating disorder (FED), and 160 subjects with no mental disorders (CTL) were recruited from 7 Italian University Departments of Psychiatry and administered the following: SCID-5, Autism-Spectrum Quotient (AQ), Ritvo Autism and Asperger Diagnostic Scale 14-item version (RAADS-14), and AdAS Spectrum. Results The AdAS Spectrum demonstrated excellent internal consistency for the total score (Kuder–Richardson’s coefficient = .964) as well as for five out of seven domains (all coefficients > .80) and sound test–retest reliability (ICC = .976). The total and domain AdAS Spectrum scores showed a moderate to strong (r = .50) positive
correlation with one another and with the AQ and RAADS-14 total scores. ASDc subjects reported significantly higher AdAS Spectrum total scores than both FED (p<.001) and CTL (p<.001), and significantly higher scores on the Childhood/adolescence, Verbal communication, Empathy, Inflexibility and adherence to routine, and Restricted interests and rumination domains (all p<.001) than FED, while on all domains compared to CTL. CTL displayed significantly lower total and domain scores than FED (all p<.001). A significant effect of gender emerged for the Hyper- and hyporeactivity to sensory input domain, with women showing higher scores than men (p<.003). A Diagnosis* Gender interaction was also found for the Verbal communication (p=.019) and Empathy (p=.023) domains. When splitting the ASDc in subjects with one symptom criterion (ASD1) and those with a ASD, and the FED in subjects with no ASD symptom criteria (FED0) and those with one ASD symptom criterion (FED1), a gradient of severity in AdAS Spectrum scores from CTL subjects to ASD patients, across FED0, ASD1, FED1 was shown. Conclusions The AdAS Spectrum showed excellent internal consistency and test–retest reliability and strong convergent validity with alternative dimensional measures of ASD. The questionnaire performed differently among the three diagnostic groups and enlightened some significant effects of gender in the expression of autistic traits.


Objective: The Predictors of Remission to Individual and Combined Treatments [PReDiCT] study aimed to identify clinical and biological factors predictive of treatment outcomes in major depressive disorder among treatment-naïve adults. The authors evaluated the efficacy of cognitive-behavioral therapy (CBT) and two antidepressant medications (escitalopram and duloxetine) in patients with major depression and examined the moderating effect of patients’ treatment preferences on outcomes. Method: Adults aged 18–65 with treatment-naïve major depression were randomly assigned with equal likelihood to 12 weeks of treatment with escitalopram (10–20 mg/day), duloxetine (30–60 mg/day), or CBT (16 50-minute sessions). Prior to randomization, patients indicated whether they preferred medication or CBT or had no preference. The primary outcome was change in the 17-item Hamilton Depression Rating Scale (HAM-D), administered by raters blinded to treatment. Results: A total of 344 patients were randomly assigned, with a mean baseline HAM-D score of 19.8 (SD=3.8). The mean estimated overall decreases in HAM-D score did not significantly differ between treatments (CBT: 10.2, escitalopram: 11.1, duloxetine: 10.4). Last observed carried forward remission rates did not significantly differ between treatments (CBT: 41.9%, escitalopram: 46.7%, duloxetine: 54.7%). Patients matched to their preferred treatment were more likely to complete the trial but not more likely to achieve remission. Conclusions: Treatment guidelines that recommend either an evidence-based psychotherapy or antidepressant medication for nonpsychotic major depression can be extended to treatment-naïve patients. Treatment preferences among patients without prior treatment exposure do not significantly moderate symptomatic outcomes.


(Available in full text) Major depressive disorder (MDD) is a prevalent and disabling psychiatric disease with rates of non-responsiveness to antidepressants ranging from 30–50%. Historically, the monoamine depletions hypothesis has dominated the view on the pathophysiology of depression. However, the lack of responsiveness to antidepressants and treatment resistance suggests that additional mechanisms might play a role. Evidence has shown that a subgroup of depressive patients may have an underlying immune deregulation that could explain the lack of therapeutic benefit from antidepressants. Studies linking inflammation and infection to depression and migraine suggest that inflammatory intervention. Here, we discuss the pre-clinical and clinical studies that have provided support for treatment with non-steroidal anti-inflammatory drugs in depressed patients with inflammatory comorbidity or an elevated immune profile, as well as evidence for anti-inflammatory properties of standard antidepressants.


Objective: The aims of this study were to investigate: (1) the prevalence and unadjusted and adjusted odds of 12-month generalized anxiety disorder (GAD) among adults with migraine in comparison to those without migraine; (2) If debilitating pain and/or chronic pain medications (IADs) are acting as a mediator of the AdAS disorder association; and (3) Factors associated with past year GAD among adults with migraine. Methods: Secondary data analysis of the nationally representative 2012 Canadian Community Health Survey-Mental Health (CCHS-MS), a population-based survey of community dwellers with a response rate of 68.9%. The first subsample included those with (n = 2232) and without migraine (n = 19,270), and the second subsample was restricted to those with migraine (n = 2232). GAD was based on the WHO-CIDI scale. Results: Fully, 6% of those with migraine had past year GAD in comparison of 2.1% of those without migraine (P <.001). The socio-demographically adjusted odds of past year GAD were two and a half times higher among those with migraine than those without migraine (95% CI: 1.97–2.98, P <.001). A Chi square test indicated that debilitating pain and/or chronic pain medications (IADs) are mediating the relationship between migraine and GAD. In the sample restricted to migraineurs, the odds associated with higher odds of 12-month GAD included having a university degree, having low income, being without a confidant, and being male. Conclusions: Generalized anxiety disorder is robustly associated with migraine and targeted outreach and interventions are warranted.


Abstract Background The attention given to anger and aggression in psychiatric patients pales in comparison to the attention given to depression and anxiety. Most studies have focused on a limited number of psychiatric disorders, and results have been inconsistent. The present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project sought to replicate and extend prior findings examining which psychiatric disorders and demographic characteristics were independently associated with elevated levels of anger and aggression. Method 3800 individuals presenting to the Rhode Island Hospital Department of Psychiatry outpatient practice underwent a semi-structured interview to determine current Axis I (N = 3800) and Axis II (N = 2151) pathology. Severity of subjective anger and overt aggression within the past week were pain and/or chronic pain medications for each patient, and odds ratios were determined for each disorder. Multiple regression analyses were conducted to determine which diagnoses independently contributed to increased levels of anger and aggression. Results Almost
half of the sample reported moderate-to-severe levels of current subjective anger, and more than 20% endorsed moderate-to-severe levels of current overt aggression. The frequency of anger was similar to the frequencies of depressed mood and psychic anxiety. Anger and aggression were elevated across all diagnoses except adjustment disorder. Anger and aggression were most elevated in patients with major depressive disorder, panic disorder with agoraphobia, post-traumatic stress disorder, intermittent explosive disorder, and cluster B personality disorders. Conclusions Anger is as common as depressed mood and psychic anxiety amongst psychiatric outpatients, and problems with anger cut across diagnostic categories. Given the high prevalence of problems with anger in psychiatric patients, more research should be directed towards its effective treatment.


(Available in free full text) Antidepressants are efficacious but we do not know which antidepressant is best suited to which person. We investigated the working hypothesis that obesity and sex may together be differential predictors of acute remission of specific symptoms for commonly used antidepressant medications. Data were acquired for 659 outpatients (1876years of age) who completed the iSPOT-D practical randomized controlled clinical trial. We measured adiposity by body mass index (BMI). By WHO criteria, 42% of patients were normal weight, 28% overweight and 31%, obese [class I (15%), II (10%) and III (6%)]. Patients were randomly assigned to 8-weeks of treatment with escitalopram, sertraline or venlafaxine extended-release (venlafaxine-XR) and then defined as remitters (17-item Hamilton Rating Scale for Depression score 77) or non-remitters. In logistic regression models, BMI was a differential predictor of remission according to antidepressant type.

Morbidly obese patients, compared to those with normal weight, were more likely to remit on venlafaxine-XR in particular. This effect was driven by a reduction specifically in physical symptoms, including sleep disturbance, somatic anxiety and appetite. The number needed to treat to achieve remission with venlafaxine-XR in obese III participants was 6. Higher BMI females but not males were more likely to remit regardless of medication type; this effect was related to a change in cognitive symptoms, including suicidal ideation, guilt, and psychomotor changes. Our findings suggest that considering BMI and sex, and assessing specific symptoms, could help tailor antidepressant choices to improve remission from depression in specialty and primary care settings.


Importance Obsessive-compulsive disorder (OCD) is a neuropsychiatric disorder associated with significant impairment and a lifetime prevalence of 1% to 3%; however, it is often missed in primary care settings and frequently undertreated. Objective To review the most current data regarding screening, diagnosis, and treatment options for OCD. Evidence Review We searched PubMed, EMBASE, and PsycINFO to identify randomized controlled trials (RCTs), meta-analyses, and systematic reviews that addressed screening and diagnostic and treatment approaches for OCD among adults (≥18 years), published between January 1, 2011, and September 30, 2016. We subsequently searched references of retrieved articles for additional reports. Meta-analyses and systematic reviews were prioritized; case series and reviews were included only for interventions for which RCTs were not available. Findings Among 792 unique articles identified, 27 (11 RCTs, 11 systematic reviews or meta-analyses, and 5 reviews/guidelines) were selected for this review. The diagnosis of OCD was revised for the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, which addresses OCD separately from anxiety disorders and contains specifiers to delineate the presence of tics and degree of insight. Treatment advances include increasing evidence to support the use of selective serotonin reuptake inhibitors as first-line pharmacologic interventions for OCD; however, more recent data support the adjunctive use of neuroleptics, deep-brain stimulation, and neurosurgical ablation for treatment-resistant OCD. Preliminary data suggest safety of other agents (eg, riluzole, ketamine, memantine, N-acetylcysteine, lamotrigine, celecoxib, ondansetron) either in combination with selective serotonin reuptake inhibitors or as monotherapy in the treatment of OCD, although their efficacy has not yet been established. Conclusions and Relevance The dissemination of computer-based cognitive behavioral therapy and other evidence-based interventions in community settings could provide a major advancement in the treatment of OCD. Although cognitive behavioral therapy with or without selective serotonin reuptake inhibitors remains a preferred initial treatment strategy, increasing evidence that supports the safety and efficacy of neuroleptics and neuromodulatory approaches in treatment-resistant cases provides alternatives for patients whose condition does not respond to first-line interventions.


Background: Effective treatments for the core symptoms of autism spectrum disorder (ASD) are still lacking. Objective: We aimed to update the data on the effectiveness of ω-3 (n=3) fatty acid (FA) supplementation as a treatment for ASD.Methods: The Cochrane Library, MEDLINE, and EMBASE databases were systematically searched up until August 2016 with no language restrictions for randomized controlled trials (RCTs) comparing ω-3 FA supplementation with placebo or with no supplementation. Participants were children diagnosed with ASD. All functional outcome measures reported were considered. For dichotomous outcomes, the results for individual studies and pooled statistics were reported as RRs. Meta-analysis was performed on outcomes that met the criteria for homogeneity. Results: Of 4662 abstracts identified (excluding duplicates), 51 articles were potentially relevant, of which 44 were excluded. Of 4 exceptions, there were no statistically significant differences in ASD symptoms between groups measured by validated scales. Among studies that used the Aberrant Behavior Checklist, parents’ ratings indicated significant improvement in lethargy symptoms in the ω-3 FA group compared with the placebo group (2 RCTs) (pooled MD: 1.98; 95% CI: 0.32, 3.63). Among studies that used the Behavioral Assessment System for Children, parents’ ratings indicated significant worsening of both externalizing behavior (2 RCTs) (pooled MD: −6.22; 95% CI: −10.9, −1.59) and social skills (1 RCT) (MD: −7; 95% CI: −13.62, −0.38) in the ω-3 FA group compared with the placebo group. One RCT reported a significant improvement in the ω-3 FA group for the daily-living component of the Vineland Adaptive Behavior Scale (MD: 6.2; 95% CI: 0.37, 12.03). Adverse effects were similar in both groups.Conclusions: Due to the limited number of included studies and small sample sizes, no firm conclusions can be drawn. However, the limited data currently available suggest that ω-3 FA supplementation does not enhance the performance of children with ASD.

mental disorders and as monotherapies for conditions such as ADHD. Finally, new studies focused on understanding the biological pathways that mediate the observed relationships between diet, nutrition and mental health are pointing to the immune system, oxidative biology, brain plasticity and the microbiome-gut-brain axis as key targets for nutritional interventions. On the other hand, the field is currently limited by a lack of data and methodological issues such as heterogeneity, residual confounding, measurement error, and challenges in measuring and ensuring dietary adherence in intervention studies. Key challenges for the field are to: replicate, refine and scale up promising clinical and population level dietary strategies; identify a clear set of biological pathways and targets that mediate the identified associations; conduct scientifically rigorous nutraceutical and ‘psychobiotic’ interventions that also examine predictors of treatment response; conduct observational and experimental studies in psychosis focused on dietary and related risk factors and treatments; and continue to advocate for policy change to improve the food environment at the population level.


Objective: The purpose of this study was to clarify the magnitude and nature of the relationship between divorce and risk for alcohol use disorder (AUD). Method: In a population-based Swedish sample of married individuals (N=942,366), the authors examined the association between divorce or widowhood and risk for first registration for AUD. AUD was assessed using medical, criminal, and pharmacy registries. Results: Divorce was strongly associated with risk for first AUD onset in both men (hazard ratio=5.98, 95% CI=5.65-6.33) and women (hazard ratio=7.29, 95% CI=6.72-7.91). The hazard ratio was estimated for AUD onset given divorce among discordant monozygotic twins to equal 3.45 and 3.62 in men and women, respectively. Divorce was also associated with an AUD recurrence in those with AUD registrations before marriage. Furthermore, widowhood increased risk for AUD in men (hazard ratio=3.85, 95% CI=2.81-5.28) and women (hazard ratio=4.10, 95% CI=2.98-5.64). Among divorced individuals, remarriage was associated with a large decline in AUD in both sexes (men: hazard ratio=0.56, 95% CI=0.52-0.64; women: hazard ratio=0.61, 95% CI=0.55-0.69). Divorce produced a greater increase in first AUD onset in those with a family history of AUD or with prior externalizing behaviors. Conclusions: Spousal loss through divorce or bereavement is associated with a large enduring increased AUD risk. This association likely reflects both causal and noncausal processes. That the AUD onset and subsequent occurrence of AUD postmenopause highlights the importance of spouse characteristics for the behavioral health consequences of spousal loss. The pronounced elevation in AUD risk following divorce or widowhood, and the protective effect of remarriage against subsequent AUD, speaks to the profound impact of marriage on problematic alcohol use.


Objective: The authors compared medication-induced mood switch risk (primary outcome), as well as treatment response and side effects (secondary outcomes) with three acute-phase treatments for bipolar II depression. Method: In a 16-week, double-blind, multisite comparison study, 142 participants with bipolar II depression were randomly assigned to receive lithium monotherapy (N=49), sertraline monotherapy (N=45), or combination treatment with lithium and sertraline (N=48). At each visit, mood was assessed using standardized rating scales. Rates of combination were switched, as were rates of treatment response and the presence and severity of treatment-emergent side effects. Results: Twenty participants (14%) experienced a switch during the study period (hypomania, N=17; severe hypomania, N=3). Switch rates did not differ among the three treatment groups, and no new manic switches were observed. Conclusions: The combination was associated with similar switch and treatment response rates in participants with bipolar II depression. The dropout rate was higher in the lithium/sertraline combination treatment group, without any treatment acceleration advantage.


(Available in free full text) The global market for probiotics is projected to be worth almost $USD 100 billion by 2020, reflecting growing consumer acceptance that our intestinal microbiota can influence physiologic systems, including but not limited to the gut. Many lay publications enthusiastically tout the potential health benefits of an optimized microbiome — or conversely, the risks of dysbiosis. Depression, stress, anxiety and autism are all proposed to be at least partially sensitive to manipulation of the gut microbiome. Studies have suggested that a variety of conditions are influenced by the microbiome, including obesity, functional gastrointestinal (GI) disorders, chronic fatigue syndrome and inflammatory illnesses. All of these disorders also have an important central nervous system component. It is likely that a substantial portion of people who consume probiotics or prebiotics will do so with the aim of improving symptoms related to the brain … There is interest among both the research and lay communities in understanding the effects of the microbiome on the brain. Patients and clinicians alike are keen to understand whether modifying the microbiome might provide a treatment avenue for various neuropsychiatric conditions. Despite a relative abundance of reviews of the microbiome in human mental health and disease, actual data are sparse, and the scientific community is not yet prepared to support the many research programs that are comprehensive and bring together investigators from various disciplines may provide the best opportunity to move this exciting but challenging field forward in the next decade.


Objective: To assess the potential association between prenatal use of antidepressants and the risk of attention-deficit/hyperactivity disorder (ADHD) in offspring. Design: Population based cohort study. Setting: Data from the Hong Kong population based electronic medical records on the Clinical Data Analysis and Reporting System. Participants: 190,618 children born in Hong Kong public hospitals between January 2001 and December 2009 and followed up to December 2015. Main outcome measure: Hazard ratio of maternal antidepressant use during pregnancy and ADHD in children aged 6 to 14 years, with an average follow-up time of 9.3 years (range 7.4-11.0 years). Results: Among 190,618 children, 1252 had a mother who used prenatal antidepressants, 5659 children (3.0%) were given a diagnosis of ADHD or received treatment for ADHD. The crude hazard ratio of maternal antidepressant use during pregnancy was 2.26 (P=0.01) compared with non-use. After adjustment for potential confounding factors, including maternal psychiatric disorders and use of other psychiatric drugs, the adjusted hazard ratio was reduced to 1.39 (95% confidence interval 1.07 to 1.82, P=0.01). Likewise, similar results were observed when comparing children of mothers who had used antidepressants before pregnancy with those who were never users (1.76, 1.36 to 2.21)
The risk of ADHD in the children of mothers with psychiatric disorders was higher compared with the children of mothers without psychiatric disorders even if the mothers had never used antidepressants (1.84, 1.54 to 2.18, P=0.01). All sensitivity analyses yielded similar results. Sibling matched analysis identified no significant difference in risk of ADHD in siblings exposed to antidepressants during gestation and those not exposed during gestation (0.54, 0.17 to 1.74, P=0.30). Conclusions The findings suggest that the association between prenatal use of antidepressants and risk of ADHD in offspring can be partially explained by confounding by indication of antidepressants. If there is a causal association, the size of the effect is probably smaller than that reported previously.


Abstract

Introduction

St John’s wort is a popular herbal remedy recommended by Traditional Chinese Medicine (TCM) practitioners and licensed and widely prescribed for depression in many European countries. However, conflicting data regarding its benefits and risks exist, and the last large meta-analysis on St John’s wort use for depression was done in 2008, with no updated meta-analysis available. Methods Using the keywords [St John’s Wort OR Hypericum perforatum OR hypericin OR hyperforin OR johanniskraut OR Hypericum perforatum] AND [depression OR antidepressant OR SSRI], a preliminary search (without language restriction) on the PubMed, Ovid, Clinical Trials Register of the Cochrane Collaboration Depression, Anxiety and Neurosis Group, Cochrane Rehabilitation Group, Cochrane Gastrointestinal Outcomes Group, and Chinese National Knowledge Infrastructure database yielded 5428 papers between 1 Jan-1960 and 1 May-2016. Results 27 clinical trials with a total of 3808 patients were reviewed, comparing the use of St John’s wort and SSRIs. In patients with depression, St John’s wort demonstrated comparable rate (pooled RR 0.983, 95% CI 0.924–1.042, p=0.001), remission (pooled RR 1.013, 95% CI 0.892–1.134, p<0.001) rate, and significantly lower discontinuation/dropout (pooled OR 0.587, 95% CI 0.407–0.797, p=0.001) compared to standard SSRIs.

Discussions

Bradley and colleagues compared the effects of the herbal antidepressant St John’s wort against the standard antidepressant, the SSRI, paroxetine. They found that St John’s wort was as effective as paroxetine and had a lower discontinuation rate. St John’s wort has been shown to reduce the risk of developing depression and to have a lower discontinuation rate compared to paroxetine.

However, the authors also note the need for new approaches to prevent depression or to delay its progression. While in its early stages, converging evidence from laboratory, population research, and clinical trials now suggests that dietary patterns and specific dietary factors may influence the risk for depression. However, largely as a result of the recency of the nutritional psychiatry field, there are currently no dietary recommendations for depression. AIM: The aim of this paper is to provide a set of practical dietary recommendations for the prevention of depression, based on the public health evidence, in order to support the best available dietary guidelines.

Results

The results showed that the use of St John’s wort and SSRIs was comparable. The pooled RR for St John’s wort was 0.983, 95% CI 0.924–1.042, p=0.001, and the pooled RR for remission was 1.013, 95% CI 0.892–1.134, p<0.001. The pooled OR for discontinuation/dropout was 0.587, 95% CI 0.407–0.797, p=0.001.

Conclusion

The results of this meta-analysis suggest that St John’s wort is as effective as SSRIs in the treatment of depression. Further research is needed to explore the mechanisms by which St John’s wort may be effective in the treatment of depression.


Nutritional Neuroscience

1-15.

Nutritional Neuroscience

1-15.

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Background & Aims Probiotics can reduce symptoms of irritable bowel syndrome (IBS), but little is known about their effects on psychiatric comorbidities. We performed a prospective study to evaluate the efficacy of Bifidobacterium longum NCC3001 (BL) on anxiety and depression in patients with IBS. Methods We performed a randomized, double-blind, placebo-controlled study of 44 adults with IBS and diarrhea or a mixed-stool pattern (based on Rome III criteria) and mild to moderate anxiety and/or depression (based on the Hospital Anxiety and Depression scale) at McMaster University in Canada, from March 2011 to May 2014. At the screening visit, clinical history and symptoms were assessed and blood samples were collected. Patients were then randomly assigned to groups and given daily BL for 4 weeks. At weeks 0, 6, and 10, patients’ self-rated levels of anxiety and depression, IBS symptom, quality of life, and somatization using validated questionnaires. At weeks 0 and 6, stool, urine and blood samples were collected, and functional magnetic resonance imaging (fMRI) test was performed. We assessed brain activation patterns, fecal microbiota, urine metabolome profiles, serum markers of inflammation, neurotransmitters, and neurotrophin levels. Results At week 6, 14 out of 22 patients in the BL group had a reduction in depression scores of 2 points or more on the Hospital Anxiety and Depression scale, vs 7 of 22 patients in the placebo group (P=.04). BL had no significant effect on anxiety or IBS symptoms. Patients in the BL group had a mean increase in quality of life score compared with the placebo group. The fMRI analysis showed that BL reduced responses to negative emotional stimuli in multiple brain regions, including amygdala and fronto-limbic regions, compared with placebo. The groups had similar fecal microbiota profiles, serum markers of inflammation, and levels of neurotrophins and neurotransmitters, but the BL group had reduced urine levels of methanethiol and aromatic amino acids metabolites. At week 10, depression scores were significantly lower in the BL group compared with the placebo group. Conclusions These findings provide new insights into the potential of probiotics in the management of depressive symptoms in patients with IBS.
Aim: The purpose of study was to assess the effect of zinc sulfate (ZS) supplementation on premenstrual syndrome (PMS) and health-related quality of life (QoL). Methods: This was a double-blind randomized and placebo-controlled trial using the parallel technique conducted between June 2013 and May 2014. A total of 142 women (age, 20–35 years) with PMS were allocated to either the ZS or placebo group. The women in the intervention group received ZS 220-mg capsules (containing 50 mg elemental zinc) from the 16th day of the menstrual cycle to the second day of the next cycle. Data were collected using the Premenstrual Symptoms Screening Tool (PSST) and 12-item Short-Form Health Survey Questionnaire. Result: The prevalence of moderate to severe PMS in the ZS group significantly decreased throughout the study period (9.5% in the first, 6% in the second and 2.6% in the third month of the study, P < 0.001), but in the control placebo group this reduction was seen only in the first month of the study (14.2% in the first, 13.7% in the second and 13.5% in the third month, P = 0.08). Also, ZS improved the PSST component scores throughout the study period. The mean scores of QoL in physical and mental components were significantly improved in the ZS intervention group. However, the differences were statistically significant only 3 months after the intervention. Conclusion: Zinc sulfate, as a simple and inexpensive treatment, was associated with improvement of PMS symptoms and health-related QoL. Additional studies are warranted to confirm these findings.


BACKGROUND: Persistent low-grade immune-inflammatory processes, oxidative and nitrosative stress (O&NS), and hypothalamic-pituitary-adrenal axis activation are integral to the pathophysiology of major depressive disorder (MDD). The microbiome composition and dysbiosis, internal translocation of bacterial elements, and their capacity to influence the bidirectional interactions of the gut-brain axis; new evidence implicates these pathways in the patho-aetiology of MDD. In addition, abnormalities in the gut-brain axis are associated with several chronic non-communicable disorders, which frequently co-occur in individuals, including but not limited to irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), obesity, and type 2 diabetes mellitus (T2DM). METHODS: We searched the PubMed/MEDLINE database up until May 1, 2016 for studies which investigated intestinal dysbiosis and bacterial translocation (the 'leaky gut') in the pathophysiology of MDD and co-occurring somatic comorbidities with an emphasis on IBS, CFS, obesity, and T2DM. RESULTS: The composition of the gut microbiota is influenced by several genetic and environmental factors (e.g. diet). Several lines of evidence indicate that gut-microbiota-diet interactions play a significant pathophysiological role in MDD and related medical comorbidities. Gut dysbiosis and the leaky gut may influence several pathways implicated in the biology of MDD, including but not limited to immune activation, O&NS, and neuroplasticity cascades. However, methodological inconsistencies and limitations limit comparisons across studies. CONCLUSIONS: Intestinal dysbiosis and the leaky gut may constitute a key pathophysiological link between MDD and its medical comorbidities. This emerging literature opens relevant preventative and therapeutic perspectives.


Importance Prenatal antidepressant exposure has been associated with adverse outcomes. Previous studies, however, may not have adequately accounted for confounding. Objective To evaluate alternative hypotheses for associations between first-trimester antidepressant exposure and birth and neurodevelopmental problems. Design, Setting, and Participants This retrospective cohort study included Swedish offspring born between 1996 and 2012 and followed up through 2013 or censored by death or emigration. Analyses were performed for preterm (birth ≤37 weeks), small for gestational age (birth weight <10th percentile), autism spectrum disorder, timing of exposure comparisons, and paternal comparisons, were used to examine the associations. Exposures Maternal self-reported first-trimester antidepressant use and first-trimester antidepressant dispensations. Main Outcomes and Measures Preterm birth (<37 gestational weeks), small for gestational age (birth weight <2nd percentile), autism spectrum disorder, and attention-deficit/hyperactivity disorder in offspring. Results Among 1 580 629 offspring (mean gestational age, 279 days; 48.6% female; 1.4% [n = 22 544] with maternal first-trimester self-reported antidepressant use) born to 943 776 mothers (mean age at childbirth, 30 years), 6.98% of exposed vs 4.78% of unexposed offspring were preterm, 2.54% of exposed vs 2.19% of unexposed were small for gestational age, 5.28% of exposed vs 2.14% of unexposed were diagnosed with autism spectrum disorder by age 15 years, and 12.63% of exposed vs 5.46% of unexposed were diagnosed with attention-deficit/hyperactivity disorder by age 15 years. At the population level, first-trimester exposure was associated with all outcomes compared with unexposed offspring (preterm birth odds ratio [OR], 1.47 [95% CI, 1.40–1.55]; small for gestational age OR, 1.15 [95% CI, 1.06–1.25]; autism spectrum disorder hazard ratio [HR], 2.02 [95% CI, 1.80–2.26]; attention-deficit/hyperactivity disorder HR, 2.21 [95% CI, 2.04–2.39]). However, in models that compared siblings while adjusting for pregnancy, maternal, and paternal traits, first-trimester antidepressant exposure was associated with birth weight (OR, 1.01 [95% CI, 0.81–1.25]) but not with small for gestational age (OR, 1.01 [95% CI, 0.81–1.25]) autism spectrum disorder (HR, 0.83 [95% CI, 0.62–1.13]), or attention-deficit/hyperactivity disorder (HR, 0.99 [95% CI, 0.79–1.25]). Results from analyses assessing associations with maternal dispensions before pregnancy and with paternal first-trimester dispensations were consistent with findings from the sibling comparisons. Conclusions and Relevance Among offspring born in Sweden, after accounting for confounding factors, first-trimester exposure to antidepressants, compared with no exposure, was associated with a small increased risk of preterm birth but no increased risk of small for gestational age, autism spectrum disorder, or attention-deficit/hyperactivity disorder.


Background Major depressive disorder (MDD) is a leading cause of disability worldwide. Aims To examine the: (a) 12-month prevalence of DSM-IV MDD; (b) proportion aware that they have a problem needing treatment and who want care; (c) proportion of the latter receiving treatment; and (d) proportion of such treatment meeting minimal standards. Method Representative community household surveys from 21 countries as part of the World Health Organization World Mental Health Surveys. Results Of 51 547 respondents, 4.6% met 12-survey criteria for DSM-IV MDD and of these 56.7% reported needing treatment. Among those who recognised their need for treatment, most (71.1%) made at least one visit to a service provider. Among those who received treatment, only 41.0% received treatment that met minimal standards. This reduced in patients given BL vs placebo. Conclusion In a placebo-controlled trial, we found that the probiotic BL reduces depression but not anxiety scores and increases quality of life in patients with IBS. These improvements were associated with changes in brain activation patterns that indicate that this probiotic reduces limbic reactivity.
resulted in only 16.5% of all individuals with 12-month MDD receiving minimally adequate treatment. Conclusions Only a minority of participants with MDD received minimally adequate treatment: 1 in 5 people in high-income and 1 in 27 in low-/lower-middle-income countries. Scaling up care for MDD requires fundamental transformations in community education and outreach, supply of treatment and quality of services.


Importance Recognition that adult attention-deficit/hyperactivity disorder (ADHD) is common, seriously impairing, and usually undiagnosed has led to the development of adult ADHD screening scales for use in community, workplace, and primary care settings. However, these scales are all calibrated to DSM-IV criteria, which are narrower than the recently developed DSM-5 criteria. Objectives To update for DSM-5 criteria and improve the operating characteristics of the widely used World Health Organization Adult ADHD Self-Report Scale (ASRS) for screening. Design, Setting, and Participants Probability subsamples of population-based adult samples from the USA (n = 119; 2004–2005 managed care subscriber survey [n = 218]) who completed the full 29-question self-report ASRS, with both subsamples over-sampling ASRS-screened positives, were blindly administered a semistructured research diagnostic interview for DSM-5 adult ADHD. In 2016, the Risk-Calibrated Subscale Linear Integer Model, a novel machine-learning algorithm designed to create screening scales with optimum integer weights and limited numbers of screening questions, was applied to the pooled data to create a DSM-5 version of the ASRS screening scale. The accuracy of the new scale was then confirmed in an independent 2011-2012 clinical sample of patients seeking evaluation at the New York University Langone Medical Center Adult ADHD Program (NYU Langone) and 2015-2016 primary care controls (n = 300). Data analysis was conducted from April 4, 2016, to September 22, 2016. Main Outcomes and Measures The sensitivity, specificity, area under the curve (AUC), and positive predictive value (PPV) of the revised ASRS. Results Of the total 637 participants, 44 (37.0%) household survey respondents, 51 (23.4%) managed care respondents, and 173 (57.7%) NYU Langone respondents met DSM-5 criteria for adult ADHD in the semistructured diagnostic interview. Of the respondents who met DSM-5 criteria for adult ADHD, 123 were male (45.9%); mean (SD) age was 33.1 (11.4) years. A 6-question screening scale was found to be optimal in distinguishing cases from noncases in the first 2 samples. Operating characteristics were excellent at the diagnostic threshold in the weighted (to the 8.2% DSM-5/Adult ADHD Clinical Diagnostic Scale population prevalence) data (sensitivity, 91.4%; specificity, 96.0%; AUC, 0.94; PPV, 67.3%). Operating characteristics were similar despite a much higher prevalence (57.7%) when the scale was applied to the NYU Langone clinical sample (sensitivity, 91.9%; specificity, 74.0%; AUC, 0.83; PPV, 82.8%). Conclusions and Relevance The new ADHD screening scale is short, easily scored, detects the vast majority of general population cases at a threshold that also has high specificity and PPV, and could be used as a screening tool in specialty treatment settings.


Objective: The authors sought to determine the risk of treatment-emergent mania associated with methylphenidate, used in monotherapy or with a concomitant mood-stabilizing medication, in patients with bipolar disorder. Method: Using linked Swedish national registries, the authors identified 2,307 adults with bipolar disorder who initiated therapy with methylphenidate between 2006 and 2014. The cohort was divided into two groups: those with and those without concomitant mood-stabilizing treatment. To adjust for individual-specific confounders, including disorder severity, genetic makeup, and early environmental factors, Cox regression analyses were used, conditioning on individual to compare the rate of mania (defined as hospitalization for mania or a new dispensation of stabilization medication) – 0–3 months and 3–6 months after medication start following non-treated periods. Results: Patients on methylphenidate monotherapy displayed an increased rate of manic episodes within 3 months of medication initiation (hazard ratio=6.7, 95% CI=2.0–22.4), with similar results for the subsequent 3 months. By contrast, for patients taking mood stabilizers, the risk of mania was lower after starting methylphenidate (hazard ratio=0.6, 95% CI=0.4–0.9). Comparable results were observed when only hospitalizations for mania were counted. Conclusions: No evidence was found for a positive association between methylphenidate and treatment-emergent mania among patients with bipolar disorder who were concomitantly receiving a mood-stabilizing medication. This is clinically important given that up to 20% of people with bipolar disorder suffer from comorbid ADHD. Given the markedly increased hazard ratio of mania following medication initiation in both patients not taking mood stabilizers, careful assessment to rule out bipolar disorder is indicated before initiating monotherapy with psychostimulants.


Significant controversy surrounds the efficacy of the newer antidepressants for children and adolescents with depression. The controversy largely hinges on meta-analyses of studies that suggest that antidepressants are minimally effective, not effective, or equivalent to placebo. In this review, the authors discuss several scientific and clinical complexities that are important to understand in reviewing the antidepressant literature: the strengths and weaknesses of meta-analyses; the scientific and regulatory context for the large number of antidepressant trials in the late 1990s and early 2000s; and the distinction between a negative trial, where the treatment does not demonstrate efficacy, and a failed trial, where methodological problems make it impossible to draw any conclusion about efficacy. It is the premise of this review that meta-analyses that include poorly designed or powered antidepressant trials distort the picture of antidepressant efficacy for teen depression. Industry-sponsored child and adolescent depression trials suffer from a number of implementation challenges and should be considered failed trials that are largely uninformative and not eligible to be included in efficacy meta-analyses. In contrast to the industry-sponsored trials, depression trials funded by the National Institute of Mental Health (NIMH) (N=2) are characterized by many methodological strengths, lower placebo response rates (30%–35%), and meaningful between-group differences (25%–30%) that support antidepressant efficacy. The NIMH-funded trials, taken together with the demonstrated efficacy of the serotonin reuptake inhibitors for childhood-onset obsessive-compulsive disorder and the anxiety disorders, suggest a broad and important role for antidepressant medications in pediatric internalizing conditions.

Wallace, C. J. K. and R. Milev (2017). “The effects of probiotics on depressive symptoms in humans: A systematic review.” Annals of General Psychiatry 16: 14. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5319175/ (Available in free full text) BACKGROUND: Patients suffering from depression experience significant mood, anxiety, and cognitive symptoms. Currently, most antidepressants work by altering neurotransmitter activity in the brain to improve these symptoms. However, in the last decade, research has revealed an extensive bidirectional communication network between the gastrointestinal tract and the central nervous system, referred to as the “gut–brain axis.” Advances in this field have linked psychiatric disorders to changes in the microbiome, making it a potential target for novel antidepressant treatments. The aim of this review is to analyze the current body of research assessing the effects of probiotics, on symptoms of depression in humans.
METHODS: A systematic search of five databases was performed and study selection was completed using the preferred reporting items for systematic reviews and meta-analyses process. RESULTS: Ten studies met criteria and were analyzed for effects on mood, anxiety, and cognition. Five studies assessed mood symptoms, seven studies assessed anxiety symptoms, and three studies assessed cognition. The majority of the studies found positive results on all measures of depressive symptoms; however, the strain of probiotic, the dosing, and duration of treatment varied widely and no studies assessed sleep. CONCLUSION: The evidence for probiotics alleviating depressive symptoms is compelling but additional double-blind randomized control trials in clinical populations are warranted to further assess efficacy.


Abstract
Background Major depressive disorder is a relatively common diagnosis with onset across the lifespan. There is a recent belief that major depressive episodes (MDE) are increasing in adolescence; however, it is not clear if this is truly an increase in prevalence or reflective of other causes such as change in diagnostic patterns. This study aimed to determine whether evidence supports an epidemic of MDE in Canadian adolescents. Methods Past year MDE prevalence estimates were derived from a series of nationally representative surveys. Random effects meta-regression and graphical analyses were used to evaluate trends. A post hoc analysis compared trends in MDE prevalence to trends in self-reported mood disorder diagnosis (made by a health professional). The sample was split into 9 birth cohorts to examine whether MDE prevalence increased in more recent cohorts. Results Prevalence of MDE did not significantly change between 2000 and 2014 (β=0.001; p=0.532), and there was no modification of trends by sex or age. However, prevalence of self-reported mood disorder diagnosis by a health professional increased from 2003 to 2014 (β=0.001; p=0.024). There was no indication that MDE prevalence differed by birth cohort. Limitations Limitations include reduced precision in subgroup analyses, lack of clinical judgement in the structured diagnostic interview, and inability to differentiate mild, moderate and severe episodes of depression. Conclusion These findings do not support an epidemic of MDE in adolescents, however as more individuals report diagnoses by a health professional, future policy may need to incorporate an increase in need of mental health services.