

Obsessive-Compulsive Disorder

ABSTRACTS

- Blier P., 1996. Sequential administration of augmentation strategies in treatment-resistant obsessive-compulsive disorder: preliminary findings.
- Brenner R., 2000. Comparison of an extract of hypericum (LI 160) and sertraline in the treatment of depression: a double-blind, randomized pilot study.
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- Vadnal R., 1997. Role of inositol in the treatment of psychiatric disorders. Basic and clinical aspects.
- Sequential administration of augmentation strategies in treatment-resistant obsessive-compulsive disorder: preliminary findings.**

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Int Clin Psychopharmacol 1996 Mar;11(1):37-44

Given that an important proportion of patients with obsessive-compulsive disorder (OCD) fail to respond adequately to serotonin (5-HT) reuptake inhibitors (SRI), augmentation strategies aimed at enhancing further 5-HT transmission by different mechanisms were attempted sequentially in 13 SRI-resistant patients. Addition of the 5-HT_{1A} beta-adrenergic antagonist pindolol did not alter OCD symptomatology but produced a rapid improvement of depressive symptoms. The 5-HT_{1A} agonist buspirone as well as 5-

hydroxytryptophan, the immediate precursor of 5-HT, added to the SRI-pindolol regimen, were not effective in attenuating the intensity of OCD. Tryptophan, added to the SRI-pindolol regimen, produced a significant improvement after 4 weeks, with further amelioration after 6 weeks (36% decrease of the Yale-Brown Obsessive Compulsive Score), which was maintained with treatment prolongation.

Comparison of an extract of hypericum (LI 160) and sertraline in the treatment of depression: a double-blind, randomized pilot study.

Brenner R, Azbel V, Madhusoodanan S, Pawlowska M. St. John's Episcopal Hospital, Far Rockaway, New York 11691, USA.

Clin Ther 2000 Apr;22(4):411-9

BACKGROUND: Hypericum (St. John's wort) has been shown to be as efficacious and well tolerated as standard antidepressants in the treatment of depression but has not been compared with selective serotonin reuptake inhibitors (SSRIs).

OBJECTIVE: This study compared hypericum and the SSRI sertraline in the treatment of depression.

METHODS: In a double-blind, randomized study conducted in a community hospital, 30 male and female outpatients (19 women, 11 men; mean age, 45.5 years) with mild to moderate depression received 600 mg/d of a standardized extract of hypericum (LI 160) or 50 mg/d sertraline for 1 week, followed by hypericum 900 mg/d or sertraline 75 mg/d for 6 weeks.

RESULTS: The severity of symptoms, as assessed by scores on the Hamilton Rating Scale for Depression (HAM-D) and the Clinical Global Impression scale, was significantly reduced in both treatment groups (< 0.01). Clinical response (defined as a $<$ or $=50\%$ reduction in HAM-D scores) was noted in 47% of patients receiving hypericum and 40% of those receiving sertraline. The difference was not statistically significant. Both agents were well tolerated. A post hoc power analysis indicated that failure to reach statistical significance between treatments resulted primarily from an absence of clinical differences rather than the small sample size.

CONCLUSION: The hypericum extract was at least as effective as sertraline in the treatment of mild to moderate depression in a small group of outpatients.

Faith-assisted cognitive therapy of obsessive-compulsive disorder.

Gangdev PS. Community Mental Health Service, Tokoroa Hospital, New Zealand.

Aust N Z J Psychiatry 1998 Aug;32(4):575-8

OBJECTIVE: The aim of this paper is to report the rapid resolution of obsessions when the patient invoked Christ to treat her obsessions.

CLINICAL PICTURE: A 25-year-old female presented with obsessions (doubts) that: (i) while driving she will knock down a pedestrian; and (ii) she will be charged with sex abuse.

TREATMENT AND OUTCOME: Cognitive therapy (cognitive restructuring and thought-stopping) was offered. After a single session a complete remission was reported when she replaced her doubts with firm convictions that 'Christ will help me drive safely' and 'Christ will not let me do anything wrong'. She was reported to have remained well at the end of 5 months at which time she relocated and was then lost to follow-up.

CONCLUSION: Religious faith can have a healing effect, and cognitive therapy is not incompatible with religion. Although unusual in standard clinical practice, rapid resolution of obsessions is possible.

Group behavioral therapy of obsessive-compulsive disorder: seven vs. twelve-week outcomes.

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Depress Anxiety 2001;13(4):161-5

Previous research has demonstrated that individualized behavioral exposure and response prevention therapy is an effective treatment for Obsessive-Compulsive Disorder. In our prior preliminary report, 7-week group exposure and response prevention

therapy was also found effective in reducing obsessions and compulsions. The present report describes a larger sample (N=113) of treatment seeking obsessive-compulsives who received group behavioral therapy. As before, group exposure and response prevention significantly improved ratings of obsessions, compulsions, and depression. These improvements were maintained at 3-month and long-term follow-up. A sub-sample of patients who received 12 weeks of treatment had outcomes at the end of the group and at follow-up that did not significantly differ from those who received 7 weeks of treatment. These results confirm the efficacy of a 7-week behavioral treatment program administered in a group format. Copyright 2001 Wiley-Liss, Inc.

Relapse prevention program for treatment of obsessive-compulsive disorder.

Hiss H, Foa EB, Kozak MJ. Department of Psychiatry, Hamburg University, Germany.

J Consult Clin Psychol 1994 Aug;62(4):801-8

Eighteen participants with obsessive-compulsive disorder received 3 weeks of intensive treatment by exposure and response prevention, which were followed by either a relapse prevention (RP) program or associative therapy (AT; an attention-control program). Independent evaluators conducted assessments of obsessive-compulsive symptoms, anxiety, and depression, before and after intensive behavior therapy, after the week of intensive RP or AT and at a 6-month follow-up. Results indicated that the RP program was effective in preventing relapse: Both treatment groups improved immediately after the intensive treatment, but the RP group remained improved at follow-up, whereas the AT group showed some return of symptoms.

The tryptophan depletion test. Impact on sleep in healthy subjects and patients with obsessive-compulsive disorder.

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Adv Exp Med Biol 1999;467:35-42

The tryptophan depletion test is a research tool to study the functional consequences of decreasing the brain serotonin metabolism. Since serotonin is involved in sleep regulation and assumed to be of high importance in the etiology of psychiatric disorders, the acute polysomnographic effects of tryptophan depletion were studied in healthy subjects and patients with obsessive compulsive disorder (OCD). According to the reciprocal interaction model of non-REM and REM-sleep regulation we expected that tryptophan depletion in healthy controls should provoke alterations of sleep similar to depression, whereas we assumed that these effects would be more pronounced in patients with OCD.

METHODS: 12 healthy subjects with a mean age of 34 years and 12 patients suffering from OCD with a mean age of 30 years had 4 polysomnographic investigations. After 1 adaption and 1 baseline night subjects received a low protein diet on day 3 and 4 until midday. On day 4 at 18.00 h subjects ingested an amino acid mixture devoid of tryptophan. This procedure resulted in a decrease of 85% in healthy subjects and 80% in OCD patients at 22.00 h.

RESULTS: The tryptophan depletion led to more pronounced disturbances of sleep continuity in OCD patients than in healthy subjects in terms of an increase of wake time and a decrease of total sleep time. In both groups a decrease of sleep stage 2 could be observed. Healthy subjects showed significant alterations of phasic REM parameters as REM density and total number of rapid eye movements, what was not the case for OCD patients.

CONCLUSIONS: Our results indicate the important role of the serotonergic system for sleep maintenance and the phasic aspects of REM sleep. Furthermore our data demonstrate that the tryptophan depletion test is a useful tool to evaluate the hypothesis of a serotonergic involvement in sleep regulation and the etiology of psychiatric disorders.

Inhibiting effects of theanine on caffeine stimulation evaluated by EEG in the rat.

Kakuda T, Nozawa A, Unno T, Okamura N, Okai O. Central Research Institute, Itoen Ltd., Shizuoka, Japan. ITN00527@nifty.ne.jp

Biosci Biotechnol Biochem. 2000 Feb;64(2):287-93.

In this study, the inhibiting action of theanine on the excitation by caffeine at the concentration regularly associated with drinking tea was investigated using electroencephalography (EEG) in rats. First, the stimulatory action by caffeine i.v. administration at a level higher than 5 micromol/kg (0.970 mg/kg) b.w. was shown by means of brain wave analysis, and this level was suggested as the minimum dose of caffeine as a stimulant. Next, the stimulatory effects of caffeine were inhibited by an i.v. administration of theanine at a level higher than 5 micromol/kg (0.781 mg/kg) b.w., and the results suggested that theanine has an antagonistic effect on caffeine's stimulatory action at an almost equivalent molar concentration. On the other hand, the excitatory effects were shown in the rat i.v. administered 1 and 2 micromol/kg (0.174 and 0.348 mg/kg) b.w. of theanine alone. These results suggested two effects

of theanine, depending on its concentration.

Electroconvulsive Therapy in Obsessive-Compulsive Disorder.

Khanna S, Gangadhar BN, Sinha V, Rajendra PN, Channabasavanna SM. Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bangalore, India.

Convuls Ther 1988;4(4):314-320

An open trial of electroconvulsive therapy was conducted in nine subjects who met DSM-III criteria for obsessive-compulsive disorder. There was an initial reduction in symptomatology that lasted from 1 to 4 months. Subjects who had less obsessive-compulsive (anankastic) personality traits responded better. There was also the post hoc observation that subjects who were agitated did better. We observed correlations between depression and interference scores, but not with symptom scores, suggesting that ECT has anti-obsessional activity.

[Behavior therapy of obsessive compulsive disorders] [Article in French]

Legeron P, Wajsgros A. Service Hospitalo-Universitaire de Sante Mentale et Therapeutique, Centre Hospitalier Sainte-Anne, Paris.

Encephale. 1989 May-Jun;15(3):343-50.

Obsessive-Compulsive Disorders (OCD) were once considered a relatively rare condition and highly refractory to treatment. Behavioral treatments consisting primarily of various methods of exposure and response prevention are reported to be approximately 70% effective in treating this condition that may affect 2 to 3% of the population and, in many cases, the effectiveness of these interventions persists over a number of years. However much remains to be done in refining these strategies and determining which patients are most likely to respond to these interventions.

Controlled trials of inositol in psychiatry.

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Eur Neuropsychopharmacol 1997 May;7(2):147-55

Inositol is a simple polyol precursor in a second messenger system important in the brain. Cerebrospinal fluid inositol has been reported as decreased in depression. A double-blind controlled trial of 12 g daily of inositol in 28 depressed patients for four weeks was performed. Significant overall benefit for inositol compared to placebo was found at week 4 on the Hamilton Depression Scale. No changes were noted in hematology, kidney or liver function. Since many antidepressants are effective in panic disorder, twenty-one patients with panic disorder with or without agoraphobia completed a double-blind, placebo-controlled, four week, random-assignment crossover treatment trial of inositol 12 g per day. Frequency and severity of panic attacks and severity of agoraphobia declined significantly with inositol compared to placebo. Side-effects were minimal. Since serotonin re-uptake inhibitors benefit obsessive compulsive disorder (OCD) and inositol is reported to reverse desensitization of serotonin receptors, thirteen patients with OCD completed a double-blind controlled crossover trial of 18 g inositol or placebo for six weeks each. Inositol significantly reduced scores of OCD symptoms compared with placebo. A controlled double-blind crossover trial of 12 g daily of inositol for a month in twelve anergic schizophrenic patients, did not show any beneficial effects. A double-blind controlled crossover trial of 6 g of inositol daily vs. glucose for one month each was carried out in eleven Alzheimer patients, with out clearly significant therapeutic effects. Antidepressant drugs have been reported to improve attention deficit disorder (ADDH) with hyperactivity symptomatology. We studied oral inositol in children with ADDH in a double-blind, crossover, placebo-controlled manner. Eleven children, mean age 8.9 3.6 years were enrolled in an eight week trial of inositol or placebo at a dose of 200 mg/kg body weight. Results show a trend for aggravation of the syndrome with myo-inositol as compared to placebo. Recent studies suggest that serotonin re-uptake inhibitors are helpful in at least some symptoms of autism. However a controlled double-blind crossover trial of inositol 200 mg/kg per day showed no benefit in nine children with autism. Cholinergic agonists have been reported to ameliorate electroconvulsive therapy (ECT)-induced memory impairment. Inositol metabolism is involved in the second messenger system for several muscarinic cholinergic receptors. Inositol 6 g daily was given in a crossover-double-blind manner for five days before the fifth or sixth ECT to a series of twelve patients, without effect. These results suggest that inositol has therapeutic effects in the spectrum of illness responsive to serotonin selective re-uptake inhibitors, including depression, panic and OCD, and is not beneficial in schizophrenia, Alzheimer's ADDH, autism or ECT-induced cognitive impairment.

Refractory obsessive compulsive disorder and ECT.

Maletzky B, McFarland B, Burt A. Department of Psychiatry, Oregon Health Sciences University, Portland 97201.

The authors review their experience with electroconvulsive therapy (ECT) in 32 patients meeting DSM-III-R criteria for obsessive compulsive disorder. All patients had received extensive behavioral and cognitive therapy and pharmacotherapy prior to the initiation of ECT without apparent benefit. Following ECT, most subjects showed considerable improvement in obsessive compulsive symptoms and remained improved up to 1 year after therapy. Some patients also showed short-term improvements on several measures of depression. The change in obsessive compulsive symptoms, however, appeared to be independent of changes in measures of depression. Obsessive-Compulsive Disorder

Mayo Clinic.

2001 Jun 25. Rochester, NY: Mayo Clinic/Mayo Foundation for Medical Education and Research (MFMER).

Obsessive-Compulsive Disorder (OCD)

Mental Health Channel.

2002 Jan 16. Northampton, MA: Healthcommunities.com (<http://www.mentalhealthchannel.net/ocd/index.shtml>).

Facts about Obsessive-Compulsive Disorder 1990.

National Institute of Mental Health.

Publication No. OM-99 4154 (Revised), printed September 1999, updated February 21, 2003. Bethesda, MD: National Institute of Mental Health/National Institutes of Health (<http://www.nimh.nih.gov/anxiety/ocdfacts.cfm>).

Treatment of the obsessive-compulsive disorder.

Nemeth, A.

Lege Artis. Med. 1998; 8(4) 236-45.

No abstract available.

Obsessive-compulsive disorder: a treatment review.

Perse T. Department of Psychiatry, University of Arizona, Tucson 85724.

J Clin Psychiatry. 1988 Feb;49(2):48-55.

Obsessive-compulsive disorder, which may affect 2% to 3% of the U.S. population, can be severely disabling, permeating an individual's personal, social, and work life. Only within the past 2 decades have effective treatments been proposed and tested. Specific behavior therapies such as exposure in vivo and response prevention have proved successful in decreasing compulsive rituals in 70% to 80% of patients who accept and comply with treatment. For those patients who do not respond to behavior therapy, medications should be used. To date the tricyclic clomipramine is the only medication that has been consistently effective in controlled studies. However, for certain patients other medications may be of benefit. For the minority of patients who do not respond to either behavior therapy or medication, psychosurgery--specifically stereotactic limbic leucotomy--should be considered a viable option.

[Results of electroconvulsive therapy in restrictive indications. A retrospective study of 15 years] [Article in German]

Schott K, Bartels M, Heimann H, Buchkremer G. Psychiatrische Universitätsklinik, Tübingen.

Nervenarzt 1992 Jul;63(7):422-5

In Tübingen ECT is restricted to severely ill patients who do not respond to other somatic therapies; especially to patients with endogenous depression and pernicious catatonia. Between 1976 and 1990, 45 patients were treated with ECT, of whom 22 suffered from endogenous depression and 10 from pernicious catatonia. Thirteen patients with other diagnoses (schizophrenic and schizoaffective psychoses, borderline schizophrenia and obsessive-compulsive disorder) were treated with ECT for severe

depressive states after failure of psychopharmacological therapy. A positive therapeutic response to ECT was observed in 46% of patients with endogenous depression and in all 10 with pernicious catatonia. In the patients with schizophrenia and schizoaffective psychosis, borderline schizophrenia and obsessive-compulsive disorder, an amelioration of the depressive or anxiety syndrome was observed only in individual cases. Side effects of ECT were transit syndromes (20%), reversible amnesic syndromes (20%) and cardiac arrhythmias (6%). According to our results, ECT is highly effective in therapy-resistant endogenous depression and pernicious catatonia, and therefore remains a necessary part of psychiatric therapy.

Equivalence of St John's wort extract (Ze 117) and fluoxetine: a randomized, controlled study in mild-moderate depression.

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Int Clin Psychopharmacol 2000 Mar;15(2):61-8

Treatment with St John's wort extract tablets (hypericum Ze 117) and the commonly used slow serotonin reuptake inhibitor (SSRI) fluoxetine was compared in patients with mild-moderate depression with entry Hamilton Depression Scale (HAM-D) (21-item) in the range 16-24, in a randomized, double-blind, parallel group comparison in 240 subjects; fluoxetine: 114 (48%), hypericum: 126 (52%). After 6 weeks' treatment, mean HAM-D at endpoint decreased to 11.54 on hypericum and to 12.20 on fluoxetine ($P < 0.09$), while mean Clinical Global Impression (CGI) item I (severity) was significantly ($P < 0.03$) superior on hypericum, as was the responder rate ($P = 0.005$). Hypericum safety was substantially superior to fluoxetine, with the incidence of adverse events being 23% on fluoxetine and 8% on hypericum. The commonest events on fluoxetine were agitation (8%), GI disturbances (6%), retching (4%), dizziness (4%), tiredness, anxiety/nervousness and erectile dysfunction (3% each), while on hypericum only GI disturbances (5%) had an incidence greater than 2%. We concluded that hypericum and fluoxetine are equipotent with respect to all main parameters used to investigate antidepressants in this population. Although hypericum may be superior in improving the responder rate, the main difference between the two treatments is safety. Hypericum was superior to fluoxetine in overall incidence of side-effects, number of patients with side-effects and the type of side-effect reported.

Tryptophan depletion in obsessive-compulsive patients.

Smeraldi E, Diaferia G, Erzegovesi S, Lucca A, Bellodi L, Moja EA. Department of Neuropsychiatric Sciences, S. Raffaele Hospital, University of Milan, Italy.

Biol Psychiatry 1996 Sep 1;40(5):398-402

Twelve patients with obsessive-compulsive disorder were studied after the administration of a mixture of amino acids devoid of tryptophan (TRP) or a mixture containing all the essential amino acids, in a double-blind, crossover design. The TRP-free mixture caused a marked depletion of plasma TRP. After TRP decrease, mean ratings of obsessions and compulsions, measured by Visual Analogue Scales (VAS) ratings, did not worsen. In contrast with other reports in literature, TRP depletion also failed to alter mood in our subjects.

[Electroconvulsive therapy in compulsive syndromes. A case report] [Article in German]

Wohlfahrt A. Psychiatrisches Landeskrankenhaus, Weinsberg.

Nervenarzt 1996 May;67(5):397-9

We report on a case of successful ECT in serious drug-resistant and psychotherapy-resistant obsessive-compulsive disorder. The 44-year old male patient had already had symptoms of this disorder for 4 years, and they completely disappeared after seven ECTs (1 bi-, 6 unilateral). After remission of the obsessions the patient underwent a behaviour therapy to consolidate the success of the ECT treatment and to prepare the patient for returning to work. He remains free of obsessions 18 months later.

Natural Treatments

Piper methysticum (kava kava).

Anon [No authors listed]

Altern Med Rev. 1998 Dec;3(6):458-60.

Piper methysticum (kava kava) is a plant native to the Pacific Island region, and has been used ceremonially for thousands of years. The active ingredients are a group of substances known as kava lactones (AKA kava pyrones). Four lactones in kava have been

found to have significant analgesic and anesthetic effects via non-opiate pathways. Kava's most popular application is as a natural anxiolytic, comparing favorably in several studies to a number prescription medications, including benzodiazepines. CNS effects seem to be mediated by several mechanisms. Studies have been conflicting regarding its GABA-receptor-binding capacity, although this has been found to occur in some studies. In vitro kava has been found to block norepinephrine uptake. It also has some anti-convulsant capabilities, which appear to be mediated by Na⁺ channel receptor sites. The therapeutic dosage is in the range of 50-70 mg kava lactones three times daily. The most common side effect, usually seen only with long-term, heavy usage of the herb, is a scaly skin rash called "kava dermatopathy." It has also been known to potentiate other medications such as barbiturates and Xanax.

Inositol treatment of obsessive- compulsive disorder.

Fux M; Levine J; Aviv A; Belmaker RH Ministry of Health Mental Health Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beersheva, Israel.

Am J Psychiatry (United States) Sep 1996, 153 (9) p1219-21

OBJECTIVE: Earlier studies reported that inositol, a simple polyol second messenger precursor, was effective in controlled trials for patients with depression and panic. In this study its effectiveness in obsessive - compulsive disorder was investigated.

METHOD: Thirteen patients with obsessive - compulsive disorder completed a double-blind, controlled crossover trial of 18 g/day of inositol or placebo for 6 weeks each.

RESULTS: The subjects had significantly lower scores on the Yale-Brown Obsessive Compulsive Scale when taking inositol than when taking placebo.

ONCLUSIONS: The authors conclude that inositol is effective in depression, panic, and obsessive -compulsive disorder, a spectrum of disorders responsive to selective serotonin reuptake inhibitors.

Over-the-counter psychotropics: A review of melatonin, St John's wort, valerian, and kava-kava

Heiligenstein E.; Guenther G. Dr. E. Heiligenstein, University of Wisconsin-Madison, School of Medicine, Madison, WI United States

Journal of American College Health (United States) 1998, 46/6 (271-276)

Use and availability of alternative healthcare products have revived in the last few years. The prevalence of supplement use in the United States is largely unknown but is thought to be widespread. In this article, four of the common substances used to treat emotional problems are reviewed. The plant or substance description, clinical indications, evidence of therapeutic efficacy, mechanisms of therapeutic actions, dosages and regimens, different commercially available preparations, and adverse effects and toxicities are described for melatonin, St John's wort, valerian, and kava-kava. That a product is 'natural' does not mean that it is either safe or effective. Many supplements are potent drugs that lack sufficient data on safety, dose- response relationships, drug interactions, and purity.

Clinical efficacy of a kava extract in patients with anxiety syndrome. Double-blind placebo controlled study over 4 weeks

Kinzler E.; Kromer J.; Lehmann E. Forschungsstelle fur Klinische Prufungen Psychologie Haus II, Psychiatrische Universitatsklinik, Bergische Landstr. 2, W-4000 Dusseldorf Germany

Arzneimittel-Forschung/Drug Research (Germany) 1991, 41/6 (584-588)

In a randomized, placebo-controlled double-blind study two groups each containing 29 patients with anxiety syndrome not caused by psychotic disorders were treated for a period of 4 weeks with kava extract WS 1490 (Laitan(R)) 3 x 100 mg/day or a placebo preparation. Therapeutic efficacy was assessed by the Hamilton-Anxiety-Scale (main target variable), the Adjectives-List and the Clinical Global-Impression-Scale (secondary target variables) after 1, 2 and 4 weeks of treatment. The HAMA overall score of anxiety symptomatology revealed a significant reduction in the drug receiving group already after one week of treatment. This difference between the two groups of patients increased in the course of the study. The results of the secondary target variables were in agreement with the HAMA-score and demonstrate the efficacy of WS 1490 in patients with anxiety disorders. No adverse experiences caused by the medication were noted during the 4 week administration of WS 14900.

Tolerability of kava-kava extract WS 1490 on anxiety disorders (Multicentric Brazilian study)

Revista Brasileira de Medicina (Brazil) 1999, 56/4 (280-284)

The objective of the present study was to examine the efficacy and tolerability of kava extract WS 1490 on patients suffering anxiety syndrome. The instrument of analysis used was the modified hamilton-Anxiety-Scale (HAMA). The patients (n=850), 192 men and 574 women, had an average of age 42.8 +/- 13.1 years-old, and they were treated for a period of 4 weeks with kava extract (Laitan (R)), 3x100 mg/day. The HAMA overall score dropped from 30 to 9 (a reduction of 70%) after the treatment, showing statistical significance (< 0.0001). The tolerability was considered good and very good in 95.8% of patients. Based on the results we can say that kava extract WS 1490 showed positive results on the treatment of anxiety states, anxious humor, tension, insomnia and muscular symptoms (e.g. pain and fatigue).

Piper methysticum Forst: A new antianxiety agents

Rates S.M.K.; Santos L.

Revista Brasileira de Farmacia (Brazil) 1997, 78/2 (44-48)

In this work a dispensing profile of phytotherapeutics produced from Piper methysticum extracts in Porto Alegre and Caxias do Sul (RS-Brazil) was carried out in the period from September to October, 1996. It was observed that 30-40% of the pharmacies dispense galenical preparations or medicinal specialities with Piper methysticum in its composition. The main therapeutics indications were to anxiety disorders and to depression. A pharmacological and therapeutics data review was also performed following the American Society of Health-System Pharmacists (ASHP) recommendations for drug monographs. These data were compared to those from promotional literature. The later data do not match fully with scientific data. It lacks informations about adverse effects, conter indications, toxicity and drug interactions. According to ASHP recommendations, medicines obtained from P. methysticum extracts or from its active principles do not represent a reliable therapeutic advance in relation to the classical antianxiety drugs. However, they could be used for this purpose, as single drug, with concomitant medical and pharmaceutical care. The patient must be advised about possible adverse effects, as visual disturb, kava dermopathy, extrapiramidal symptom and putative addiction, drug interactions, mainly with alcohol and other depressants CNS; and special conditions, such as elderly, pregnancy and breast feeding.

Kava-kava extract in anxiety disorders: an outpatient observational study.

Scherer J Bezirkskrankenhaus Haar, Germany.

Adv Ther 1998 Jul-Aug;15(4):261-9

Fifty-two outpatients suffering from anxiety of nonpsychotic origin were included in an observational study of a kava-kava preparation. Drug efficacy was evident on measures of a global improvement scale, with 42 patients (80.8%) rating treatment as "very good" or "good". Adverse events were rare. These results support kava-kava extract as an effective and safe alternative to antidepressants and tranquilizers in anxiety disorder without the tolerance problems associated with benzodiazepines.

Inhibition of platelet MAO-B by kava pyrone-enriched extract from Piper methysticum Forster (kava-kava).

Uebelhack R, Franke L, Schewe HJ Department of Psychiatry, Humboldt-Universitat zu Berlin (Charite), Germany.

Pharmacopsychiatry 1998 Sep;31(5):187-92

Kava-kava, a psychoactive beverage, induces relaxation, improves social interaction, promotes sleep and plays an important role in the sociocultural life in the islands of the South Pacific. On the other hand, standardized extracts of kava-kava roots are used for the therapy of anxiety, tension and restlessness. Kava pyrones, the major constituents of kava kava, are generally considered to be responsible for the pharmacological activity in humans and animals. To obtain more information on the mechanisms by which kava-kava exerts psychotropic properties we investigated the in vitro effects of kava-kava extract and pure synthetic kava pyrones on human platelet MAO-B, in comparison to amitriptyline, imipramine and brofaromine. Kava-kava extract was found to be a reversible inhibitor of MAO-B in intact platelets (IC50 24 microM) and disrupted platelet homogenates (IC50 1.2 microM). Structural differences of kava pyrones resulted in a different potency of MAO-B inhibition. The order of potency was desmethoxyyangonin & (+/-)-methysticin & yangonin & (+/-)-dihydromethysticin & (+/-)- dihydrokavain & (+/-)-kavain. The two most potent kava pyrones, desmethoxyyangonin and (+/-)-methysticin displayed a competitive inhibition pattern with mean Ki 0.28 microM and 1.14 microM respectively. The inhibition of MAO-B by kava pyrone-enriched extracts might be an important mechanism for their psychotropic activity.

Role of inositol in the treatment of psychiatric disorders. Basic and clinical aspects

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CNS Drugs (New Zealand) 1997, 7/1 (6-16)

Myo-inositol is a ubiquitous carbohydrate that is present in large amounts in brain tissue and is involved in neuronal signalling and osmoregulation. This sugar is an essential component of the inositol signalling system, which is a postreceptor second messenger signalling system found in many cells. Myo-inositol is the precursor of membrane inositol phospholipids, which are critically linked to a number of CNS receptor signalling systems, including muscarinic, serotonergic, adrenergic, metabotropic and histaminergic systems, and those linked to cholecystokinin, tachykinins, neurotensin, platelet activating factor and other transmitters. Upon stimulation of these receptors, a signal is transmitted through a guanosine triphosphate (GTP)-binding protein (G(q)), which then activates the enzyme phospholipase C. This results in the release of a second messenger, inositol 1,4,5-trisphosphate (InsP₃), from membrane inositol phospholipids. InsP₃ then causes the release of free intracellular calcium into the cytosol, activating a number of enzymes or receptors. Myo-inositol in the brain is derived from 3 sources: (i) receptor stimulation (a salvage pathway); (ii) de novo synthesis from glucose; and (iii) uptake of dietary myo-inositol through plasma membrane myo-inositol transporters. Most myo-inositol is probably derived from the first 2 sources, which are controlled through the lithium-sensitive enzyme myo-inositol monophosphatase (IMPase). This enzyme acts upon myo-inositol monophosphates, hydrolysing them to release free myo-inositol. Recent biochemical, molecular and crystallographic studies have demonstrated that the overall metabolism of brain inositol is closely modulated by this enzyme. Lithium salts, which are commonly used in various psychiatric conditions, inhibit this enzyme, and this action has been implicated as a therapeutic mechanism of action of lithium. A change in the availability of CNS inositol may lead to altered brain cell signalling pathways and, eventually, to the development of a neuropsychiatric disorder. Recent evidence indicates that myo-inositol has psychoactive effects, with initial studies demonstrating effectiveness in the treatment of depression, panic disorder and obsessive - compulsive disorder. At present, the exact mechanism of these clinical effects is uncertain. The development of various inositol system-based drugs may lead to future psychoactive drugs designed to modulate a second messenger cascade of events rather than a receptor system, and will lead to further understanding of CNS disease from a post-receptor second messenger perspective.

OBSESSIVE COMPULSIVE DISORDER

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Can hypoglycaemia cause obsessions and ruminations?

Rippere V
Med Hypotheses (England) Sep 1984, 15 (1) p3-13

Two cases of obsessional ruminations apparently secondary to functional hypoglycaemia are described. Both patients are young Caucasian males with obsessional histories at the start of dietary treatment of 18 and 6 years, respectively. In both cases, reactive hypoglycaemia was confirmed by glucose tolerance test. The first case made a complete recovery on dietary treatment which has lasted over two years; previous treatment with drugs, behaviour therapy, and counselling were unsuccessful. The response of the second case has been less outstanding due to poor compliance, but improvement and worsening have been systematically related to the extent of his adherence to the suggested dietary regimen. These cases raise questions for further research on this neglected subgroup of obsessional patients.

Dietary treatment of chronic obsessional ruminations.

Rippere V
Br J Clin Psychol (England) Nov 1983, 22 (Pt 4) p314-6

Chronic obsessional ruminations may prove resistant to psychological treatment because they are not psychological in nature but epiphenomena of brain dysfunction secondary to nutritional factors. The case is described of a chronic, treatment-resistant ruminator who made a dramatic and lasting recovery when a high protein breakfast was added to his elimination diet regimen, undertaken when years of psychological and pharmacological treatment had failed. Biochemical and clinical evidence supports the hypothesis that hypoglycaemia secondary to inappropriate diet was the cause of his disorder. Dietary contributions to obsessional ruminations should probably be sought early on in the assessment of such patients.

Sequential administration of augmentation strategies in treatment-resistant obsessive-compulsive

disorder: preliminary findings.

Blier P; Bergeron R

Neurobiological Psychiatry Unit, McGill University, Montreal, Quebec, Canada.

Int Clin Psychopharmacol (England) Mar 1996, 11 (1) p37-44

Given that an important proportion of patients with obsessive-compulsive disorder (OCD) fail to respond adequately to serotonin (5-HT) reuptake inhibitors (SRI), augmentation strategies aimed at enhancing further 5-HT transmission by different mechanisms were attempted sequentially in 13 SRI-resistant patients. Addition of the 5-HT_{1A} beta-adrenergic antagonist pindolol did not alter OCD symptomatology but produced a rapid improvement of depressive symptoms. The 5-HT_{1A} agonist buspirone as well as 5-hydroxytryptophan, the immediate precursor of 5-HT, added to the SRI-pindolol regimen, were not effective in attenuating the intensity of OCD. Tryptophan, added to the SRI-pindolol regimen, produced a significant improvement after 4 weeks, with further amelioration after 6 weeks (36% decrease of the Yale-Brown Obsessive Compulsive Score), which was maintained with treatment prolongation.

Plasma melatonin and cortisol circadian patterns in patients with obsessive-compulsive disorder before and after fluoxetine treatment.

Monteleone P; Catapano F; Tortorella A; Di Martino S; Maj M

Institute of Psychiatry, Second University of Naples, Italy.

Psychoneuroendocrinology (England) 1995, 20 (7) p763-70

The circadian rhythms of melatonin and cortisol were evaluated in seven outpatients with obsessive-compulsive disorder (OCD) before and after 8 weeks of fluoxetine treatment (20 mg/day in the first 2 weeks, and 40 mg/day afterwards), and in seven healthy subjects matched to patients on age, sex and season of testing. The results confirm our previous findings of a decreased 24-h production of melatonin ($p < .05$; two-way ANOVA with repeated measures) and of an increased circadian secretion of cortisol ($p < .01$) in OCD patients with respect to matched controls, and show, for the first time, that these hormonal alterations do not significantly change after 2 months of fluoxetine administration, in spite of a good clinical improvement. These data suggest that the normalization of the biochemical changes underlying the altered endocrine parameters in obsessive-compulsive patients is not necessary for effective therapy or clinical remission.

Neuroendocrine responses to intravenous L-tryptophan in obsessive compulsive disorder.

Fineberg NA; Cowen PJ; Kirk JW; Montgomery SA

Academic Department of Psychiatry, St Mary's Hospital, London, UK.

J Affect Disord (Netherlands) Oct 1994, 32 (2) p97-104

We studied the neuroendocrine responses produced by intravenous L-tryptophan (TRP) in 16 untreated patients with obsessive compulsive disorder (OCD) and 16 matched healthy controls. The increase in plasma growth hormone seen following TRP was significantly greater in the OCD patients, while TRP-induced prolactin release did not differ from controls. Taken in conjunction with findings from other neuroendocrine studies the data suggest that some aspects of 5-HT_{1A} neurotransmission may be increased in OCD. This increase may represent a compensatory change which promotes adaptation to stress in non-depressed OCD patients.

Tryptophan depletion in patients with obsessive-compulsive disorder who respond to serotonin reuptake inhibitors.

Barr LC; Goodman WK; McDougle CJ; Delgado PL; Heninger GR; Charney DS; Price LH

Clinical Neuroscience Research Unit, Abraham Ribicoff Research Facilities, Connecticut Mental Health Center, New Haven.

Arch Gen Psychiatry (United States) Apr 1994, 51 (4) p309-17

METHODS: The effects of short-term tryptophan depletion were examined in 15 patients with DSM-III-R obsessive-compulsive disorder who had demonstrated symptom reduction following treatment with serotonin reuptake inhibitors. Patients received a 24-hour, low-tryptophan (160-mg/d) diet followed the next morning by a drink of 15 amino acids. A double-blind, placebo-controlled cross-over design was used.

RESULTS: The diet and the amino acid drink reduced free plasma tryptophan levels by a mean of 84% 5 hours later. Short-term tryptophan depletion did not significantly change mean ratings of obsessions and compulsions. In contrast, mean depression ratings were significantly increased with tryptophan depletion compared with the control (tryptophan-supplemented) testing.

CONCLUSION: Maintenance of serotonin reuptake inhibitor-induced improvement of obsessive and compulsive symptoms, unlike remission of depressive symptoms, may not depend on ongoing short-term availability of serotonin.

Circadian rhythms of melatonin, cortisol and prolactin in patients with obsessive-compulsive disorder.

Monteleone P; Catapano F; Del Buono G; Maj M
Institute of Psychiatry, First Medical School, University of Naples, Italy.
Acta Psychiatr Scand (Denmark) Jun 1994, 89 (6) p411-5

Plasma melatonin, cortisol and prolactin (PRL) levels were measured over a 24-h period in 13 drug-free patients with obsessive-compulsive disorder and in matched healthy subjects. The circadian profiles of melatonin and PRL were altered in patients; the circadian rhythm of cortisol was preserved, although at a higher level compared with normal controls. These changes were significantly related to the severity of the obsessive-compulsive symptoms. Further studies need to clarify the state- or trait-dependent character of these abnormalities.

Biological approaches to treatment-resistant obsessive compulsive disorder.

Goodman WK; McDougle CJ; Barr LC; Aronson SC; Price LH
Yale University School of Medicine, Department of Psychiatry, New Haven, CT 06519.
J Clin Psychiatry (United States) Jun 1993, 54 Suppl p16-26

Biological approaches to the patient with treatment-resistant obsessive compulsive disorder are briefly reviewed. The most commonly employed strategy involves combining a potent serotonin reuptake inhibitor (SRI) (e.g., clomipramine or fluvoxamine) with another medication that may exert effects on the brain serotonin system. Open-label reports regarding the addition of tryptophan, fenfluramine, lithium, or buspirone to ongoing SRI therapy of obsessive compulsive disorder are encouraging. However, the anti-obsessive compulsive efficacy of SRI-lithium and SRI-buspirone combination therapy has not been confirmed in recent controlled trials. Preliminary evidence suggests that addition of neuroleptic may benefit SRI-refractory obsessive compulsive disorder patients who have a comorbid chronic tic disorder. Other biological approaches (e.g., electroconvulsive therapy and psychosurgery) are considered in terms of their narrowly defined roles in the treatment of patients with SRI-resistant obsessive compulsive disorder. Finally, an algorithm is proposed for those patients with obsessive compulsive disorder who fail to respond to an adequate trial with a potent SRI. (115 Refs.)

Pharmacotherapy of obsessive compulsive disorder.

Goodman WK; McDougle CJ; Price LH
Clinical Neuroscience Research Unit, Yale University School of Medicine, New Haven, CT 06519.
J Clin Psychiatry (United States) Apr 1992, 53 Suppl p29-37

The authors briefly review studies of the efficacy of potent serotonin reuptake inhibitors (SRIs) (e.g., clomipramine, fluvoxamine) in obsessive compulsive disorder (OCD) and compare the use of antidepressants in the treatment of depression and OCD. They propose an algorithm for those patients with OCD who fail to respond to an adequate trial with a potent SRI and discuss the promise and limitations of adding tryptophan, fenfluramine, lithium, buspirone, or a neuroleptic to ongoing SRI therapy. Other biological approaches (e.g., ECT, psychosurgery) are considered in terms of their narrowly defined roles in the treatment of patients with SRI-resistant OCD. (68 Refs.)

Plasma tryptophan levels and plasma tryptophan/neutral amino acids ratio in patients with mood

disorder, patients with obsessive- compulsive disorder, and normal subjects.

Lucca A; Lucini V; Piatti E; Ronchi P; Smeraldi E

Istituto di Ricovero e Cura a carattere scientifico H. San Raffaele, Department of Neuropsychiatric Sciences, University of Milan, School of Medicine, Italy.

Psychiatry Res (Ireland) Nov 1992, 44 (2) p85-91

Fasting plasma tryptophan (TRP) levels and ratios of total plasma tryptophan to the sum of five large neutral amino acids (LNAA)--tyrosine, phenylalanine, leucine, isoleucine, and valine--that compete with tryptophan for passage across the blood-brain barrier were found to be significantly lower in a group of 28 patients with major depression compared with 29 normal subjects and 21 patients with obsessive-compulsive disorder (OCD). The OCD group was divided in two subgroups: patients with OCD alone and patients with a co-diagnosis of major depression. Since it has been considered that these biological parameters reflect brain tryptophan and serotonin levels, our results suggest their importance in relation to the presence or absence of depressive symptoms. The values of the other LNAA and their sum did not differ significantly among the groups.

Melatonin and cortisol secretion in patients with primary obsessive-compulsive disorder.

Catapano F; Monteleone P; Fuschino A; Maj M; Kemali D

Institute of Psychiatry, First Medical School, University of Naples, Italy.

Psychiatry Res (Ireland) Dec 1992, 44 (3) p217-25

Plasma levels of melatonin and cortisol were measured over a 24-hour period in seven patients with primary obsessive-compulsive disorder (OCD) and seven matched healthy control subjects. In OCD patients, the 24-hour secretion of melatonin was reduced as compared with that in healthy control subjects, whereas its circadian rhythm was preserved. In addition, in OCD patients, the overall secretion of cortisol was higher than that in control subjects, but there was no change in the circadian pattern of cortisol secretion. No correlation was found between clinical parameters and hormone levels.

Role of serotonin in obsessive- compulsive disorder.

Baumgarten HG; Grozdanovic Z

Institute of Anatomy, University Clinic Benjamin Franklin, Free University of Berlin, Germany.

Br J Psychiatry Suppl (England) 1998, (35) p13-20

BACKGROUND: Serotonin may play a role in the pathophysiology of obsessive-compulsive disorder (OCD) because of the anti-obsessional effect of selective serotonin reuptake inhibitors (SSRIs).

METHOD: The literature is reviewed on knowledge of the role of serotonergic neurons in brain function, studies on monoamine metabolites in cerebrospinal fluid (CSF), various stress neuropeptides, neuroendocrine and behavioural challenge after administration of direct and indirect serotomimetic compounds, and neuroanatomical data on brain circuits organising behaviour.

RESULTS: In most of the OCD cases analysed, CSF 5-hydroxyindoleacetic acid and homovanillic acid concentrations do not significantly differ from age-corrected controls. However, a relationship appears to exist between pre-treatment levels of these metabolites and clinical response to drugs acting on the serotonin transporter. Abnormalities in CSF arginine vasopressin, corticotropin-releasing hormone, oxytocin and somatostatin levels have been reported in OCD. Long-term treatment with high-doses of clomipramine, fluvoxamine, and fluoxetine tend to correct these neuropeptide abnormalities.

CONCLUSIONS: We hypothesise that continuous treatment with SSRIs alters serotonin turnover and neuropeptide expression patterns in OCD-entertaining functional forebrain/midbrain circuits.

Psychiatric manifestations of homocystinuria due to cystathionine beta-synthase deficiency: prevalence, natural history, and relationship to neurologic impairment and vitamin B6-responsiveness.

Abbott MH; Folstein SE; Abbey H; Pyeritz RE

Homocystinuria commonly affects the central nervous system (CNS), primarily as mental retardation, seizures, and stroke. Case reports have long suggested a predisposition to schizophrenia, but no careful study of predisposition to psychiatric illness has been performed. Accordingly, we evaluated 63 persons with homocystinuria due to cystathionine beta-synthase deficiency for psychiatric disturbance, intelligence, evidence of other CNS problems, and responsiveness to vitamin B6. The overall rate of clinically significant psychiatric disorders was 51%, predominated by four diagnostic categories: episodic depression (10%), chronic disorders of behavior (17%), chronic obsessive - compulsive disorder (5%), and personality disorders (19%). The average IQ was 80 +/- 27 (1 SD); and an IQ of less than or equal to 79 was two-thirds more common among vitamin B6-nonresponsive patients compared to vitamin B6-responsive patients. Aggressive behavior and other disorders of conduct were particularly common among patients with mental retardation and among vitamin B6-nonresponsive patients.

Alphainf 2-adrenoreceptor status in obsessive- compulsive disorder

Lee M.A.; Cameron O.G.; Gurguis G.N.M.; Glitz D.; Smith C.B.; Hariharan M.; Abelson J.L.; Curtis G.C.
Cleveland VA Med Ctr, Psychiatry Service, 10000 Brecksville Road, Brecksville, OH 44141 US
Biological Psychiatry (United States) 1990, 27/10 (1083-1093)

Ten patients with obsessive -compulsive disorder (OCD) and 13 normal control subjects received intravenous infusions of 2 x 10^{sup} -sup 6 g/kg of clonidine and normal saline on separate days. Responses to the drug relating to plasma growth hormone (GH), 3-methoxy-4-hydroxyphenylglycol (MHPG), heart rate, blood pressure, and several symptoms were determined. Additionally, platelet alphainf 2-adrenoreceptor binding was measured in most of the subjects. GH, MHPG, blood pressure, and heart rate responses to clonidine did not differ between groups. As expected, patients reported more symptoms than normal subjects, and clonidine was sedating for both groups. Patients did not differ from normal subjects in the symptom response to clonidine. The maximum number of binding sites (B(max)) for tritiated clonidine was significantly greater in OCD patients than in normals. This pattern of alphainf 2-adrenoreceptor status is different than the patterns in major depression and panic anxiety.

Vitamin Binf 1inf 2 and folic acid serum levels in obsessive compulsive disorder

Hermesh H.; Weizman A.; Shahar A.; Munitz H.
Geha Psychiatric Hospital, Beilinson Medical Center, 49 100 Petah Tiqva Israel
Acta Psychiatrica Scandinavica (Denmark) 1988, 78/1 (8-10)

Vitamin Binf 1inf 2 and folate serum levels were studied in 30 patients with obsessive compulsive disorder (OCD), and in two control groups comprised of 30 chronic schizophrenics and 30 normal healthy subjects. Six patients (20%) of the OCD group had abnormal low levels of vitamin Binf 1inf 2. This prevalence was significantly higher than that of the control groups. No clinical neurological or haematological abnormalities accompanied the reduced vitamin Binf 1inf 2 levels. Possible implication of this finding for the pathophysiology of OCD in a subgroup of patients and the possibility that the Binf 1inf 2 deficiency could be the consequence rather than the cause of OCD are suggested.

Controlled trials of inositol in psychiatry.

Levine J
Ministry of Health Mental Health Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beersheva, Israel.
Eur Neuropsychopharmacol (Netherlands) May 1997, 7 (2) p147-55

Inositol is a simple polyol precursor in a second messenger system important in the brain. Cerebrospinal fluid inositol has been reported as decreased in depression. A double-blind controlled trial of 12 g daily of inositol in 28 depressed patients for four weeks was performed. Significant overall benefit for inositol compared to placebo was found at week 4 on the Hamilton Depression Scale. No changes were noted in hematology, kidney or liver function. Since many antidepressants are effective in panic disorder, twenty-one patients with panic disorder with or without agoraphobia completed a double-blind, placebo-controlled, four week, random-assignment crossover treatment trial of inositol 12 g per day. Frequency and severity of panic attacks and severity of agoraphobia declined significantly with inositol compared to placebo. Side-effects were minimal. Since serotonin re-uptake inhibitors benefit obsessive compulsive disorder (OCD) and inositol is reported to reverse desensitization of serotonin receptors, thirteen patients with OCD completed a double-blind controlled crossover trial of 18 g inositol or placebo for six weeks each. Inositol significantly

reduced scores of OCD symptoms compared with placebo. A controlled double-blind crossover trial of 12 g daily of inositol for a month in twelve anergic schizophrenic patients, did not show any beneficial effects. A double-blind controlled crossover trial of 6 g of inositol daily vs. glucose for one month each was carried out in eleven Alzheimer patients, with no clearly significant therapeutic effects. Antidepressant drugs have been reported to improve attention deficit disorder (ADDH) with hyperactivity symptomatology. We studied oral inositol in children with ADDH in a double-blind, crossover, placebo-controlled manner. Eleven children, mean age 8.9 +/- 3.6 years were enrolled in an eight week trial of inositol or placebo at a dose of 200 mg/kg body weight. Results show a trend for aggravation of the syndrome with myo-inositol as compared to placebo. Recent studies suggest that serotonin re-uptake inhibitors are helpful in at least some symptoms of autism. However a controlled double-blind crossover trial of inositol 200 mg/kg per day showed no benefit in nine children with autism. Cholinergic agonists have been reported to ameliorate electroconvulsive therapy (ECT)-induced memory impairment. Inositol metabolism is involved in the second messenger system for several muscarinic cholinergic receptors. Inositol 6 g daily was given in a crossover-double-blind manner for five days before the fifth or sixth ECT to a series of twelve patients, without effect. These results suggest that inositol has therapeutic effects in the spectrum of illness responsive to serotonin selective re-uptake inhibitors, including depression, panic and OCD, and is not beneficial in schizophrenia, Alzheimer's ADDH, autism or ECT-induced cognitive impairment.

Inositol treatment of obsessive- compulsive disorder.

Fux M; Levine J; Aviv A; Belmaker RH

Ministry of Health Mental Health Center, Faculty of Health Sciences, Ben Gurion University of the Negev, Beersheva, Israel.

Am J Psychiatry (United States) Sep 1996, 153 (9) p1219-21

OBJECTIVE: Earlier studies reported that inositol, a simple polyol second messenger precursor, was effective in controlled trials for patients with depression and panic. In this study its effectiveness in obsessive - compulsive disorder was investigated.

METHOD: Thirteen patients with obsessive - compulsive disorder completed a double-blind, controlled crossover trial of 18 g/day of inositol or placebo for 6 weeks each.

RESULTS: The subjects had significantly lower scores on the Yale-Brown Obsessive Compulsive Scale when taking inositol than when taking placebo.

CONCLUSIONS: The authors conclude that inositol is effective in depression, panic, and obsessive -compulsive disorder, a spectrum of disorders responsive to selective serotonin reuptake inhibitors.

Role of inositol in the treatment of psychiatric disorders. Basic and clinical aspects

Vadnal R.; Parthasarathy L.; Parthasarathy R.

Dr. R. Vadnal, Mental Hlth./Behavioural Scis. Serv., VA Medical Center, 800 Zorn Avenue, Louisville, KY 40206 United States

CNS Drugs (New Zealand) 1997, 7/1 (6-16)

Myo-inositol is a ubiquitous carbohydrate that is present in large amounts in brain tissue and is involved in neuronal signalling and osmoregulation. This sugar is an essential component of the inositol signalling system, which is a postreceptor second messenger signalling system found in many cells. Myo-inositol is the precursor of membrane inositol phospholipids, which are critically linked to a number of CNS receptor signalling systems, including muscarinic, serotonergic, adrenergic, metabotropic and histaminergic systems, and those linked to cholecystokinin, tachykinins, neurotensin, platelet activating factor and other transmitters. Upon stimulation of these receptors, a signal is transmitted through a guanosine triphosphate (GTP)-binding protein (G(q)), which then activates the enzyme phospholipase C. This results in the release of a second messenger, inositol 1,4,5-trisphosphate (InsP₃), from membrane inositol phospholipids. InsP₃ then causes the release of free intracellular calcium into the cytosol, activating a number of enzymes or receptors. Myo-inositol in the brain is derived from 3 sources: (i) receptor stimulation (a salvage pathway); (ii) de novo synthesis from glucose; and (iii) uptake of dietary myo-inositol through plasma membrane myo-inositol transporters. Most myo-inositol is probably derived from the first 2 sources, which are controlled through the lithium-sensitive enzyme myo-inositol monophosphatase (IMPase). This enzyme acts upon myo-inositol monophosphates, hydrolysing them to release free myo-inositol. Recent biochemical, molecular and crystallographic studies have demonstrated that the overall metabolism of brain inositol is closely modulated by this enzyme. Lithium salts, which are commonly used in various psychiatric conditions, inhibit this enzyme, and this action has been implicated as a therapeutic mechanism of action of lithium. A change in the availability of CNS inositol may lead to altered brain cell signalling pathways and, eventually, to the development of a neuropsychiatric disorder. Recent evidence indicates that myo-inositol has psychoactive effects, with initial studies demonstrating effectiveness in the treatment of depression, panic disorder and obsessive - compulsive disorder. At present, the exact mechanism of these clinical

effects is uncertain. The development of various inositol system-based drugs may lead to future psychoactive drugs designed to modulate a second messenger cascade of events rather than a receptor system, and will lead to further understanding of CNS disease from a post-receptor second messenger perspective.

Lithium and tryptophan augmentation in clomipramine-resistant obsessive- compulsive disorder.

Rasmussen SA
Am J Psychiatry (United States) Oct 1984, 141 (10) p1283-5

Obsessive -compulsive patients with symptoms resistant to clomipramine were treated by lithium or L -tryptophan augmentation. The improvement noted supports the hypothesis that increasing serotonergic neurotransmission ameliorates obsessive symptoms.

Vitamin B12 and folic acid serum levels in obsessive compulsive disorder.

Hermesh H; Weizman A; Shahar A; Munitz H
Geha Psychiatric Hosp, Beilinson Medical Ctr, Sackler School of Medicine, Tel Aviv Univ, Israel.
Acta Psychiatr Scand (Denmark) Jul 1988, 78 (1) p8-10

Vitamin B12 and folate serum levels were studied in 30 patients with obsessive compulsive disorder (OCD), and in two control groups comprised of 30 chronic schizophrenics and 30 normal healthy subjects. Six patients (20%) of the OCD group had abnormal low levels of vitamin B12. This prevalence was significantly higher than that of the control groups. No clinical neurological or haematological abnormalities accompanied the reduced vitamin B12 levels. Possible implication of this finding for the pathophysiology of OCD in a subgroup of patients and the possibility that the B12 deficiency could be the consequence rather than the cause of OCD are suggested.

Obsessive compulsive disorder arising in a 75-year-old woman

Bajulaiye R.; Addonizio G.
New York Hospital-Cornell Medical Center, Westchester Division, 21Bloomingdale Road, White Plains, NY 10605 United States
International Journal of Geriatric Psychiatry (United Kingdom) 1992, 7/2 (139-142)

Presented is the case of a 75-year-old woman with obsessive compulsive disorder with an unusual age of onset at age 72 years. The patient was resistant to various treatments, but responded to lithium augmentation of fluoxetine.

Lithium augments fluoxetine treatment of obsessive compulsive disorder

Ruegg R.G.; Evans D.L.; Comer W.S.; Golden R.N.
Psychiatry Dept, University of North Carolina School of Medicine, Chapel Hill, NC 27599-7160 US
Lithium (United Kingdom) 1992, 3/1 (69-71)

Fluoxetine is a potent serotonin uptake inhibitor effective in the treatment of obsessive compulsive disorder (OCD). However, clinical response is often partial. Lithium carbonate (Li) has been used to potentiate clomipramine and doxepine treatment of OCD. We report our experience using Li to augment fluoxetine in four OCD patients

WS 1490 (kava extract) in the treatment of anxiety neurosis

Hahn G.
Engelstrasse 18,W-8520 Erlangen Germany
Fortschritte der Medizin (Germany) 1992, 110/9 (86)

No abstract.

Inhibition of platelet MAO-B by kava pyrone-enriched extract from *Piper methysticum* Forster (kava-kava).

Uebelhack R, Franke L, Schewe HJ

Department of Psychiatry, Humboldt-Universität zu Berlin (Charité), Germany.

Pharmacopsychiatry 1998 Sep;31(5):187-92

Kava-kava, a psychoactive beverage, induces relaxation, improves social interaction, promotes sleep and plays an important role in the sociocultural life in the islands of the South Pacific. On the other hand, standardized extracts of kava-kava roots are used for the therapy of anxiety, tension and restlessness. Kava pyrones, the major constituents of kava kava, are generally considered to be responsible for the pharmacological activity in humans and animals. To obtain more information on the mechanisms by which kava-kava exerts psychotropic properties we investigated the in vitro effects of kava-kava extract and pure synthetic kava pyrones on human platelet MAO-B, in comparison to amitriptyline, imipramine and brofaromine. Kava-kava extract was found to be a reversible inhibitor of MAO-B in intact platelets (IC₅₀ 24 µM) and disrupted platelet homogenates (IC₅₀ 1.2 µM). Structural differences of kava pyrones resulted in a different potency of MAO-B inhibition. The order of potency was desmethoxyyangonin > (+/-)-methysticin > yangonin > (+/-)-dihydromethysticin > (+/-)- dihydrokavain > (+/-)-kavain. The two most potent kava pyrones, desmethoxyyangonin and (+/-)-methysticin displayed a competitive inhibition pattern with mean K_i 0.28 µM and 1.14 µM respectively. The inhibition of MAO-B by kava pyrone-enriched extracts might be an important mechanism for their psychotropic activity.

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