

Alternative and Complementary Treatments for Extrapyrarnidal Symptoms, Schizophrenia, and Bipolar Disorder:

List of References with Conclusions or Highlights

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Introduction: The references listed contain conclusions or highlights of select articles on natural treatments and alternatives that have been queried and reviewed out of a PubMed search of over 355,000 titles. Most are complementary clinical trials with the alternative therapies used in conjunction with antipsychotic medication or mood stabilizers. This is not just a valuable resource for those currently using psychotropic drugs and wish to improve clinical outcome, it is a valuable resource for those seeking clinical efficacy of alternative treatments for schizophrenia and bipolar disorder that choose to not to use psychiatric drugs. This resource is also useful for those who are forced used psychiatric drugs, and are aware of iatrogenic harm, and are interested in methods in reducing harm, or treating dyskinesia's, dystonia, akathisia, atypical antipsychotic-induced weight gain, treating dopaminergic supersensitivity. All these conditions mentioned may be treated with by natural remedies and other alternatives methods. There are also neuroprotective treatments that can be found in current psychiatric and medical scientific literature, including treatment to reverse structural atrophy of the brain, and help reduce the oxidative damages of neuroleptic drugs. There are also references to Ayurvedic medicine, Kampo medicine, and Chinese medicine as well as alternative medicine used in the Western world such as Orthomolecular medicine. Other non-invasive therapies such as neurofeedback, biofeedback, dark therapy, and sound therapy, etc. have been included. These are some of the many alternative and natural treatments that improve the outcome of schizophrenia and bipolar disorder that have been validated by scientific literature. All these and more are included in this document.

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Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Alternative and Complementary Treatments for Extrapyramidal Symptoms

Natural Treatments for Tardive Dyskinesia in Humans

Growdon JH. Lecithin can suppress tardive dyskinesia. *New England Journal of Medicine*, Vol 298, No. 18 pp1029, May 1978

- *"The mean number of movements decreased in all patients during lecithin ingestion (Table 1), and serum choline levels rose from a mean \pm S.D. of 10.0 \pm 2.2 to 22.8 \pm 5.1 nmol per milliliter ($P < 0.01$). Lecithin was as effective as choline chloride: the number of buccal-lingual-masticatory movements decreased as they had during choline administration. In addition, lecithin may be more acceptable to patients, since it does not have a bitter taste of fishy body odor as associated with choline ingestion. These data suggest that lecithin may constitute an effective mode of neurotransmitter precursor therapy for conditions in which physicians wish to increase cholinergic tone."*

Growdon JH. Oral choline administration to patients with tardive dyskinesia. *New England Journal of Medicine*, Vol 297, No.10, pp524-527, September 1977

- *"Twenty patients with stable buccal-lingual-masticatory movements took oral doses of choline for two weeks according to a double-blind crossover protocol. Plasma choline levels rose from 12.4 \pm 1.0 to 33.5 \pm 2.5 nmol per milliliter (mean \pm S.E.M.; $P < 0.001$) during this period. Choreic movements decreased in nine patients, worsened in one and were unchanged in 10. Thus, oral doses of choline can be useful in neurologic diseases in which an increase in acetylcholine release is desired."*

Lerner V. Vitamin B6 treatment for tardive dyskinesia: a randomized, double-blind, placebo-controlled, crossover study. *J Clin Psychiatry* 2007 Nov;68(11):1648-54

- *"Vitamin B6 appears to be effective in reducing symptoms of TD."*

Zhang WF. Extract of ginko biloba treatment for tardive dyskinesia in schizophrenia: a randomized, double-blind, placebo-controlled trial. J Clin Psychiatry 2011 May;72(5):615-21

- *“EGb-761 appears to be an effective treatment for reducing the symptoms of TD in schizophrenia patient*

Miyaoka T. Yi-gan san for the treatment of neuroleptic-induced tardive dyskinesia: an open-label study. Prog Neuropsychopharmacol Biol Psychiatry 2008 Apr 1; 32(3):781-4

- *“Administration of YGS resulted in a statistically significant improvement in tardive dyskinesia and psychotic symptoms”*

Barcelos R. Effects of w-3 essential fatty acids (w-3 EFAs) on motor disorders and memory dysfunction typical neuroleptic-induced: Behavioral and biochemical parameter. Neurotox Res, 2009

- *“The FO (fish oil) decreased the motor disorders, memory dysfunction, and oxidative damage typical neuroleptic-induced”*

Krishna Vaddadi, Dyskinesia’s and their treatment with essential fatty acids: a review. Prostaglandins, Leukotrienes and Essential Fatty Acids (1996) 55(1&2), 89-94

- *“Clinical improvement in HD (Huntington’s Disease) with LA and GLA supplementation is a novel finding....” It has been suggested that in individuals at early stages of HD, or in individuals at risk of developing HD, if given EFA’s probably of both n-6 and n-3 series on long term basis might delay the onset of HD.”*

Shamir E, Melatonin treatment for tardive dyskinesia. Arch Gen Psychiatry. 2001;58:1049-1052

- *“In conclusion, the results of the present study demonstrate that melatonin treatment is beneficial for antipsychotic-induced TD.”*

Nikolaus M, Severe tardive dyskinesia in affective disorders: Treatment with Vitamin E and C. Neuropsychobiology 2002;46(suppl 1):28-30

- *“...Combining vitamin E with C was a safe and efficacious in the treatment of tardive dyskinesia in affective disorder.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Lee JG. Clinical effectiveness of the Kampo medicine kamisoyosan for adjunctive treatment of tardive dyskinesia in patients with schizophrenia: a 16 week open trial. *Psychiatry Clin Neurosci* 2007 Oct;61(5):509-14

- *"A meaningful reduction in total abnormal involuntary movement scale scores was observed in the tardive dyskinesia group"*

Vaddadi KS. A double-blind trial of essential fatty acid supplementation in patients with tardive dyskinesia. *Psychiatry Res* 1989 Mar;27(3): 313-23

- *"The antidyskinetic effect of EPA supplementation was marginally significant but not clinically important. However, active treatment produced significant improvements in total psychopathology scores and schizophrenia subscales scores, and significant improvement in memory."*

Natural Substances Used in Tardive Dyskinesia in Animals

Thaakur S, Effect of alpha lipoic acid on the tardive dyskinesia and oxidative stress induced by haloperidol in rats. *J Neural Transm* (2009) 116;807-814

- *"In conclusion, ALA improves TD and catalepsy by scavenging hydroxyl radicals, singlet oxygen hypochlorous acid, and regenerating other antioxidants such as glutathione, vitamin C, ubiquinol (coenzyme Q 10) an indirectly vitamin E...."*

Bhattacharya S. Effect of Embilica officinallis tannoids on a rat model of tardive dyskinesia. *Indian J of Experimental Biology*, Vol. 38, September 2000, pp. 945-947

- *"The results suggest that EOT exerts a prophylactic effect against neuroleptic-induced TD....."*

Thaakur SR. Effects of spirulina maxima on haloperidol induced tardive dyskinesia and oxidative stress in rats. *J Neural Transm* 2007 Sep;114(9):1217-25

- *"Spirulina suppletion at a dose of 180mg/kg significantly improved enzymatic and nonenzymatic antioxidants and decreased tardive dyskinesia induced by haloperidol. In conclusion the results of the present investigation suggest that spirulina decreases haloperidol induced oxidative stress and TD by many mechanisms as it is a cocktail of antioxidants."*

Bhattacharya SK. Effect of *Withania sominifera* glycowithanolides on rat model of tardive dyskinesia. *Phytomedicine* 2002 Mar;9(2):167-70

- *“The results indicate the reported antioxidant effect of WSG rather than its GABA-mimetic action, may be responsible for the prevention of haloperidol-induced TD.”*

Selvakumar GP. Morin attenuates Haloperidol induced tardive dyskinesia and oxidative stress in mice. *Journal of Natural Sciences Research* Vol.2, No.8, 2012

- *“ These results indicate that morin have beneficial role in mitigating HP-induced damage of dopaminergic neurons, possibly via its neuroprotective and its antioxidant potential.”*

Chiropractic Management of Musculoskeletal Pain Secondary to Tardive Dyskinesia

Schoonderwoerd K. Chiropractic management of musculoskeletal pain secondary to tardive dyskinesia. *J Can Chiropr Assoc* 2005; 49(2)

- *“A case report is presented of a patient affected by TD who suffered mechanical musculoskeletal pain secondary to its effects, and was managed by chiropractic care.”*

Natural Treatments of Oral Dyskinesia's in Humans and Animals

Naidu P. Reversal of reserpine-induced orofacial dyskinesia and cognitive dysfunction by quercetin. *Pharmacology* 2004;70:59-67

- *“In conclusion, the results of the present study clearly indicated that quercetin has a protective role against reserpine-induced orofacial dyskinesia and associated cognitive dysfunction. Consequently, quercetin could be considered as a potential therapeutic agent for the treatment of TD.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Colpo G. Ilex paraguariensis has antioxidant potential and attenuates Haloperidol-induced orofacial dyskinesia and memory dysfunction in rats. Neurotoxicity Research, 2007, Vol. 12(3), pp.171-180

- *“Rats treated with “mate” did not exhibit an increase in vacuous chewing movements observed in rats treated with haloperidol.” The “mate” prevented the effects of haloperidol in this behavioral paradigm.”*

Naidu P. Effect of Withania somnifera root extract on Haloperidol-induced orofacial dyskinesia: Possible mechanism of action. Journal of Medicinal Food, Vol. 6, No. 2, 2003

- *“These findings strongly suggest that oxidative stress plays a significant role in HP-induced orofacial dyskinesia and that Ws could be effective in preventing neuroleptic-induced extrapyramidal side effects.”*

Bishnoi M. Protective effect of Curcumin, the active principle of turmeric (Curcuma longa) in haloperidol-induced orofacial dyskinesia and associated behavioral, biochemical and neurochemical changes in rat brain. Pharmacol Biochem Behav. 2008 Feb;88(4):511-22

- *“In present study, curcumin was able to reverse the behavioral, biochemical and neurochemical changes caused by exposure to haloperidol possibly by virtue of its antioxidant effect....”*

Nade V. S. Effect of Hibiscus rosa sinensis on reserpine-induced neurobehavioral and biochemical alterations in rats. Indian Journal of Experimental Biology, Vol. 47, July 2009, pp. 559-563

- *“The results from the presents study suggested Hibiscus rosa sinensis had a protective role against reserpine-induced orofacial dyskinesia and oxidative stress.”*

Naidu P. Possible mechanism of action in melatonin attenuation of haloperidol-induced orofacial dyskinesia. Pharmacology, Biochemistry and Behavior 74(2003) 641-648

- *“In conclusion, melatonin could be screened as a potential drug candidate for the prevention or treatment of neuroleptic-induced orofacial dyskinesia”*

Bishnoi M. Protective effect of rutin, a polyphenolic flavonoid against haloperidol-induced orofacial dyskinesia and associated behavioral, biochemical and neurochemical changes. *Fundamental and Clinical Pharmacology* 21(2007) 521-529

- *“The findings of the present study suggested the involvement of free radicals in the development of neuroleptic-induced orofacial dyskinesia, a putative model of TD, and rutin as a possible therapeutic option to treat this hyperkinetic movement disorder.”*

Macedo DS. B vitamins attenuate haloperidol-induced orofacial dyskinesia in rats: possible involvement of antioxidant mechanisms. *Behav Pharmacol* 2011 Oct;(7):674-80

- *“All groups treated with B vitamins presented a decrease in lipid peroxide formation. The data suggest a promising role for B vitamins in the prevention of OD.”*

Maxia A. Ethanolic extract of *Rubia pergrina* L. (Rubiaceae) inhibits haloperidol-induced catalepsy and reserpine-induced orofacial dyskinesia. *Nat Prod Res* 2012;26(5):438-45

- *“The extract of R. peregrine intraperitoneally significantly inhibited haloperidol-induced catalepsy in mice. In rats, the extract significantly inhibited orofacial dyskinesia induced by reserpine.”*

Sanghavi CR. Korean ginseng extract attenuates reserpine-induced orofacial dyskinesia and improves cognitive dysfunction in rats. *Nat Prod Res* 2011 Apr;25(7):704-15

- *“The present study concludes that oxidative stress might play an important role in reserpine-induced abnormal oral movements and Korean ginseng extract could be useful in the treatment of drug-induced dyskinesia and amnesia.”*

Pathan AA. *Mucuna pruriens* attenuates haloperidol-induced orofacial dyskinesia in rats. *Nat Prod Res* 2011 Apr;25(8):764-71

- *“The results of the present study suggest that MEMP by virtue of its free radical scavenging activity prevents neuroleptic-induced TD.”*

Nade VS. Protective effect of *Morbus alba* leaves on haloperidol-induced orofacial dyskinesia and oxidative stress. *Pharm Biol* 2010 Jan;48(1): 17-22

- *“The results suggest a protective effect of Morbus alba extract against haloperidol-induced orofacial dyskinesia and oxidative stress.”*

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Patil RA. Protective effect of *Rubia cordifolia* on reserpine-induced orofacial dyskinesia. *Nat Prod Res* 2011 Nov 18

- *"It is concluded that oxidative stress might play an important role in reserpine-induced abnormal oral movements and MERC significantly protected animals against reserpine-induced orofacial dyskinesia and has great potential in the treatment of neuroleptic induced orofacial dyskinesia."*

Busanello A. Resveratrol reduces vacuous chewing movements induced by acute treatment with fluphenazine. *Pharmacol Biochem Behav* 2012 Apr; 101(2):307-10

- *"Fluphenazine treatment produced VCM in 70% of rats and concomitant treatment with resveratrol decreased the prevalence to 30%, but did not modify the intensity of the VCM's. Furthermore, the fluphenazine administration reduced the locomotor and exploratory activity of animals in the open field test. Resveratrol treatment was able to protect the reduction of both parameters. Taken together, our data suggest that resveratrol could be considered a potential neuroprotective agent by reducing motor disorders induced by fluphenazine treatment."*

Patil R. Reversal of haloperidol-induced orofacial dyskinesia by *Murraya koenigii* leaves in experimental animals. *Pharm Biol* 2012 Jun;50(6):691-7

- *"The study concludes the *M. koenigii* could be screened as a potential drug for the prevention or treatment of neuroleptic-induced OD."*

Patil RA. Reversal of reserpine-induced orofacial dyskinesia and catalepsy by *Nardostchys jatamansi*. *Indian J Pharmacol* 2012 May;44(3): 340-4

- *"The study concludes that ANJ and TNJ significantly protected animals against reserpine-induced orofacial dyskinesia as well as catalepsy suggesting its potential value in the treatment of neuroleptic-induced orofacial dyskinesia and Parkinson's disease."*

Sookram C. Curcumin prevents haloperidol-induced development of abnormal orofacial movements: possible implications of Bcl-XL in its mechanism of action. *Synapse* 2011 Aug;65(8):788-94

- *"These results suggest that curcumin may be a promising treatment to prevent the development of AOFMs and further suggest some therapeutic value in the treatment of movement disorders."*

Sekiguchi K. Ameliorative effect of yokukansan on vacuous chewing movement in haloperidol-induced rat tardive dyskinesia model and involvement of the glutamatergic system. *Brain Res Bull* 2012 Dec 1;89(5-6):151-8

- *“Oral administration of YKS (0.1 and 0.5g/kg) once a day for three weeks (21 days) from the 12th week to 15th week ameliorated the haloperidol decanoate-induced increase in VCM in a dose-dependent manner.”*

Trevizol F. Comparative study between two animal models of extrapyramidal movement disorders: prevention and reversion by pecan nut shell aqueous extract. *Behav Brain Res* 2011 Aug 1;221(1):13-8

- *“Comparatively, the pecan shell AE was able to both prevent and reverse OD but only prevent catalepsy.”*

Batool F. Protective effects of aqueous fruit extract from Sea Buckthorn (*Hippophae rhamnoides* L. Spp. *Turkestanica*) on haloperidol-induced orofacial dyskinesia and neuronal alterations in the striatum. *Med Sci Monit* 2010 Aug;16(8);BR285-92

- *“Hippophae rhamnoides fruit extract has a protective role against haloperidol-induced orofacial dyskinesia. Consequently, use of Hippophae rhamnoides as a possible therapeutic agent for the treatment of tardive dyskinesia should be considered.”*

Natural Treatments for Tardive Dystonia

Dannon P. Vitamin E treatment in tardive dystonia. *Clinical Neuropharmacology*. Vol. 20, No.5, pp. 434-437

- *“We present a case of one young man with tardive dystonia secondary to neuroleptic treatment, whose condition substantially improved with treatment by 1200mg/d(IU) of vitamin E.”*

Tani M. Effect of acupuncture treatment for a patient with severe axial dystonia appearing during treatment for schizophrenia. *Selshin Shinkeigaku Zasshi* 2005;107(8):802-10

- *“It is suggested that acupuncture treatment has had a positive effect on tardive dystonia including axial dystonia. The patient also achieved improved stability with regards to symptoms of schizophrenia.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Okamoto H. Orengedoku-to augmentation in cases showing partial response to yokukan-san treatment: a case report and literature review of evidence for the use of Kampo herbal formulae. *Neuropsychiatric Disease and Treatment* 2013;9 151-155

- *“A 44-year-old male had started to use methamphetamine at the age of 20. When he was 32 years old, he began to exhibit signs of methamphetamine-induced psychotic disorder accompanied by perceptual delusions and auditory hallucinations and started to take antipsychotic medication irregularly. After twice serving prison time, the patient stopped using methamphetamine and began taking 6mg of risperidone regularly at the age of 42, which caused severe tardive dystonia affecting his whole body. His tardive dystonia was refractory to conventional medications such as the maximum doses of tizanidine—a centrally acting skeletal muscle relaxant—benzodiazepines, and anticholinergic drugs, as well as other atypical antipsychotics like 10mg of olanzapine or 30mg of aripiprazole. When he arrived at our hospital he was unable to sit still in the waiting room. In addition, he had been irritable and aggressive toward his mother, who lived with him, which often resulted in destruction of property at the home. When yokukan-san (7.5g/day) was added to his conventional medication, his involuntary movements were reduced by 30% after 2 weeks. Then, when orengedoku-to (7.5g/day) augmentation was started after 4 weeks, the tardive dystonia was reduced by 80% after 6 weeks. He was able to sit on the same bench with other patients in the waiting room for the first time in 2 years and property destruction became much less common occurrence, although the attitude toward his mother remained abrupt.”*

Natural Treatments for Extrapyramidal Side Effects

Dorfman-Etrog P. The effect of vitamin E addition to acute neuroleptic treatment on the emergence of extrapyramidal side effects in schizophrenic patients: An open label study. *European Neuropsychopharmacology* 9 (1999) 475-477

- *“Addition of vitamin E to neuroleptics may reduce the severity of acute neuroleptic-induced Parkinsonism (NIP) in schizophrenic patients.”*

Miodownik C. Vitamin B6 add-on therapy in treatment of schizophrenic patients with psychotic symptoms and movement disorders. *Harefuah* 2003 Sep;142(8-9):592-6, 647

- *The authors suggest that vitamin B6 may be efficient as a treatment for tardive dyskinesia and parkinsonism induced by neuroleptic agents.”*



Ali O. Effects of tryptophan and valine administration on behavioral pharmacology of haloperidol. Pak J Pharm Sci 2005 Apr;18(2):23-8

- *“These findings suggest a possible serotonergic involvement in neuroleptic induced tardive dyskinesia and amelioration of the disorder through TRP supplementation.”*

Boerner RJ. Attenuation of neuroleptic-induced extrapyramidal side effects by Kava special extract WS 1490. Wien Med Wochenschr 2004 Nov;154(21-22):508-10

- *“We studied at 42 patients (17 female, 25 male) with different psychiatric diagnoses, who were pretreated by neuroleptics, the efficacy and tolerability of Kava special extract WS 1490 on extrapyramidal side effects. In both patient and physician questionnaires as well as in the physicians global ratings, significant improvements were found for all extrapyramidal signs and symptoms recorded. The concomitant intake of WS 1490 was well tolerated by the patients. The findings of this observational study suggest that extrapyramidal side effects of neuroleptic drugs may be attenuated by Kava special extract WS 1490.”*

Natural Treatment for Antipsychotic-Induced Parkinsonism

Sandyk R. Pyridoxine improves drug-induced parkinsonism and psychosis in a schizophrenia patient. Int J Neurosci 1990 Jun;52(3-4):225-32

- *“A schizophrenia patient with severe neuroleptic-induced Parkinsonism and Tardive Dyskinesia is presented in whom administration of pyridoxine (vitamin B6) (100mg/d) resulted in a dramatic and persistent attenuation of the movement disorder as well as a reduction of psychoatic behavior.”*

Miodownik C. Vitamin B6 add-on therapy in the treatment of schizophrenic patients with psychotic symptoms and movement disorders. Harefuah 2003 Sep;142 (8-9):592-6647

- *“The authors suggest that vitamin B6 may be efficient as the treatment for tardive dyskinesia and parkinsonism induced by neuroleptic agents.”*

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Ishikawa T. Effectiveness of the kampo kami-shoyo-san (TJ-24) for tremor of antipsychotic-induced parkinsonism. *Psychiatry Clin Neurosci* 2000 ;54(5):579-82

- *“The results showed a statistical significant reduction in tremor after administration of kami-shoyo-san, with 62.5% patients showing improvements of one point or more.”*

Natural Treatment of Tardive Oculogric Spasms

Coupland N. Successful treatment of tardive oculogric spasms with vitamin E. *Journal of Clinical Psychopharmacology*, Vol. 15(4), August 1995, pp 285-286

- *“The baseline frequencies of episodes accorded with his history and their number fell substantially within a month on vitamin E, 1200 IU daily.” “A trial of vitamin E seems merited in oculogric spasms that have not responded to standard approaches....”*

Natural Treatments for Neuroleptic Malignant Syndrome

Dursun SM. High-dose vitamin E plus vitamin B6 treatment of risperidone-related neuroleptic malignant syndrome. *J Psychopharmacol* 1998;12(2):220-1
PMID# 9694035

- *“ This patient responded satisfactorily to the supportive management and vit E plus vit B6.*

Natural Treatments for Catalepsy

Naidu P.S. Quercetin, a bioflavonoid, reverses Haloperidol-induced catalepsy. *Methods Find Exp Clin Pharmacol* 2004, 26(5):323-326

- *“In conclusion, the findings of the present study strongly suggest that quercetin can be screened as a potential drug candidate or as an adjuvant for the treatment of neuroleptic-induced extrapyramidal side effects.”*

Natural Attenuation of Tics

Garcia-Lopez R. An open study evaluating the efficiency and security of magnesium and vitamin B6 as a treatment of Tourette syndrome in children. *Med Clin (Barc)* 2008 Nov 22;131(18):689-91

- *The total tic score decreased from 26.7 (t0) to 12.9 (t4) and the total effect on the YGTSS was a reduction from 58.1 to 18.8."*

Natural Improvement of Akathisia

Lerner V. Vitamin B6 treatment in acute neuroleptic-induced akathisia: a randomized, double-blind, placebo-controlled study. *J Clin Psychiatry* 2004 Nov;65(11):1550-4

- *"The vitamin B6-treated patients in comparison with the placebo group showed a significant on the subjective-awareness of restlessness, subjective distress, and global subscales of BAS. Our preliminary results indicate that high doses of vitamin B6 may be useful additions to the available treatments for NIA....."*

Berk M. N-Acetyl Cysteine as glutathione precursor for Schizophrenia-A double-blind, randomized, placebo-controlled trial. *Biol Psychiatry* 2008;64:361-368

- *"A moderate benefit of NAC at end point for akathisia was also evident on the BAS, which approached significance."*

Miodownik C. Vitamin B6 verses mianserin and placebo in acute neuroleptic-induced akathisia: a randomized, double blind, controlled study.

- *"Our results indicate that high doses of B6 and low dose of mianserin may be a useful addition to current treatments of NIA."*

Kramer MS. L-tryptophan in neuroleptic-induced akathisia. *Biol Psychiatry* 1990 Mar 15;27(6):671-2

- *"Akathisia scores decreased an average of 39% of base line. Some patients and referring physicians felt that L-tryptophan was quite helpful and requested its continuation.. L-tryptophan, along with nicotinic acid appeared to reduce both objective and subjective components of akathisia in most patients."*

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Gold R. Is there a rationale for iron supplementation in the treatment of akathisia? A review of the evidence. *J Clin Psychiatry* 1995 Oct;56(10):476-83

- *The rationale for iron supplementation in the treatment of akathisia is relatively weak, and there are potentially adverse long-term consequences as outlined in our review. More research is required to directly measure the level of iron in the brains of patients with akathisia.before such therapeutic intervention can be recommended."*

Cotter PE. Improvement in neuroleptic-induced akathisia with intravenous iron treatment in a patient with iron deficiency. *J Neurol Neurosurg Psychiatry* 2007 May;78(5):548

- *"The close temporal relationship between administration of intravenous iron deficiency can contribute to the development or persistence of akathisia in some patients. Iron repletion may be valuable in such cases, although this requires further evaluation."*

Structured Relaxation in the Treatment of Akathisia

Hansen LK. Structured relaxation in the treatment of akathisia. *Neuropsychiatr Dis Treat* 2010 May 25;6:269-71

- *"...the relaxation program appears to be a promising alternative to traditional treatment of akathisia. The patients appreciated the relaxation sessions but none of them managed to carry it out on their own without professional encouragement."*

Natural Treatment for Lithium-induced Tremor

Miodownik C. Lithium-induced tremor treated with vitamin B6: a preliminary case series. *Int J Psychiatry Med* 2002; 32(1):103-8

- *"After the addition of vitamin B6 to their treatment, according to their SAS scores four patients showed impressive improvement until total disappearance of their tremor. The subjective scale, on which the patients scored their impression of clinical improvement, showed similar results."*

Alternative and Complementary Treatments for Schizophrenia

Natural Therapies for Treatment Resistant Schizophrenia

Miyaoka T. Yi-gan san as adjunctive therapy for treatment-resistant schizophrenia: an open-label study. Clin Neuropharmacol 2009 Jan-Feb;32(1):6-9

- *“A significant decrease was observed at 2 weeks and at 4 weeks in each Positive and Negative Syndrome Scale for Schizophrenia subscale score in the YGS group, but not observed in the control group.”*

Bulut M. Beneficial effects of N-acetylcysteine in treatment resistant schizophrenia. World J Biol Psychiatry 2009;10(4 Pt 2):626-8

- *“This paper reports a case of a poorly responsive schizophrenia patient who improved considerably with add-on NAC 600 mg/day.”*

Natural Symptom Reduction and Improved Clinical Outcome

Dakhale G.N. Supplementation of vitamin C with atypical antipsychotics reduces oxidative stress and improves the outcome of schizophrenia. Psychopharmacology (2005) 182:494-498

- *“BPRS change scores at 8 weeks improved statically significant with vitamin C as compared to placebo.”*

Berk M. N-Acetyl-Cysteine as a glutathione precursor for schizophrenia-a double blind, randomized, placebo-controlled trial. Biol Psychiatry 2008;64:361-368

- *“Improvement was seen on the CGI-I at 2 weeks and the CGI-S at 4 weeks, while improvement on the PANSS and a trend for improvement on the BAS emerged only toward 24 weeks of treatment.”*

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Arvindakshan M. Supplementation with a combination of w-3 fatty acids and antioxidants (vitamin E and C) improves the outcome of schizophrenia. *Schizophrenia Res* 62 (2003) 195-204

- *“Concomitantly, there was significant reduction in psychopathology based on reduction in individual total scores for brief psychiatric rating scale (BPRS) and positive and negative syndrome scale (PANSS), general psychopathology-PANSS and increase in Henrich’s Quality of Life (QOL) scale.”*

Lane HY. A randomized, double –blind, placebo-controlled comparison study of sacosine (N-methylglycine) and D-serine add-on treatment for schizophrenia. *Int J Neuropsychopharmacolgy* 2010 May; 13(4):451-60

- *“Treatment group x treatment duration interaction analysis by multiple linear regression showed that sacosine was superior to placebo at all four outcome measures of Positive and Negative Syndrome Scale (PANSS)..., Scale for the Assessment of Negative Symptoms (SANS), Quality of Life (QOL) and Global Assessment of Functioning (GAF). However, d-serine did not differ in effect significantly from placebo in any measure.”*

Heresco-Levy U. D-serine efficiency as add-on pharmacotherapy to risperidone and olanzapine for treatment-refractory schizophrenia. *Biol Psychiatry* 2005 Mar 15;57(6):577-85

- *“D-serine administration induced increased serine serum levels and resulted in significant improvements in negative, positive, cognitive, and depression symptoms, as measured by the Positive and Negative Syndrome Scale.”*

Lou HC. Therapeutic effect of shuxening combining neuroleptics for the treatment of chronic schizophrenia—double blind study. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 1997 Mar;17(3): 139-42

- *“SXN presented a better therapeutic effect for chronic schizophrenics than the control group when rated with traditional global rating method as well, in which 44.98% marked improvement was obtained in the SXN group compared to 20.98% in the control group.”*

Zeng DZ. Clinical observation on effect of Jieyu Anshen Decoction combined with aripiprazole in treating chronic schizophrenia. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2007 Apr;27(4):358-61

- *“JAD combined with aripiprazole has definite effect in treating chronic schizophrenia, shows advantages of quickly initiating effect, high safety and with no harm for increasing adverse reactions, so it is better than using aripiprazole alone.”*

Reduced Hospital Readmission Rates with Nicotinic Acid

Hoffer A. Treatment of Schizophrenia with Nicotinic Acid: A ten year follow-up. *Acta Psychiatrica Scandinavica*, Volume 40, Issue 2, pages 171-189, June 1964

- *“The group which received nicotinic acid had the best record which showed most clearly in the total days of rehospitalization, i.e. about 11 days per patient per year. The comparison group required about 19 days per patient per year.”*

Hoffer A. Nicotinic acid: An adjunct in the treatment of schizophrenia. *Am J Psychiatry* 1963 Aug; 120:171-3

- *“Of the first 16 patients treated in 1952, 75% have not required any further readmissions, 4 have between them had 6 brief readmissions and none now in the hospital. A comparison group of 27 did not fare so well. Of them 17 have required readmission 63 times. These 27 patients required 34 years of admissions over a ten-year period. The nicotinic acid group required only 1.4 years..”*

Osmond H. Massive niacin treatment in schizophrenia. Review of a nine year study. *Lancet*, 1962 Feb 10; 1 (7224): 316-319

- *“Table IV shows the effect of niacin and other treatments on the time spent in the hospital. One way of summarizing this table would be to say that, during the four-year follow-up, patients who had never had nicotinic acid spent two-fifths of a year in hospital, while for those who received it the average was only a sixth of a year.”*
- *“...Schizophrenics treated in Saskatchewan without niacin or nicotinamide had an equally gloomy prognosis (table III): over half were readmitted at least once within five years of discharge. But of those receiving this vitamin only about a sixth required readmission during the same period.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Natural Reduction of Positive Symptoms

Atmaca M. The effect of extract of ginko biloba addition to olanzapine on therapeutic effect and antioxidant enzyme levels in patients with schizophrenia. *Psychiatry and Clinical Neurosciences* (2005),59. 652-656

- *“At the evaluation of week 8, a significant difference in mean Scale for the Assessment of Positive Symptoms (SAPS) scores but not in Scale for the Assessment of Negative Symptoms between groups was found.”*

Laan W. Adjuvant aspirin therapy reduces symptoms of schizophrenia spectrum disorders: results from a randomized, double-blind, placebo-controlled trial. *J Clin Psychiatry* 2010 May;71(5):520-7

- *“Aspirin given as adjunctive therapy to regular antipsychotic treatment reduces the symptoms of schizophrenia spectrum disorders.”*

Ritsner MS. L-theanine relieves positive, activation, and anxiety symptoms in patients with schizophrenia and schizoaffective disorder: an 8 week, randomized, double-blind, placebo-controlled, 2-center study. *J Clin Psychiatry* 2011 Jan;72(1):34-42

- *“40 patients completed the study protocol. Compared with placebo, L-theanine augmentation was associated with reduction of anxiety (P= .015; measured by the HARS scale) and positive (P= .009) and general psychopathology (P<.001) scores (measured by PANSS 3-dimensional model). According to the 5-dimension model of psychopathology, L-theanine produced significant reductions on PANSS positive (P= .004) and activation factor (P= .006) scores compared to placebo.”L-theanine augmentation of antipsychotic therapy can ameliorate positive, activation and anxiety symptoms in schizophrenia and schizoaffective disorder patients,*

Natural Improvement of Negative Symptoms

Lane H Y. Sarcosine or D-Serine add-on treatment for acute exacerbation of schizophrenia. *Arch Gen Psychiatry*, 2005;62:1196-1204

- *“The evidence most strongly supports the benefit of sarcosine for general psychiatric symptoms and depression and possible benefit for negative symptoms (blunted effect and alogia) but not for positive symptoms during acute phase.”*

Doruk A. A placebo-controlled study of extract of ginko biloba added to clozapine in patients with treatment-resistant schizophrenia. *Int Clin Psychopharmacol* 2008 Jul;23(4):223-7

- *“These preliminary data suggested that EGb was found useful for enhancing the effect of clozapine on negative symptoms in patients with treatment resistant schizophrenia”*

Heresco-Levy U. High-dose glycine added to olanzapine and risperidone for the treatment of schizophrenia. *Biol Psychiatry* 2004 Jan 15;55(2):165-71

- *“The negative symptoms improvement remained significant even following covariation for changes in other symptom clusters and extrapyramidal side effects.”*

Strous RD. Dehydroepiandrosterone augmentation in the management of negative, depressive, and anxiety symptoms in schizophrenia. *Arch Gen Psychiatry* 2003 Feb;60(2): 133-41

- *“Increases in DHEA and DHEA-S levels were correlated with improvement in negative symptoms ($P<.05$), but not with improvement in depressive and anxiety symptoms.”*

Strous RD. Dehydroepiandrosterone (DHEA) augmentation in the management of schizophrenia symptomology. *Essent Psychopharmacol* 2005;6(3):141-7

- *“In the authors study, administering DHEA to patients with schizophrenia who had moderate to severe negative symptoms and who were maintained on antipsychotic medications induced significant improvement, more so in women and corresponding to increased plasma levels of DHEA and DHEA-S.”*

Liu JL. Clinical observation on effect of modified Daotan Decoction combined with small dose risperidone in treating chronic schizophrenia. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2007 Mar;27(3):208-10

- *“There was no significant difference in the overall efficiency between the two groups, but the improvement of the negative symptoms, illness provocation and general psychopathologic condition was significantly better in the treatment group than that in the control group respectively ($P< 0.05$).”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Prevention of Psychotic Disorders Using Natural Substances

Amminger GP. Long-chain Omega-3 Fatty Acids for indicated prevention of psychotic disorders: A randomized, placebo-controlled trial. Arch Gen Psychiatry Vol 67 (No. 2) Feb 2010

- *“Long-chain Omega-3 PUFAs reduce the risk of progression to psychotic disorder and may offer a safe and efficacious strategy for indicated prevention in young people with subthreshold psychotic states.”*

Asevedo E. N-acetylcysteine as a potentially useful medication to prevent conversion to schizophrenia in at-risk individuals. Rev Neurosci 2012;23(4):353-62

- *“In this article, we propose that NAC could be a useful medication to prevent evolution of schizophrenia in individuals at risk for psychosis.”*

Woods S.W.. Glycine treatment of prodromal symptoms. Schizophrenia Res Vol. 86 Suppl 2006 pp S7

- *“Of seven completers, three met early remission criteria during the 8 weeks on glycine. No patients converted to psychosis. In MMRM analyses, patients improved significantly from baseline on SOPS total (-18.2+9.9, p<0.001) and on positive symptom, disorganization, and general symptom subscales. Negative symptoms improved only at the trend level.”*

Omega-3 Fatty Acids as Psychotherapeutic Agent for Pregnant Schizophrenic Patient

Su KP. Omega-3 fatty acids as a psychotherapeutic agent for a pregnant schizophrenic patient. *Eur Neuropsychopharmacol* 2001 Aug;11(4):295-9

- *“Because of the potential adverse events and teratogenesis of antipsychotic drugs, it is important to find a safe and effective treatment for pregnant women with severe mental illness. The membrane hypothesis of schizophrenia provides a rationale to treat symptoms of schizophrenia with omega-3 PUFAs. We report a 30-year-old married woman with chronic schizophrenia, who experienced an episode of acute exacerbation of psychotic symptoms during pregnancy. After entering into an opening trial of omega-3 PUFAs monotherapy, she showed a dramatic improvement in both positive and negative symptoms of schizophrenia and a significant increase of omega-3 composition in erythrocyte membrane. There were no adverse effects in this treatment. Thus, omega-3 PUFAs could be both beneficial and therapeutic to pregnant schizophrenic women.”*

Prevention of Oxidative Stress Neuropathology in Schizophrenia

Mahadik S. P. Prevention of oxidative stress-mediated neuropathology and improved clinical outcome by adjunctive use of a combination of antioxidants and omega-3 fatty acids in schizophrenia. *International Review of Psychiatry*, April 2006: 18(2):119-131

- *“In summary, oxidative stress and cell damage likely exist at very early stages of schizophrenia and if not treated early, it can trigger progressive deterioration of neuropathology and thereby symptomology; dietary antioxidants and omega-3 fatty acids are found to effectively prevent and restore the oxidative neuropathology and improve the outcome under a variety of situations. Moreover, these supplements are also found to prevent and cure important medical morbidities such as obesity, hypertension, diabetes, and cardiovascular abnormalities that are often associated with illness and treatment.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Antioxidants for the Treatment of Schizophrenia

Singh V. Review and meta-analysis of usage of ginkgo as an adjunct therapy in chronic schizophrenia. *Int J Neuropsychopharmacol* 2010 Mar;13(2):257-71

- *“Ginkgo as an add-on therapy to antipsychotic medication produced statistically significant moderate improvement (SMD=0.50) in total and negative symptoms of chronic schizophrenia. Ginkgo as an add-on therapy ameliorates the symptoms of chronic schizophrenia. The role of antioxidants in the pathogenesis of schizophrenia has also been explored.”*

Milner G. Ascorbic Acid in Chronic Psychiatric Patients—A Controlled Trial. *Brit J Psychiat* (1963), 109, 294-299

- *“Statistically significant improvement in depressive, manic and paranoid symptom complexes, together with an improvement in overall personality functioning, was obtained following saturation with ascorbic acid.”*

Mahadik SP. Oxidative injury and the potential use of antioxidants in schizophrenia. *Prostaglandins Leukot Essent Fatty Acids* 1996 Aug;55(1-2):45-54

- *“Adjunctive treatment with antioxidants (e.g. vitamins E and C, beta-carotene and quinones) at the initial stages of illness may prevent further oxidative injury and thereby ameliorate and prevent further possible deterioration of associated neurological and behavioral deficits in schizophrenia.”*

Natural Treatment for Very-late-onset Schizophrenia-like Psychosis

Miyaoka T. Yokukansan (TJ-54) for the treatment of very-late-onset schizophrenia-like psychosis: an open label study. *Phytomedicine* 2013 May 15;20(7):654-8

- *“A highly significant ($p < 0.001$) improvement on all measures of psychotic symptomology was observed in all patients. TJ-54 was very well tolerated by the patients, and no clinically significant adverse effects were observed. Scores on all abnormal movement scales did not differ significantly prior to and after TJ-54 treatment.”*

Natural Treatment of Visual Hallucinations

Miyaoka T. Yi-gan san for the treatment of Charles bonnet syndrome (visual hallucinations due to vision loss): an open-label study. Clin Neuropharmacol 2011 Jan-Feb;34(1):24-7

- *“Yi-gan san may be effective and safe therapy to control visual hallucinations in patients with CBS and should be further tested in double-blind, placebo controlled trials.”*

Natural Improvement in Cognition

Chen EY. HT1001, a proprietary North American ginseng extract, improves working memory in schizophrenia: a double-blind, placebo-controlled study. Phyther Res 2012 Aug;26(8):1166-72

- *“Visual working memory was significantly improved in the HT1001 group, but not in the placebo group. Furthermore, extrapyramidal symptoms were significantly reduced after 4 weeks treatment with HT1001, whereas no difference in extrapyramidal effects was observed in the placebo group. These results provide a solid foundation for the further investigation of HT1001 as an adjunct therapy in schizophrenia, as an improvement in working memory and a reduction in medication related side effects has considerable potential to improve functional outcome in this population.”*

Chen ZH. Effects of warm-supplementing kidney yang (WSKY) capsule added on risperidone on cognition in chronic schizophrenic patients: a randomized, double-blind, placebo-controlled, multi-center clinical trial. Hum Psychopharmacol 2008 Aug;23(6)465-70

- *“WSKY capsule added on risperidone may improve cognitive function, social function of the chronic schizophrenics patients, and the WSKY safely during treatment”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Ritsner MS. Improvement of sustained attention and visual and movement skills, but not clinical symptoms, after dehydroepiandrosterone augmentation in schizophrenia: a randomized, double-blind, placebo-controlled crossover trial. *J Clin Psychopharmacol* 2006 Oct;26(5):495-9

- *Compared to placebo, DHEA administration did not produce significant improvement in clinical symptoms, side effects, and quality-of-life scores. However, 6 weeks of DHEA administration (but not placebo) was associated with a significant improvement in Positive and Negative Symptom Scale ratings compared with baseline. Furthermore, 6 weeks of DHEA treatment was associated with significant improvement in cognitive functions of visual sustained attention and visual and movement skills compared with placebo conditions."*

Neuroprotection from Neuroleptics

Post A. Mechanisms underlying the protective potential of α -Tocopherol (Vitamin E) against Haloperidol-associated neurotoxicity. *Neuropsychopharmacology*. 2002, Vol. 26, No. 3

- *"...the present study shows that pre- and co-treatment with vitamin E interferes with the stimulation of apoptotic cascades by haloperidol and, in addition, attenuates some of the undesirable behavioral side-effects of the neuroleptic."*

Heiser P. Effects of antipsychotics and vitamin C on the formation of reactive oxygen species. *Journal of Psychopharmacology*, (2009) 1-6

- *"Vitamin C reduced the ROS production of all drugs tested and for haloperidol and clozapine the level of significance was reached. Our study demonstrated that induce the formation of ROS in whole blood of rats, which can be reduced by application of vitamin C."*

Dietrich-Muszalska A. Inhibitory effects of polyphenol compounds on lipid peroxidation caused by antipsychotics (haloperidol and amisulpride) in human plasma in vitro. *The World Journal of Biological Psychiatry*, 2009, 1-6

- *"We showed that in the presence of polyphenols: resveratrol and quercetin, lipid peroxidation in plasma samples treated with tested drugs was significantly decreased."*

Bishnoi M. Protective effect of curcumin and its combination with piperine (bioavailability enhancer) against haloperidol-associated neurotoxicity: cellular and neurochemical evidence. *Neurotox Res* 2011 Oct;20(3):215-25

- *“Interestingly, co-administration of curcumin (25 and 50mg/kg, i.p., 21 days) dose dependently prevented all behavioral, cellular, and neurochemical changes associated with administration of haloperidol.”*

Dietrich-Muszalska A. Epicatechin inhibits human plasma lipid peroxidation caused by haloperidol in vitro. *Neurochem Res* 2012 Mar;37(3):557-62

- *“In conclusion, the presented results indicate that epicatechin-the major polyphenolic component of green tea reduced significantly human plasma lipid peroxidation caused by haloperidol. Moreover, epicatechin was found to be more effective antioxidant, than the solution of pure resveratrol or quercetin.”*

Dietrich-Muszalska A. Beta-glucan from *Saccharomyces cerevisiae* reduces plasma lipid peroxidation induced by haloperidol. *Int J Biol Macromol* 2011 Jul 1;49(1): 113-6

- *“The presented results indicate that beta-glucan seems to have distinctly protective effects against the impairment of plasma lipid molecules induced by haloperidol.”*

Reversal of Cerebral Atrophy in Schizophrenia

Puri BK. Eicosapentaenoic acid treatment in schizophrenia associated with symptom remission, normalization of blood fatty acids, reduced neuronal membrane phospholipid turnover and brain structure changes. *Int J Clin Pract* 2000; 54(1):57-63

- *“These results demonstrate that EPA can reverse both the phospholipid abnormalities previously described in schizophrenia and cerebral atrophy.”*

Attenuation of Dopaminergic Supersensitivity

Gattaz W. F. Vitamin E attenuates the development of haloperidol-induced dopaminergic hypersensitivity in rats: possible implications for tardive dyskinesia. *J Neural Transm* (1993) 92: 197-201

- *“Within the context of the present experiment vitamin E attenuated the development of behavioral DA-supersensitivity after haloperidol treatment.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

The Use of GLA & LA to Differentiate Between Temporal Lobe Epilepsy and Schizophrenia

Vaddadi KS. The use of gamma-linolenic acid and linoleic acid to differentiate between temporal lobe epilepsy and schizophrenia. *Prostaglandins Med* 1981 Apr;6(4):375-9

- *“Three long-stay, hospitalized schizophrenics who failed to respond adequately to conventional drug therapy were treated with gamma-linolenic acid and linoleic acid in the form of evening primrose oil. They became substantially worse and electroencephalographic features of temporal epilepsy became apparent. In all three the clinical state dramatically improved when carbamazepine, the conventional therapy for temporal lobe epilepsy was introduced. It can be extremely difficult to distinguish on clinical grounds between schizophrenia and temporal lobe epilepsy, and electroencephalographic studies do not always reveal an abnormality in the temporal lobe syndrome, unless additional procedure such as sphenoidal electroencephalography is undertaken. A trial of therapy with gamma-linolenic acid may prove of considerable value in distinguishing between these two states, so allowing specific therapy to be introduced.”*

Natural Antipsychotics

In-Won Chung. Pharmacologic Profile of Natural Products Used to Treat Psychotic Illnesses. *Psychopharmacology Bulletin* 31:139-145, 1995

- *“Authors Summary; In this article there are 31 extracts prepared from natural products frequently used to treat psychotic illnesses were identified from prescriptions in the Korean Tongeuibogam. The screening assays determined the receptor binding of each natural product used to treat psychotic illness.”*

Zhang-Jin Zhang. Therapeutic effects of herbal extracts and constituents in animal models of psychiatric disorders.

- *“Authors Summary; This article contains a section with numerous neuroleptic herbs that have been tested in animal models of psychosis.”*

Elenbroek BA. Effects of (-)stepholidine in animal models for schizophrenia.

Acta Pharmacol Sin 2006 Sep;27(9):1111-8

- *“The data showed that SPD showed antipsychotic-like effects in both the prepulse inhibition paradigm and in the paw test. Moreover, the results of the paw test suggest that SPD has an atypical character with relatively small potency to induce extrapyramidal symptoms.”*

Natesan S. The antipsychotic potential of l-stepholidine – a naturally occurring

dopamine receptor D1 agonist and D2 antagonist. Psychopharmacology (Berl) 2008 Aug; 199(2):275-89

- *“Thus, l-stepholidine shows efficacy like an “atypical” antipsychotic in traditional animal models predictive of antipsychotic activity and shows in vitro and vivo D91) agonism, and, if its rapid elimination does not limit its actions, it could provide a unique therapeutic approach to schizophrenia.”*

Feifel D. Adjunctive intranasal oxytocin reduces symptoms in schizophrenic patients.

Biol Psychiatry 2010;68:678-680

- *“We found that 3 weeks of intranasal oxytocin given adjunctive to standard antipsychotic medications, caused significantly greater reductions in schizophrenia symptoms at the end point compared with placebo. This result supports our hypothesis that oxytocin exhibits antipsychotic properties and validates preclinical studies, case reports, and less well controlled clinical studies suggesting oxytocin’s ability to ameliorate symptoms of schizophrenia”*

Samanta M. K. Development of mono ingredient herbal neuroleptic tablet for better psychiatric therapy. Indian J Pharm Sci, 2005, 67(1):51-56

- *“A tablet containing A. calamus, W. somnifera, and G. glabra” “...three neuroleptic plant extracts were used for the formulation based on ayurvedic neuroleptic formulations and available literatures. ...It was found that these formulations containing three plant extracts were having similar effects as those of marketed formulations. The prepared tablet formulation has not shown any drug induced parkinsonian syndrome or any other relevant side effects, whereas the synthetic drug, chlorpromazine showed maximum pyramidal side effects.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Pedersen CA. Intranasal oxytocin reduces psychotic symptoms and improves Theory of Mind and social perception in schizophrenia. *Schizophrenia Res* 2011 Oct;132(1):50-3

- *“PANSS scores declined significantly and several social cognition measures improved significantly or near significantly in oxytocin but not placebo.”*

Zuardi AW. A critical review of the antipsychotic effects of cannabidiol: 30 years of a translational investigation. *Curr Pharm Des* 2012; 18(32):5131-40

- *“Subsequent studies have demonstrated that CBD has antipsychotic effects as observed using animal models and in healthy volunteers. Thus, this article provides a critical review of the research evaluating antipsychotic potential of this cannabinoid. CBD appears to have pharmacological profile similar to that of atypical antipsychotic drugs as seen using behavioral and neurochemical techniques in animal models. Additionally, CBD, prevented human experimental psychosis and was effective in open case reports and clinical trials in patients with schizophrenia with remarkable safety profile.”*

Pandy V. Antipsychotic-like activity of noni (*Norinda citrifolia* Linn.) in mice. *BMC Complement Altern Med* 2012 Oct 19; 12:186

- *“ The present study results demonstrated the antidopaminergic effect of *Morinda citrifolia* Linn. In mice, suggesting that noni has antipsychotic-like activity which can be utilized in the treatment of psychiatric disorders.”*

Sonibare MA. Antipsychotic property of aqueous and ethanolic extracts of *Lonchocarpus cyanescens* (Schumach and Thonn.) Benth. (Fabaceae) in rodents.

- *“Taken together, these findings suggest that the extracts possess phytochemically active constituents with antipsychotic property. Thus, this investigation provides evidence that may justify the ethnomedicinal applications of *Lonchocarpus cyanescens* as the major constituent of the recipe used for the management of psychosis in Nigeria.”*

Chatterjee M. Evaluation of the antipsychotic potential of *Panax quinquefolium* in ketamine induced experimental psychosis model in mice. *Neurochem Res* 2012 Apr;37(4):759-70

- *“Overall our findings suggest that PQ posses antipsychotic like properties, which may lead to future studies with its specific constitutes which may particularly be beneficial in predominant negative and cognitive symptoms of schizophrenia.”*

de Sousa DP. Neuroleptic-like properties of the chloroform extract of *Maytenus obtusifolia* MART. Roots. *Biol Pharm Bull* 2005 Feb;28(2):224-5

- *“The results suggest that chloroform extract of Maytenus obtusifolia MART. possesses neuroleptic-like properties.”*

Yadav AV. Anti-dopaminergic effect of the methanolic extract of *Morbus alba* L. leaves. *Indian J Pharmacol* 2008 Oct;40(5):221-6

- *“The results suggest that the methanolic extract of Morbus alba L. possesses antidopaminergic activity. Further neurochemical investigation can explore the mechanism of action of the plant drug with respect to dopaminergic functions and help to establish the plant as an antipsychotic agent.”*

Gupta G. Sedative, antiepileptic and antipsychotic effects of *Viscum album* L. (Loranthaceae) in mice and rats. *J Ethnopharmacol* 2012 Jun 14;141(3):810-6

- *“The results obtained in present study suggested that title plant exhibited sedative, antiepileptic and antipsychotic activity in mice and rats.”*

Sotoing Taiwe G. Antipsychotic and sedative effects of the leaf extract of *Crassocephalum bauchiense* (Hutch.) Milne-Redh (Asteraceae) in rodents. *J Ethnopharmacol* 2012 Aug 30;143(1): 213-20

- *“The results show that the antipsychotic and sedative properties of Crassocephalum bauchiense are possibly mediated via the blockade of dopamine D-2 receptors and GABAergic activation, respectively.”*

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Omogbiya IA. Jobelyn® pretreatment ameliorates symptoms of psychosis in experimental models. *J Basic Clin Physiol Pharmacol* 2013;24(4):331-6

- *“Taken together, these findings suggest that JB exhibits antipsychotic-like activity, devoid of the adverse effect of cataleptic behavior, and may offer some beneficial effects in the symptomatic relief of psychotic ailments.”*

Ueda T. Geissoschizine methyl ether has third-generation antipsychotic-like actions at the dopamine and serotonin receptors. *Eur J Pharmacol* 2011 Dec 5;671(1-3):79-86

- *“GM and GM derivatives may compromise a new set of candidates for atypical antipsychotics.”*

Wakabayashi C. Behavioral and molecular evidence for psychotropic effects in L-theanine. *Psychopharmacology (Berl)* 2012 Feb;219(4):1099-109

- *“Our results suggest that L-theanine has antipsychotic-like and possibly antidepressant-like effects. It exerts these effects, at least in part, through induction of BDNF in the hippocampus and the agonistic action of L-theanine on the NMDA receptor.”*

Arowona IT. Antipsychotic property of solvent-partitioned fractions of *Lonchocarpus cyanescens* leaf extract in mice. *J Basic Clin Physiol Pharmacol* 2013 Dec 19: 1-6

- *“These findings suggest that EAF contains the major active constitute(s) mediating the antipsychotic property of LC and further support its use for the management of psychosis in traditional medicine.”*

Costa-Campos L. Antipsychotic-like profile of alstonine. *Pharmacology Biochemistry and Behavior*, Vol. 60, No.1, pp. 133-141, 1998

- *“An ethnopharmacological study in Nigeria has led to the investigation of a plant-based extract used by traditional psychiatrists with anecdotal antipsychotic-like effects. This extract was later found to bear antipsychotic profile (Elisabetsky et al., unpublished results) using a behavioral approach similar to the present study. Phytochemical studies have identified alstonine as one of the major components of this extract. The following study investigates the putative antipsychotic profile of alstonine using behavioral and neurochemical strategies.”*

Recovery of Psychosis with Chinese Herb

Panosian A. Pharmacology of Schsandria Chinensis Bail: An overview of Russian research and uses in medicine. *Journal of Ethnopharmacology* 118(2008) 183-212

- *“Galant et. Al. (1957) claimed total recovery in psychosis following a trial involving the administration of SSP over a period of ten days (0.5g, three times daily) to 36 patients (19 with schizophrenia, 6 with reactive psychosis, 4 with alcoholic psychosis, 3 with involuntional depression, and 4 with psychopathology) presenting astheno-depressive syndrome. However, in the treatment showed no effect in psychopathology, whilst in schizophrenic group, six patients recovered, seven patients improved, and six (the hardest) cases the treatment was ineffective.”*

Natural Improvement of Mismatch Negativity

Lavoie S. Glutathione precursor, N-Acetyl-Cysteine, Improves mismatch negativity in schizophrenic patients. *Neuropsychopharmacology*, 2008, 33, 2187-2199

- *“MMN improvement was observed in the absence of robust changes in assessments of clinical severity, though the latter was observed in larger and more prolonged clinical study”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Potential of Therapeutic Effects of Nicotinic Acid by Pyridoxine (vitamin B6) in Schizophrenia

Ananth JV. Potential of therapeutic effects of nicotinic acid by pyridoxine in chronic schizophrenics. The Canadian Psychiatric Association Journal, Volume 18(5), Oct 1973, 377-383

- *“Based on these findings it was hypothesized that the administration of pyridoxine will enhance the therapeutic effect of nicotinic acid in schizophrenic patients by opening up kynurenine cycle of tryptophan metabolism and thereby decreasing the formation of indoles.*
- *In this 48-week placebo-controlled study, the therapeutic effect of a combination of nicotinic acid and pyridoxine was compared with that of treatment with either nicotinic acid or pyridoxine alone. Of the three indices of therapeutic effects, global improvement in psychopathology (BPRS and NOSIE) scores was seen in all three groups; the number of days of hospitalization during the period of the clinical study was lower in both the nicotinic acid and combined treatment group; and only in the combined treatment group was the daily average dosage of phenothiazine medication decreased. Thus, improvement in all three indices was noted in the combined treatment group.”*

Antidepressant Effect of Pyridoxine (vitamin B6) in Schizophrenic Patients with Co-morbid Minor Depression

Shiloh R. Antidepressant effect of pyridoxine (vitamin B6) in neuroleptic-treated schizophrenic patients with co-morbid minor depression — preliminary open-label trial. Harefuah 2001 May;140(5):369-73,456.

- *“Two of nine patients (22%), characterized by higher initial HAM-D and SANS scores, and by older age and longer duration of illness, experienced marked improvements in depressive symptoms (23% and 28% decrease in HAM-D scores) following 4 weeks of pyridoxine administration. In one of these two, the improvement in depressive symptoms was accompanied by a parallel decrease in SANS scores.”*

Natural Attenuation of Amphetamine Induced Positive Psychotic Symptoms

Irwin MR. L-5-hydroxytryptophan attenuates positive psychotic symptoms induced by D-amphetamine. *Psychiatric Res* 1987 Dec;22(4):283-9

- *“Pre-administration with 5HTP significantly antagonized amphetamine-elicited elevations in thought disturbance, activation, and hallucinations.”*

Dietary Modification for Symptom Remission in Schizophrenia

Dohan FC. Relapsed schizophrenics: more rapid improvement on a milk-and cereal free diet. *Br J Psychiatry* 1969 May; 115(522):595-6

- *“Relapsed schizophrenic men randomly assigned to a milk-and cereal free diet on admission to a locked ward were released to an open ward considerably more rapidly than those assigned a high-cereal diet. When gluten was secretly added to the cereal-free diet the difference did not occur. Release of non-schizophrenic patients was not related to diet. These findings support the hypotheses that ingestion of cereals may be pathogenic for those with the genotype for schizophrenia.”*

Dohan FC. Relapsed schizophrenics: Earlier discharged from the hospital after cereal-free, milk-free diet. *Am J Psychiatry* 130;6, June 1973

- *“During the first 90 days after admission to the hospital, those schizophrenics assigned to the CFMF diet were discharged more than twice as fast as those in the HC (high cereal) control group. In contrast to the beneficial effects of the CFMF diet, the relapsed schizophrenics on the CFMF diet to which wheat gluten was added (without the February 12, 2014 knowledge of staff or patients) were not discharged from hospital significantly faster than their temporal controls on the HC diet.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

De Santis A. Schizophrenic symptoms and SPECT abnormalities in a coeliac patient: regression after a gluten-free diet. *J Internal Medicine* 1997;242:421-423

- *"A 33 year-old patient, with pre-existing diagnosis of 'schizophrenic' disorder, came to our observation for severe diarrhea and weight loss. Use of SPECT, demonstrated hypoperfusion of the left frontal brain area, without evidence of structural cerebral abnormalities. Jejunal biopsy showed villous atrophy. Antiendomysial antibodies were present. A gluten-free diet was started, resulting in disappearance of psychiatric symptoms, and normalization of histological duodenal findings and of the SPECT pattern....the SPECT demonstrating a dysfunction of the frontal cortex disappearing after a gluten free diet."*

Cade R. Autism and Schizophrenia: Intestinal Disorders Nutritional Neuroscience, Vol. 3, pp. 52-72, 2000

- *"...with a gluten-casein free diet alone. Patients 1 and 6 showed significant improvement after only two months on the diet. After four months on the diet, all seven patients had improved and there was a statistically significant improvement for the group as a whole comparing control with experimental values."*

Kraft BD. Schizophrenia, gluten and low-carbohydrate, ketogenic diets. *Nutr Metab (Lond)* 2009 Feb 26;6-10

- *A case report of a 70 year old schizophrenic with severe medical problems who used a ketogenic diet. "Over the course of 12 months, C.D. has continued the low-carbohydrate, ketogenic diet and has had no recurrence of auditory or visual hallucinations. She has also continued to lose weight and experience improvements in her energy level. She acknowledged having 2-3 isolated episodes of dietary non-compliance that lasted several days, where she ate pasta, bread, and cakes around the holidays: however she had no recurrence of her hallucinations."*

Pacheco A. A pilot study of the ketogenic diet in schizophrenia. *Am J Psychiatry* 121, May 1965, pp. 1110-1

- *"The average scores showed a statistically significant decrease in symptomology after 2 weeks on the ketogenic diet. The third rating taken one week after discontinuing the diet, showed that in 7 out of 10 patients there was a slight to fairly large increase in symptomology."*

Attenuation of Schizophrenic Symptoms Using Milk Containing A2 Genetic Variant

Bell SJ. Health implications of milk containing beta-casein with the A2 genetic variant. *Crit Rev Food Sci Nutr* 2006;46(1):93-100

- *“Furthermore, consumption of milk with A2 variant may be associated with less severe symptoms of autism and schizophrenia”*

Treatment of Psychosis and Tardive Dyskinesia with Low Protein, Imbalanced Amino Acid Dietary Intervention

Aschheim E. Dietary control of psychosis. *Medical Hypotheses* (1993) 41, 327-328

- *“The purported dietary intervention derives from established animal work dealing with the feeding of diets in which the essential amino acid (EAA) composition has been modified so as to produce a defined imbalance. It has been demonstrated that when animals are kept on a low but adequate protein diet balanced in terms of EAAs the addition of extra amount of single amino acids induces a deficiency of other EAAs...It is likely the biochemical effects of this treatment will become apparent in a matter of hours because amino acids, in contrast to carbohydrates and fats are not stored in the body. Consequently, the change in psychiatric presentation may become noticeable within a short time.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Effect of Low –Tryptophan Diet as an Adjunct to Neuroleptic Therapy in Schizophrenia

Rosse RB. Effect of a low-tryptophan diet as an adjuvant to conventional neuroleptic therapy in schizophrenia. *Clinical Neuropharmacology* Vol. 15, No. 2, pp. 129-141

- *“Authors Summary; Dietary manipulations of TRP have been shown to alter levels of 5-HT, kynurenic acid, and quinolinic acid. Conceivably, decreasing dietary ingestion of TRP would (a) diminish central serotonergic transmission due to a reduction of presynaptic stores of 5-HT, (b) relieve antagonism of NMDA-mediated neural transmission by decreasing levels of kynurenic acid, and (c) reduce excitotoxic levels of quinolinic acid. As reviewed above, a reduction in serotonergic transmission and alternation of glutamatergic transmission at a specific receptor subclass may be associated with salutary therapeutic effects in patients with schizophrenia.*
- *In this investigation, we examined the safety and adjunctive therapeutics effects of 4-day TRP-deficient diet on the behavioral symptomology of schizophrenic patients maintained on a stable dose of their conventional antipsychotic medications.*
- *Interestingly, however, some of the behavioral rating measures (BPRS, CGI) reached statistical significance in the last 2 days of the diet, suggesting a beneficial adjuvant effect for the low-TRP that was not immediate but delayed a few days.*
- *Potentially, the most important finding of this study is improved performance on the Stroop Color and Word Test during the diet phase that largely dropped off during the post-diet phase.*

Dietary Glycomacropeptide: A Novel Nutritional Treatment for Manic and Psychotic Disorders

Badawy A. Novel nutritional treatment for manic and psychotic disorders: a review of tryptophan and tyrosine depletion studies and the potential of protein-based formulations using glycomacropeptide. *Psychopharmacology* (2013) 228: 347-358

- *“A palatable alternative lacking Trp, Tyr and Phe has been identified in the whey protein fraction caseino-glycomacropeptide (c-GMP). The absence of these three aromatic amino acids renders GMP suitable as a template for seven formulations for separate and combined depletion or loading and placebo control. The absence of Phe and Tyr enables GMP to provide a unique nutritional therapy of manic and psychotic disorders by inhibition of cerebral dopamine synthesis and release and possibly also by enhancing*

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glutamatergic function, in general, and in patients resistant to antipsychotic medication, in particular."

Dietary Improvement in Schizophrenia

McCreadie RG. Dietary improvement in people with schizophrenia: randomized controlled trial. *Br J Psychiatry* 2005 Oct; 187:346-51

- *"People with schizophrenia make poor dietary choices. Aims were to measure the impact of giving free fruits and vegetables for 6 months on eating habits in schizophrenia. Conclusions: The diet of people with schizophrenia improved when they were given free fruits and vegetables but this was not sustained after withdrawal of intervention. A support group added no benefit."*

Natural Treatment for Insomnia in Schizophrenia

Suresh Kumar PN. Melatonin in schizophrenic outpatients with insomnia: a double-blind, placebo-controlled study. *J Clin Psychiatry* 2007 Feb;88(2):237-41

- *"The modal stable dose of melatonin was 3mg. Relative to placebo, melatonin significantly improved the quality and depth of sleep of nighttime sleep, reduced the number of nighttime awaking's, and increased the duration of sleep without producing a morning hangover. Subjectively, melatonin also reduced sleep-onset latency, heightened freshness on awaking, improved mood, and improved daytime functioning."*

Natural Treatment for Anxiety in Schizophrenia

Ritsner MS. L-theanine relieves positive, activation, and anxiety symptoms in patients with schizophrenia and schizoaffective disorder: and 8 week, randomized, double-blind, placebo-controlled, 2-center study. *J Clin Psychiatry* 2011 Jan;72(1):34-42 "

- *According to the 5-dimension model of psychopathology, L-theanine produced significant reductions on PANSS positive and activation factor scores compared to placebo."*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Estrogen for Treatment of Schizophrenia

Grigoriadis S. The role of estrogen in schizophrenia: implications for schizophrenia practice guidelines for women. *Can J Psychiatry*. 2002 Jun;47(5):437-42

- *“Estrogen has been used effectively as an adjunctive treatment in women with schizophrenia. Estrogen may also play a preventive role in TD.”*

Kulkarni J. Estrogen in severe mental illness: a potential new treatment approach. *Arch Gen Psychiatry* 2008 Aug; 65(8):955-60

- *“Estradiol appears to be a useful treatment for women with schizophrenia and may provide a new adjunctive therapeutic option for severe mental illness.”*

Kulkarni J. Estrogens and men with schizophrenia: is there a case for adjunctive therapy? *Schizophr Res* 2011 Feb;125(2-3):278-83

- *“Results demonstrated for estradiol participants a more rapid reduction in general psychopathology that occurred in the context of greater increases in serum estrogen levels and reductions in FSH and testosterone levels.”*

Natural Treatment with Prolyl Oligopeptidase Inhibitors

Tarrango T. The natural product berberine is a human prolyl oligopeptidase inhibitor. *ChenMedChem* 2007 Mar;2(3):354-9

- *“As berberine is a natural compound that has been safely administered to humans, it opens up new perspectives for the treatment of neuropsychiatric diseases.”*

Tarrago T. Identification by 19F NMR of traditional Chinese medicinal plants possessing prolyl oligopeptidase inhibitory activity. *Chembiochem* 2006 May;7(5):827-33

- *“This peptidase has been associated with schizophrenia, bipolar affective disorder, and related neuropsychiatric disorders and might therefore have important clinical implications.”*

Ayurvedic Medicine for Schizophrenia

Agarwal V. Ayurvedic medicine for schizophrenia. Cochrane Database Syst Rev 2007 Oct 17;(4):CD006867

- *"....Ayurvedic treatment, in the case a complex mixture of many herbs, is compared with chlorpromazine in acutely ill people with schizophrenia, it is equally, but skewed data seems to favor the chlorpromazine group. Ayurvedic medication may have some effects for treatment of schizophrenia...."*

Chinese Herbal Medicine for Schizophrenia

Rathbone J. Chinese herbal medicine for schizophrenia: Cochrane systematic review of randomized trials. Br J Psychiatry 2007 May;190:379-84

- *"Results suggest that combining Chinese herbal medicine with antipsychotics is beneficial"*

Schizophrenia Mainly Treated with Jinpudan Tablets

Yang CL. Schizophrenia mainly treated with jinpudan tablets. Zhongh XJ YI Jie He Ze Zhi 1987 Sep;7(9):529-31

- N/A

Chinese Medical Treatment to Relieve Blood Stasis in Schizophrenia

Wang B. Traditional Chinese medical treatment to invigorate blood and relieve stasis treatment of schizophrenia: comparison with antipsychotic treatment. Psychiatry Clin Neurosci 1996 Dec;52 Suppl:S329-30

- *"Traditional Chinese medicine is superior to antipsychotic drugs in the effects of anti-anxiety-depression and antipsychomotor inhibition, but is less effective in controlling psychomotor excitation compared with antipsychotic drugs"*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Zhu YZ. Clinical study of shuizhi-dahuang mixture in treating schizophrenics with blood stasis syndrome. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 1996 Nov;16(11):646-8

- *A clinical study of 67 female schizophrenics was conducted. Thirty two patients of them treated with Shuizhi (leech)-Dahuang (rhubarb) mixture mainly with low dosage of antipsychotic drugs (combined therapy group). The results showed that their overall therapeutic effects were similar and the combined therapy group could reduce the dosages of antipsychotic drugs and its side effects, and tended to normalize the hemorheologic indices."*

Zhang JZ. Xuefu zhuyu decoction in treating blood stasis syndrome of schizophrenia. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 1993 Jul; 13(7):397-401

- *"The clinical and experimental study of 66 schizophrenics were conducted. Based on mental symptoms, four-diagnostic method of TCM and hemorheology, it presented preliminarily the clinical and experimental criteria for schizophrenia. The combined therapy of Xuefu Zhuyu Decoction and low dosage of antipsychotic drug could relieve the mental symptoms and the abnormal hemorheologic index normalized. Its therapeutic index was higher than that of the control group."*

Integrative Treatments for Medication-Induced Side Effects for Schizophrenia & Bipolar Disorder

Natural Reduction of Atypical Antipsychotic-Induced Weight Gain

Eosu K. A preliminary investigation of a-lipoic acid treatment of antipsychotic drug-induced weight gain in patients with schizophrenia. *J Clin Psychopharmacol* 2008;28:138-146

- *"The mean weight loss at the 12 week end point was 3.16 (3.20)kg; median, 3.03kg;range 0-8.85kg"*

Yamamoto N. Bofu-tsusho-san effectively attenuates the weight gain observed after receiving olanzapine. *Psychiatry Clin Neurosci* 2008 Dec;62(6):747

- *A 20 year old woman with schizophrenia on medication, experiencing weight gain, lost 2.7kg of weight in 6 months with additional use of Bofu-tsusho-san with no changes of food intake . "In study of obese mice, bofu-tsusho-san produced a significant decrease in fat mass and weight compared with placebo, with-out effecting amount of food ingested"*

Katzman M. Weight gain and psychiatric treatment: is there as role for green tea and conjugayed linoleic acid? *Lipids in Health and Disease* 2007, 6:14

- *"In these four adults who were taking quietiapine, the concurrent self-administration of green tea and conjugated linoleic acid appeared to be protective against gains in body fat. The results were fairly consistent; each had a decrease in body fat percentage and increase in lean body mass."*

Natural Treatments for Hypersalivation in Schizophrenia

Hung CC. Treatment effects of traditional Chinese medicines Suoquan Pill and Wuling Powder on clozapine-induced hypersalivation in patients with schizophrenia: study protocol of randomized, placebo-controlled trial. *Zhong Xi Yi Jie He Xue Bao* 2011 May;9(5):495-502

- *"It is hypothesized that SQP and WLP will have a beneficial effect in controlling clonzapine-induced hypersalivation symptoms."*

Kang B. Effect of suo quan pill for reducing clozapine induced salivation. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 1993 Jun; 13(6) 347-8

- *"There was a significant difference in effect on salivation between the therapeutic group (21 cases) and the controlled group (19 cases), P<0.01."*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Natural Treatment for Hyperprolactinemia in Schizophrenia

Yuan HN. A randomized, crossover comparison of herbal medicine and brocriptine against risperidone-induced hyperprolactinemia in patients with schizophrenia. *J Clin Psychopharmacol* 2008 Jun;28(3):264-370

- *“Peony-Glycyrrhiza Decoction treatment produced a significant baseline-endpoint decrease in serum PRL levels, without exacerbating psychosis and changing other hormones, and decreased the amplitudes were similar to those of BMT (24% vs 21%-38%).”*

Yamanda K. Effectiveness of Herbal Medicine (Shakuyaku-kanzo-to) for Neuroleptic_Induced Hyperprolactinemia. *J Clin Psychopharmacol* Vol 17/No 3 June 1997

- *“There were statistically significant changes in p-PRL levels from 26.6 (SD 10.8) ng/mL at baseline to 20.8 (SD 11.2) mg/mL at 4 weeks and 24.0 (SD 11.4) ng/mL at 8 weeks ($F=8.408$, $df=2,38$, $p=0.0009$). Post hoc analysis demonstrated statistically significant differences between p-PRL levels at 4 and 8 weeks ($p<0.01$) and between p-PRL levels at 4 and 8 weeks ($p<0.05$). Plasma PRL levels at 8 weeks were not significantly different from those at baseline. In five patients, the p-PRL levels decreased by more than 50% with TJ-68 treatment. Three of 10 patients, who had complained of reduced sexual desire, experienced subjective improvement. Potassium levels and other laboratory data showed no significant changes with TJ-68 administration. Neither exacerbation of psychosis nor other adverse effects occurred.”*

Hori H. Herbal medicine (Shakuyaku-kanzo-to) improves Olanzapine-associated hyperprolactinemia: A case report. *Letters to the Editor, Journal of Clinical Psychopharmacology*, Volume 33, Number 1, February 2013

- *“In conclusion, shakuyaku-kanzo-to might be useful for treating amenorrhea without worsening psychotic symptoms in patients with schizophrenia.”*

Omega-3 Fatty Acids for Hypertriglyceridemia in Patients Taking Second Generation Antipsychotics

Fetter JC. N-3 fatty acids for hypertriglyceridemia in patients taking second-generation antipsychotics. *Clin Schizophr Relat Psychoses* 2013 Summer;7(2):73-77A

- *“Mean triglyceride levels decreased by 70.4+-50.4 mg/dL (p=0.001). Among secondary endpoints, mean HDL increased by 2.6+-3.5(p=0.03). However, LDL and total cholesterol, blood pressure, HOMA-IR and CPR did not significantly change.”*

Caniato RN. Effect of omega-3 fatty acids on the lipid profile of patients taking clozapine. *Aust N Z J Psychiatry* 2006 Aug; 40 (8):691-7

- *Participants taking omega-3 fatty acids demonstrated a statistically significant reduction in mean serum triglyceride levels of 22%. There was an associated increase in total cholesterol (6.6%) and low-density lipoprotein cholesterol (22%). Common side-effects included fishy burps or breath, but no serious side effects or interactions were observed. Omega-3 fatty acids may be of value in patients taking clozapine and who have elevated serum triglyceride levels.”*

Hypolipidemic and Hypoglycemic Actions of Withania somnifera for Treatment in Schizophrenia

Agnihotri AP. Effects of Withania somnifera in patients of schizophrenia: A randomized, double blind, placebo controlled pilot trial study. *Indian Journal of Pharmacology* 45. 4 (2013): 417

- *“No change in all three biochemical parameters was found after 1 month of treatment in the placebo group. However, a statistically significant (p<0.05) reduction in serum triglycerides and FBG was observed after 1 month of WS treatment compared to the placebo group.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Natural Treatment of Antipsychotic-induced Amenorrhea Syndrome

Ding Y. Effect of Tongdatang Serial Recipe on antipsychotic drug-induced glactorrhea-amenorrhea syndrome. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2008 Mar;28(3):263-5

- *Therapeutic efficacy on the 49 patients of the treatment group was cured in 31 (63.3%), markedly effective in 11 (22.4%), effective in 4 (8.2%) and ineffective in 3 (6.1%), with a total effective rate of 93.9%, while in 47 patients of the control group, the corresponding cases (%) was 0, 3(6.4%), 7(14.9%) and 37 (78.7%), respectively, with the total effective rate of 21.3%. “*

Yamanda K. Herbal medicine (Shakuyaku-kanzo-to) in the treatment of risperidone-induced amenorrhea. *J Clin Psychopharmacol*, Vol. 19/No.1 August 1999

- *“This report demonstrates TJ-68 to be effective in correcting neuroleptic-induced amenorrhea and hyperprolactinemia. Addition of TJ-68 lowered the p-PRL level from 22 to 9.5ng/mL, and menstruation recovered after 3 weeks of administration. Discontinuation of this compound resulted in the return of irregularity of menstruation and hyperprolactinemia.”*

Kanofsky JD. Ascorbic Acid action in neuroleptic-associated amenorrhea. *J Clin Psychopharmacol*, Vol 9/No. 5 Oct. 1989

- *“The above cases suggest that ascorbic acid at the dose of 2 g orally three times a day may obviate the negative effect neuroleptics can have on menstruation. Given, the wide array of suggestive evidence, we believe that ascorbic acid supplementation should be systematically studied in women who are amenorrheic secondary to neuroleptic use.”*

Yi-Gan San Add-on Treatment for Neuroleptic-induced Nocturnal Eating/Drinking Syndrome with Restless Legs Syndrome

Kawabe K. Nocturnal eating/drinking syndrome with restless legs syndrome caused by neuroleptics improved by Yi-Gan San add-on treatment: a case report Clin Neuropharmacol 2012 Nov-Dec;35(6):290-1

- *We report a middle-aged male patient with schizophrenia who had nocturnal eating/drinking syndrome with restless leg syndrome whose condition improved with the administration of the herbal medicine Yi-Gan San (Yokukan-San in Japanese).*

Herbal Treatment for Antipsychotic-induced Hyperprolactinemia

Yuan HN. A randomized, crossover comparison of herbal medicine and bromocriptine against risperidone-induced hyperprolactinemia in patients with schizophrenia. J Clin Psychopharmacol 2008 Jun;28(3):264-370

- *“These results suggest that herbal therapy can yield additional benefits while having comparable efficacy in treating antipsychotic-induced hyperprolactinemia in individuals with schizophrenia.”*

Herbal Treatment for SSRI-induced Nausea and Dyspepsia

Yamada K. Herbal medicine in the treatment of fluvoxamine-induced nausea and dyspepsia. Psychiatry and Clinical Neurosciences (1999), 53, 681

- *In summary, our results suggest that a herbal medicine, Gorei-san, may be effective for fluvoxamine-induced nausea and dyspepsia, without severe adverse events. Further studies are needed to confirm our results.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Yamada K. Effectiveness of Gorei-san (TJ-17) for the treatment of SSRI-induced nausea and dyspepsia: preliminary observations. Clin Neuropharmacol 2003 May-Jun;26(3):112-4

- *“Gorei-san (TJ-17), which is composed of five herbs (Alismatis rhizome, Atractylodis lanceae rhizome, Polyporus, Hoelen, and Cinnamomi cortex), is a Japanese herbal medicine that has been used to treat nausea, dry mouth, edema, headache, and dizziness. The authors investigated the efficacy of TJ-17 for patients who experienced nausea or dyspepsia induced by SSRIs. Twenty outpatients who experienced nausea or dyspepsia induced by SSRIs were recruited for the study. Seventeen patients were female, three were male, and patient age ranged from 21 to 74 years (49.8 +/- 17.0 years). TJ-17 was added to the previous regimen. Nausea and dyspepsia disappeared completely in nine patients, decreased in four patients, decreased slightly in two, and did not change in five patients. No adverse events were associated with the addition of TJ-17 in any patient.”*

Herbal Treatment of Antipsychotic –induced Hypoperistalsis

Sato K. Effect of Dai-kenchu-to (Da-Jian-Zhong-Tang) on the delayed intestinal propulsion induced by chlorpromazine in mice. J Ethnopharmacol 2003 May;86(1):37-44

- *“These results demonstrated that Dai-kenchu-to improves chlorpromazine-induced hypoperistalsis via cholinergic systems and that Zanthoxylum Fruit is the main contributor to this action of Dai-kenchu-to.”*

Herbal Treatment of Nausea and Vomiting Associated with SSRIs

Oka T. Rikkunshi-to attenuates adverse gastrointestinal symptoms induced by fluvoxamine. Biopsychosoc Med 2007 Nov 15;1:21

- *“This study suggests that Rikkunshi-to reduces FLV-induced adverse events, especially nausea, and improves QOL related to GI symptoms without affecting the antidepressant effect of FLV.”*

Efficiency of Milk Thistle in Preventing Psychotropic Drug-Induced Hepatic Damage

Palasciano G. The effect of silymarin on plasma levels of malon-dialdehyde in patients receiving long-term treatment with psychotropic drugs. *Current Therapeutic Research*, Vol 55(5), May 1994, 537-545

- *“The data show that silymarin, when used at submaximal doses, reduces the lipoperoxidative hepatic damage that occurs during treatment with butyrophenones or phenothiazines. Results suggest that increased lipoperoxidation may contribute to PD-induced hepatotoxicity.”*

Protective Action of Coenzyme Q10 on Neuroleptic-induced Cell Damage in Rat Myocardial Cells

Chiba M. A protective action of coenzyme Q10 on chlorpromazine-induced cell damage in cultured rat myocardial cells. *Jpn Heart J* 1984 Jan;25(1):127-37

- *“These findings suggest that CoQ may protect myocardial cells from CPZ-induced injury, and that prostaglandins may play an important role in the action of CoQ.”*

Acupuncture Treatment of Sexual Dysfunction Secondary to Antidepressants

Khamba B. Efficacy of Acupuncture Treatment of Sexual Dysfunction Secondary to Antidepressants. *J Altern Complemt Med* 2013 Jun 21

- *“This study suggests a potential role for acupuncture in the treatment of sexual side effects of SSRIs and SNRIs as well for a potential benefit of integrating medical and complementary and alternative practitioners.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Aspirin Reduces Clinical Deterioration in Subjects on Lithium

Stolk P. Is aspirin useful in patients on lithium? A pharmacoepidemiological study related to bipolar disorder. Prostaglandins Leukot Essent Fatty Acids 2010 Jan;82(1):9-14

- “Low dose aspirin produced a statistically significant duration-independent reduction in relative risk of clinical deterioration in subjects on lithium, whereas other NSAIDs and glucocorticoids did not.”

Aspirin for Treatment of Lithium-associated Sexual Dysfunction in Men

Saroukhani S. Aspirin for the treatment of lithium-associated sexual dysfunction in men: randomized double-blind placebo-controlled study. Bipolar Disord 2013 Sep;15(6):650-6

- “By week 6, patients in the aspirin group showed significantly greater improvement in the total (63.9% improvement from baseline) and erectile function domain (85.4% improvement from baseline) scores than the placebo group (14.4% and 19.7% improvement from baseline, p -values=0.002 and 0.001, respectively). By week 6, 12 (80%) patients in aspirin group and three (20%) patients in placebo group met the criteria of minimal clinically important change [$\chi^2(1)=10.800, p=0.001$]. Other IIEF domains also showed significant improvement at end of trial.”

Non-Invasive Therapies and Treatments for Schizophrenia

Hydrotherapy as a Neuroleptic and Sedative Treatment

Nikolia S. Hydrotherapy as a possible neuroleptic and sedative treatment. *Medical Hypotheses* (2008) 70, 230-238

- *“As described previously, an adapted cold shower could work as a mild electroshock applied to the sensory and therefore, it might have an antipsychotic effect similar to that of electroconvulsive therapy. Additionally, a cold shower is a vivid example of stress-induced analgesia and would also be expected to “crowd out” or suppress psychosis related neurotransmission with-in the mesolimbic system.”*

Harmon RB. Hydrotherapy in the state mental hospitals in the mid-twentieth century. *Issues Ment Health Nurs* 2009 Aug;30(8):491-4

- *“Student and graduate nurses were required to demonstrate competence in hydrotherapy treatments used to calm agitated or manic patients in the era before neuroleptics. The nurses interviewed for this study indicated that, although labor intensive, hydrotherapy worked, at least temporarily.....”*

Sound Therapy for Remission of Auditory Hallucinations in Treatment Resistant Schizophrenia

Kaneko Y. Two cases of intractable auditory hallucination successfully treated with sound therapy. *International Tinnitus Journal* 2010;16(1):29-31

- *“We report two cases of AVHs successfully treated with sound therapy safely using a tinnitus control instrument (sound generator). The present study showed that sound therapy induced a complete remission of AVHs safely in two patients 2 years 7 months and 1 year 6 months. These results imply that the neuromechanism of AVHs is sensitive to sound therapy.”*

Alternative and Complementary Treatments for Extrapyrarnidal Symptoms, Schizophrenia, and Bipolar Disorder

Morning Sunlight Reduces Length of Hospitalization

Benedetti F. Morning sunlight reduces length of hospitalization in bipolar depression. *J Affect Disord* 2001 Feb;62(3):221-3

- *“Natural sunlight can be an underestimated and controlled light therapy for bipolar depression.”*

Dark Therapy for Schizoaffective Disorder

German Gomez-Bernal. Dark therapy for schizoaffective disorder: A case report. *Med Hypotheses* Volume 72, Issue 1, pp. 105-6, January 2009

- *“James Phelps describes how amber-tinted safety glasses, could be useful for patients with rapid cycling bipolar disorder. These lens could block more than 90% wavelenghts around 450mm (blue to blue-green) of light spectrum creating “virtual darkness” which could has a physiologic effect equivalent to true darkness, at least at the level of melatonin synthesis. I report a case that could support Phelps hypotheses.”*
-

Computer-assisted Therapy for Medication-resistant Auditory Hallucinations

Leff J. Computer-assisted therapy for medication-resistant auditory hallucinations: proof-of-concept study. *Br J Psychiatry* 2013 Jun;202:428-33

- *“Avatar therapy was evaluated by a randomized, single blind, partial crossover trial comparing the novel therapy with treatment as usual (TAU). We used three main outcome measures: (a) the Psychotic Symptom Rating Scale (PSYRATS), hallucination section; (b) the Omnipotence and Malevolence subscales of Revised Beliefs About Voices Questionnaire (BAVQ-R); and (c) the Calgary Depression Scale (CDS). The control group showed showed no change over time in their scores on three assesments, whereas the novel therapy group showed mean reductions in total PSYRATS score (auditory hallucinations) of 8.75 (P=0.003) and in the BAVQ-R combined score of omnipotence and malevolence of the voices of 5.88 (P=0.004). There was no significant reduction in the CDS total score for depression. For the crossover group, comparison of the period of the*

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TAU with the period of avatar therapy confirmed the findings of the previous analysis. The effect size of therapy was 0.8. Avatar therapy represents a promising treatment for medication resistant auditory hallucinations."

Virtual Reality for Treatment of Schizophrenia

De Costa RM. The acceptance of virtual reality devices for cognitive rehabilitation: a report of positive results with schizophrenia. *Comput Methods Programs Biomed* 2004 Mar;73(3):173-82

- *"The subjects that participated in this experiment accepted to work with computers and immersive glasses and demonstrated a high level of interest in the proposed tasks. No problems of illness have been observed."*

Virtual Reality for Paranoia

Fornells-Ambrojo M. Virtual reality and persecutory delusions: safety and feasibility. *Schizophr Res* 2008 Sep; 104(1-3):228-36

- *"Exposure to social situations using VR has the potential to be incorporated into cognitive behavioral interventions for paranoia."*

Computer-assisted Attention Training for Schizophrenia

Hermanutz M. Computer-assisted attention training in schizophrenics. A comparative study. *Eur Arch Psychiatry Clin Neurosci*

- *"The evaluation of computer-assisted attention training program is compared with cognitive group training program. Both programs were devised to reduce cognitive deficits in schizophrenics. Both were shown to be effective in reducing distraction of schizophrenics in reaction-time tasks. By the means of training, schizophrenics may attain the same results in reaction time tasks as healthy individuals."*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Exposure Control of Chronic Auditory Hallucinations in Schizophrenia

Persaud R. A pilot study of exposure control of chronic auditory hallucinations in schizophrenia. *Br J Psychiatry* 1995 Jul;167(1):45-50

- *“Many patients complain less of their auditory hallucinations per se than of lack of control of the experiences. There is reason to believe that a non-distraction (exposure) approach could help patients gain more control over persistent auditory hallucinations and teach them that their experience is a form of thinking and has no external source. This study is a pilot test of that idea. Five DSM-III-R schizophrenic outpatients with medication-resistant auditory hallucinations improved with a mean of 31 hour-long sessions over 3 months of therapist-guided exposure to their hallucinations and situations likely to evoke them. Improvement was the greatest in the patients anxiety and sense of control over their hallucinations, less in social use of leisure and hallucinating time. These mildly encouraging pilot results warrant a controlled study of exposure for drug-resistant chronic auditory hallucinations and other psychotic experiences which are associated with anxious avoidance.”*

Bright Light Therapy for Schizophrenia

Aichhorn W. Bright light therapy for negative symptoms in schizophrenia: a pilot study. *J Clin Psychiatry* 2007 Jul;68(7):1146

- *“Bright light therapy was safe in our patients and did not result in psychotic exacerbation, as seen in unchanged positive scores on the PANSS. The subjective improvement in drive was statistically significant after 4 weeks, but did not persist after discontinuation of bright light therapy.”*

Heim M. Bright light therapy in schizophrenic diseases. *Psychiatr Neurol Med Psychol (Leipz)* 1990 Mar;42(3):146-50

- *“20 patients with schizophrenic disorders, displaying a depressive syndrome, were given bright-light therapy, and compared with 11 patients treated by means of partial deprivation of sleep. Against a figure of 27% in the case of sleep-deprivation, syndrome remittance was 55% in the case of bright-light therapy. As depressive syndromes improve under bright-light therapy, schizophrenic syndromes also recede, which suggests close syndromatologic links....”*

Oren D. Bright Light Therapy for Schizoaffective Disorder. Am J Psychiatry 158:12, December 2001

- *“Bright light therapy proved comparable or superior to treatment with previous medications for depression for this patient.”*

Hyperbaric Oxygen Treatment for Schizophrenia

Kutko II. The use of hyperbaric oxygenation in treating mental patients resistant to psychopharmacotherapy. Zh Nervol Psikhaitr Im S S Korsakova 1996;96(5):47-51

- *“A positive clinical effect was marked in 72.5% of cases (in 67.4% of schizophrenic patients and in 77.4% of patients with vascular disease).”*

Isakov IuV. Clinical effectiveness of hyperbaric oxygenation in the combined treatment of patients with schizophrenia. Zh Nevropatol Psikhiatr Im S S Korsakova 1987;87(12):1832-5

- *“The maximum therapeutic effect was observed after 10-12 sessions”*

CPAP for Negative Symptoms and Remission of Auditory Hallucination in Schizophrenia

Sugishita K. Continuous positive airway pressure for obstructive sleep apnea improved negative symptoms in patient with schizophrenia. Psychiatry and Clinical Neurosciences 2010;64:663-667

- *“The present case report is in line with previous reports, including a patient with delusional schizophrenia showing improvement of negative symptoms and a case of hebephrenic schizophrenia showing complete remission of auditory hallucinations after successful treatments of OSA with CPAP.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Vestibular Stimulation Improves Schizophrenic Behavior

Baker G. Vestibular stimulation with autistic and schizophrenic children. 14(4) 1977 434-5

- *“ Behavior changes such as increased awareness, increased eye contact and verbalization, and decrease of self-destructive behaviors were also observed in the experimental group. The hypothesis was supported that vestibular stimulation can lower the threshold for vestibular activation to improve system functioning.”*

Effectiveness of Spiritual Emotional Freedom Technique (SEFT) in Schizophrenia

Puspitaningrum Ike. Effectiveness of spiritual emotional freedom technique (SEFT) intervention in schizophrenia with depression anxiety stress. Nursing Intervention, Complementary and Alternative Therapy, In JAVA International Nursing Conference 2012 October 6-7, Semarang

- *The results of statistical tests concluded that the variables had a significant result (0.017). It can be concluded that SEFT intervention was effective to reduce depression anxiety stress levels in patients with schizophrenia.”*

Application of Autogenic Training to Schizophrenic Patients

Shibata J. The application of autogenic training to a group of schizophrenic patients. The American Journal of Clinical Hypnosis, Volume X, Number 1, July 1967

- *“ The progress of the Standard Exercises of the Autogenic Training program in 65 schizophrenic patients was favorable, being the same as for normal persons, the patients learning them in about two months and being able to proceed on to the Meditation Exercises. All patients progressed favorably during the Standard Exercises, but after proceeding on to the Meditation Exercises there were several patients whose symptoms aggravated.”*

Shibata J. Clinical evaluation with psychological tests of schizophrenic patients treated with autogenic training. *The American Journal of Clinical Hypnosis*, Volume X, Number 1, July 1967

- *“What we can say from the results of the psychological tests alone, is that evidently we can obtain good results in some recuperating schizophrenic patients who take up AT as a medium for rehabilitation.”*

Neurofeedback for Schizophrenia

Surmeli T. Schizophrenia and efficacy of qEEG-guided neurofeedback treatment: clinical case series. *Clin EEG Neurosci* 2012 Apr;43(2):133-44

- *“Changes in PANSS, MMPI, and TOVA were analyzed to evaluate the effectiveness of NF treatment. The mean number of sessions completed by the participants was 58.5 sessions within 24 to 91 days. Three dropped out of treatment between 30 and 40 sessions on NF, and one did not show any response. Of the remaining 48 participating 47 showed clinical improvement after NF treatment, based on changes in their PANSS scores. The participants who were able to take the MMPI and the TOVA showed significant improvements in these measures as well. Forty were followed up for more than 22 months, 2 for 1 year, 1 for 9 months, and 3 for between 1 and 3 months after completion of NF. Overall NF was shown to be effective.”*

Bolea AS. Neurofeedback Treatment of Chronic Inpatient Schizophrenia. *Journal of Neurotherapy: Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience*, Volume 14, Issue 1, 2010

- *“ This is a study on the effect of neurofeedback on chronic inpatient complex paranoid schizophrenics. The purpose of this research was twofold: first, to determine the effects of the application of neurofeedback to very chronic cases of schizophrenia that had been resistant to years of inpatient medical and psychological treatment and second, to propose a connection paradigm of schizophrenia. The author obtained progress using affective neurofeedback with more than 70 hospital in patients with chronic schizophrenia. Improvements were seen in the EEG patterns and in cognitive, affective and behavioral patterns that often resulted in successful release from the hospital to live in the community. A 2-year follow up found that positive changes were sustained. It is the authors impression that reinforcement of right parietal alpha and inhibiting frontal delta and fast beta activity obtained the best results.”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Neurofeedback Treatment to Enhance Cognitive Performance in Schizophrenia

Rocha N. Neurofeedback treatment to enhance cognitive performance in Schizophrenia.
Porto 17-18 June 2011

- *“Following treatment, patients showed evidence of improved performance in different cognitive measures. The most important and consistent increases were observed in attention/vigilance, working memory and processing speed. We also observed changes in EEG patterns during the treatment, suggesting a learning effect. Patients were very collaborative during the treatment sessions and showed increased interest in their performance. Results from this exploratory study support the feasibility of using neurofeedback to enhance cognition in schizophrenia, but this method should not be considered alone for this purpose.”*

Biofeedback for Schizophrenia

Pharr OM. The use and utility of EMG biofeedback with chronic schizophrenic patients.
Biofeedback Self Regul 1989 Sept;14(3):229-45

- *“On the nurses observation scale for inpatient evaluation the biofeedback group significantly improved on the Social Competence and Social Interest factors”*

Schneider SJ. Neuroleptic-like electroencephalographic changes in schizophrenics
through biofeedback. Biofeedback Self Reg 1982 Dec;7(4):479-90

- *“The results suggest that the EEG of schizophrenics can be temporarily altered, using feedback techniques, in a way that mimics the EEG changes that have been shown to occur with neuroleptic induced clinical improvement*

Biofeedback for the Treatment of Polydipsia in Schizophrenia

Walter G. A "biofeedback" approach to the treatment of chronic polydipsia. *J Behv Ther Exp Psychiatry* 1993 Sep;24(3):225-9

- *"The patient showed substantially increased sodium concentration, which was maintained despite the withdrawal of feedback. This behavioral method appears promising in settings where restriction of fluid intake is not practical or ethical."*

Anxiety Reduction in Schizophrenia through Thermal Biofeedback and Relaxation Training

Hawkins RC 2nd. Anxiety reduction in hospitalized schizophrenics through thermal biofeedback and relaxation training. *Percept Mot Skills* 1980 Oct;51(2):475-82

- *"The present study investigated the efficacy of thermal biofeedback and relaxation as adjunctive treatments to antipsychotic medication for reduction of anxiety in 40 hospitalized schizophrenics who were randomly assigned to four groups: biofeedback, relaxation, biofeedback and relaxation, and minimal treatment control. Significant reduction in anxiety followed treatment, but there were no between-group differences. One year follow-up and post hoc analyses indicated a subgroup of "anxious" schizophrenics who showed substantial reduction in anxiety following treatment with biofeedback and relaxation."*

Energy Healing as a Complementary Treatment for Paranoid Schizophrenia

Chhibber K. Energy healing as a complementary treatment for paranoid schizophrenia: A case report. 141st APHA Annual Meeting (November 2-November 6, 2013) APHA 2013

- *"Energy Healing Treatments: The subject received 4 energy healing treatments daily for a period of 16 weeks, consisting of both Pranic healing and Reiki. Additional treatments were administered as necessary, when hallucinations or abnormal behavior persisted. Results: Subject noted feelings of lightness, with sustained periods of calmness and coherence. The subjects mother/father also observed changes in mood and behavior, including increased responsiveness and social proclivity. Hallucinations and erratic behavior diminished in frequency and magnitude. Physician recommended lowering dosage of main antipsychotic based on observations. The subject continues to exhibit improvement. These results indicate Energy healing to be a potent and effective method of complementary therapy for schizophrenia."*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Bioenergetics Therapy for Negative Symptoms of Schizophrenia

Rohricht F. Effect of body-oriented psychotherapy on negative symptoms in schizophrenia: a randomized controlled trial. *Psychol Med* 2006 May;36(5):669-78

- *“ Patients receiving BPT attended more sessions and had significantly lower negative symptom scores after treatment (PANSS negative, blunted affect, motor retardation). The differences held true at 4 month follow-up. Other aspects of psychopathology and subjective quality of life did not change significantly in either group. Treatment satisfaction and ratings of the therapeutic relationship were similar in both groups. BPT may be an effective treatment for negative symptoms in patients with chronic schizophrenia.”*

Acupuncture for Schizophrenia

Lee MS. Acupuncture for schizophrenia: a systematic review and meta-analysis. *Int J Clin Pract* 2009 Nov;63(11):1622-33

- *“Thirteen RTC’s, all originating from China, met the inclusion criteria. One RTC reported significant effects of electro-acupuncture plus drug therapy for improving auditory hallucinations and positive symptoms compared to sham EA plus drug therapy. Four RTCs showed significant effects of acupuncture for response rate compared with antipsychotic drugs. Seven RTCs showed significant effects of acupuncture plus antipsychotic therapy for response rate compared with antipsychotic drug therapy. Two RTCs tested laser acupuncture on hallucinations against sham laser acupuncture. One RTC found beneficial effects of laser acupuncture on response rate, Brief Psychiatric Rating Scale and clinical global index compared with sham laser.”*

Auricular Acupuncture for the Treatment of Auditory Hallucinations

Shi Zx. Observation on the curative effect of 120 cases of auditory hallucination treated with auricular acupuncture. *Journal of Traditional Chinese Medicine* , 9(3): 176-178, 1989

- *“We have treated auditory hallucination with different kinds of psychosis, mainly using auricular acupuncture and yielding certain cumulative effect. We also noted there is no significant difference in curative effects among groups of simple auricular acupuncture, auricular plus body acupuncture and auricular acupuncture plus chlorpromazine. Therefore, we recommend auricular acupuncture for treating hallucinations.”*

Electroacupuncture for Treatment of Schizophrenia

Jing Cheng. Electro-acupuncture verses sham electro-acupuncture for auditory hallucinations in patients with schizophrenia: a randomized controlled trial. Clin Rehabil 2009 Jul;(7):579-88

- *“The clinical response rates in electro-acupuncture and sham electro-acupuncture group were 43.3% and 13.3% respectively.”*

Feng-Ju Y. Short-term curative effect of electroacupuncture as adjunctive treatment on schizophrenia. Zhongguo Zhong Xi Yi Zhi 2006 Mar;26(3):253-5

- *“With effect equal to CZ (clonzapine), combination of CZ and EA shows higher compliance in treating schizophrenia....*

Zhuge DY . Comparison between electro-acupuncture with chlorpromazine and chlorpromazine alone in 60 schizophrenic patients. Zhongguo Zhong Xi Yi Jie He Za Zhi 1993 Jul;13(7):408-9,388

- *“The result showed the total curative effects of the two groups were similar. However, the marked effects appeared earlier in combined therapy than using chlorpromazine alone, less chlorpromazine was needed.”*

Shiatsu Therapy for Schizophrenia

Lichtenberg P. Shiatsu as an adjunctive therapy for schizophrenia: an open-label pilot study. Altern Ther Health Med 2009 Sep-Oct;15(5):44-6

- *“On the scales of psychopathology and side effects, the subjects showed a statistically and clinically significant improvement by the end of treatment. This improvement was maintained at the 12 week follow-up.”*

Hypnosis for Schizophrenia

Izquierdo de S. Hypnosis for Schizophrenia. Cochrane Database Syst Rev. 2007 Oct;17(4):CD004160

- *“Hypnosis could be helpful for people with schizophrenia”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Abrams S. Short-term hypnotherapy of a schizophrenic patient.

- *“The only generalization that can be made from this study is that hypnotherapy may be a highly successful technique with some schizophrenic patients; but whether this is a method that might be of value for schizophrenia in general remains inconclusive. ”*

Abrams S. The use of hypnotic techniques with psychotics. American Journal of Psychotherapy

- *“The case histories of psychotics treated by hypnotic methods point up the value of this treatment modality. Some patients improved with hypnotherapy after other therapeutic techniques had failed, and other patients with long-term illness dramatically recovered when hypnosis was employed. This would strongly suggest that hypnotherapeutic methods may be valuable tool for the treatment of specific psychotic disorders.*

Yoga for Better Clinical Outcome in Schizophrenia

Vancampfort D. State anxiety, psychological stress and positive well-being responses to yoga and aerobic exercise in people with schizophrenia: a pilot study. Disabil Rehabil 2011;33(8):684-9

- *“After single sessions of yoga and aerobic exercises individuals with schizophrenia or schizoaffective disorder showed significantly decreased state anxiety, decreased psychological stress and increased subjective well-being compared to no exercise control.”*

Visciglia E. Yoga therapy as an adjunctive treatment for schizophrenia: a randomized, controlled pilot study. J Altern Complement Med 2011 Jul;17(7):601-7

- *“The YT group obtained significant improvements in positive and negative symptoms of schizophrenia symptoms compared to WL, including PANSS scores on positive syndrome, negative syndrome, general psychopathology. Activation, paranoia, and depression subscales. YT had improved perceived quality of life in physical and psychological domains.”*

Duraiswamy G. Yoga therapy as an add-on treatment in the management of patients with schizophrenia-a randomized controlled trial. Acta Psychiatr Scand 2007 Sep;116(3):226-32

- *“Subjects in the YT group had significantly less psychopathology than those in the PT group at the end of four months”*

Effect of Yoga Therapy on Facial Emotion Recognition Deficits in Schizophrenia

Behere RV. Effect of yoga therapy on facial emotion recognition deficits, symptoms, and functioning in patients with schizophrenia. Acta Psychiatr Scand 2011 Feb;123(2):147-53

- *“There was a significant positive correlation between baseline FERD and socio-occupational functioning ($r=0.3$, $P=0.01$). Paired samples t test showed significant improvement in positive and negative symptoms, socio-occupational functioning and performance on TRENDS ($P<0.05$) in the Yoga group., but not in the other two groups. Maximum improvement occurred at the end of 2 months, and improvement in positive and negative symptoms persisted at the end of 4 months.”*

Bibliotherapy for Schizophrenia

Alexander RH. Bibliotherapy with chronic schizophrenics. J Rehabil 1967 Nov-Dec;33(6):26-7

- *‘Bibliotherapy should continue to play an increasingly important function in the rehabilitation of chronic schizophrenics. Schizophrenic persons have shown ready response to the reality approach of bibliotherapy when it is presented in an interesting and challenging manner by a skilled therapist. With careful professional guidance bibliotherapy can provide a significant “first step” in the rehabilitation of mental patients to become interacting members of society. A significant finding of the study of which the above is a resume and one which the study was not aimed at, is that with the application of bibliotherapy , a group of chronic schizophrenic patients under going drug therapy can learn to consistently perform tasks heretofore considered beyond their ability.’*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Mindfulness for Schizophrenia

Chadwick P. Mindfulness groups for distressing voices and paranoia: a replication and randomized feasibility trial. *Behav Cogn Psychother* 2009 Jul;37(4):403-12

- *“Secondary analysis combining both groups and comparing scores before and after mindfulness training revealed significant improvement in clinical functioning and mindfulness of distressing thoughts and images.”*

Newman TK. Impact of mindfulness on cognition and effect in voice hearing: evidence from two case studies. *Behav Cogn Psychother* 2009 Jul;(4):397-402

- *“Findings show that mindfulness training has an impact on cognition and affect specifically associated with voices, and thereby beneficially alters relationship with voices.”*

Deckersbach T. Mindfulness-based cognitive therapy for nonremitted patients with bipolar disorder. *CNS Neurosci Ther* 29=012 Feb;18(2):133-41

- *“These findings suggest that treating residual mood symptoms with MBCT may be another avenue to improving mood, emotion regulation, well being, and functioning in individuals with bipolar disorder.”*

Mindfulness for Treatment of Auditory Hallucinations and Improvement of Cognition

Newman Taylor K. Impact of mindfulness on cognition and affect in voice hearing: evidence from two case studies. *Behav Cogn Psychother* 2009 Jul;37(4):397-402

- *“Findings show that mindfulness training has an impact on cognition and affect specifically associated with voices, and thereby beneficially alters relationship with voices.”*

Mindfulness for Paranoid Beliefs

Ellett L. Mindfulness for paranoid beliefs: evidence from two case studies. Behav Cogn Psychother 2013 Mar;41(2):238-42

- *“Findings suggest that mindfulness training can impact on cognition and affect specifically associated with paranoid beliefs, and is potentially relevant to both Poor Me and Bad Me paranoia.”*

Treating Trauma in Schizophrenia with EMDR

David P.G. van den Berg. Treating trauma in Psychosis with EMDR: A pilot study. J Behav Ther & Exp Psychiat 43 (2012): 664-671

- *“The results of this open trial show that it is effective and safe to treat posttraumatic stress disorder using eye movement desensitization and reprocessing. Moreover treating posttraumatic stress disorder has a positive effect on other symptoms. Auditory verbal hallucinations, delusions, anxiety, and depression decrease. Self-esteem also improves. Although treatment can definitely produce some stress for a small minority of the subjects, as it does in other patients with posttraumatic stress disorder, it is generally safe and does not lead to adverse events.”*

Morita Therapy for Schizophrenia

Li C. Morita therapy for schizophrenia. Schizophrenia Bulletin vol. 34, no. 6, pp1021-1023, 2008

- *“Morita therapy may have some positive effects, but there are no data to assess whether this sustained. For schizophrenia, therefore, Morita therapy remains an experimental intervention.”*

Physically Oriented Therapy for Schizophrenia

Rohricht F. Ego-pathology, body experience, and body psychotherapy in chronic schizophrenia.

Psychol Psychother 2009 Mar;82(Pt 1):19-30

- *“In patients with chronic schizophrenia, body oriented psychological interventions may be effective for both positive therapeutic changes in ego-pathology and negative symptoms...”*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Andres K. Empirical study of a physically oriented therapy with schizophrenic patients. *Z Klin Psychol Psychopathol Psychother* 1993;41(2):159-69

- *“The study shows that this body-oriented therapy is a worthy consideration as a method for giving schizophrenic patients a greater awareness of their own body limits”*

Sex Education for Schizophrenia

Lukoff D. Sex education and rehabilitation with Schizophrenic male outpatients. *Schizophrenia Bull.* Vol 12, No. 4. 1988

- *“A sex education program for recent-onset male schizophrenic patients attending an outpatient clinic was developed in response to several incidents involving patients inappropriate sexual behaviors. To enhance our current understanding of the sexual function and needs of these patients, sex histories, were taken. Almost all of the 16 patients interviewed were sexually active, with autoerotic activity predominating. Sixty-three percent of the patients reported orgasmic and/or erectile dysfunctions. Other studies have linked sexual dysfunction to the side effects of antipsychotic medications. The objectives of the sex education program were: (1) to provide information; (2) to clarify values (3) to overcome sexual dysfunction; and (4) to enhance intimacy skills. The authors used role playing, modeling, group exercises, and explicit sex therapy audiovisual material to improve patients intimacy skills. Patients participated actively and used the group to explore sexual issues. No exacerbations of symptoms were observed among patients participating in the program.”*

Music Therapy for Diminishing Schizophrenic Symptoms

Na HJ. Effects of listening to music on auditory hallucinations and psychiatric symptoms in people with schizophrenia. *J Korean Acad Nurs* 2009 Feb;39(1):62-71

- *“...listening to music may be useful for managing auditory hallucinations in schizophrenic inpatients.*

Ulrich G. The additional effect of group music therapy for schizophrenic patients: a randomized study. *Acta Psychiatr Scand* 2007 Nov;116(5):362-70

- *“Musical activity diminishes negative symptoms and improves interpersonal contact.”*

Tang W. Rehabilitative effect of music therapy for residual schizophrenia. A one-month randomized controlled trial in Shanghai. *Br J Psychiatry Suppl* 1994 Aug;24:38-44

- *“Music therapy significantly diminished patients negative symptoms, increasing their ability to converse with one another.”*

Gold C. Music therapy for schizophrenia-like illnesses. *Cochrane Database Syst Rev* 2005 Apr 18;(2):CD004925

- *“Music therapy as an addition to standard care helps people with schizophrenia to improve their global state and may also improve mental state and functioning if sufficient number of music sessions are provided.”*

Art Therapy for Schizophrenia

Tegibaerg HS. Art therapy may reduce psychopathology in schizophrenia by strengthening the patients sense of self: a quantitative extended case report. *Psychopathology* 2011;44(5):314-8

- *“The most important benefit of the art therapy was a strengthening of the patients’ sense of self. All patients reported a good outcome, and qualitative analysis showed that the positive effect of art therapy is mainly due to a strengthening of patients’ minimal sense of self.”*

Ruddy R. Art therapy for schizophrenia or schizophrenia-like illnesses. *Cochrane Database Syst Rev* 2005 Oct 19;(4):CD003728

- *“Data from one mental state measure (SANS) showed a small but significant difference favoring the art-therapy group.a measure of social functioning (SFS) showed no clear difference between groups in endpoint scores and in quality of life, as measured by PerQol, did not indicate the effects of art therapy.”*

Noronha KJ. Working with Art in a Case of Schizophrenia. *Indian J Psychol Med.* 2013 Jan-Mar; 35(1):89-92

- *“This study used art as a therapeutic tool in therapy with a client diagnosed with schizophrenia, along with medical management. The purpose of using art was to enable the non-communicative client to communicate. The clients drawings were used as a process medium. Progress was seen in changes in social behaviors and communication evidenced by him speaking more, expressing feelings and gaining better insight.*

Alternative and Complementary Treatments for Extrapyramidal Symptoms, Schizophrenia, and Bipolar Disorder

Effect of Humorous Movies on Schizophrenics

Gelkopf M. The effect of humorous movies on inpatients with chronic schizophrenia. *J Nerv Ment Dis* 2006 Nov;194(11):880-3

- *“Reduced levels of psychopathology, anger, anxiety, and depression symptoms and improvement in social competence were revealed in the study group.”*

Gelkopf M. Therapeutic use of humor to improve social support in an institutionalized schizophrenic inpatient community. *J Soc Psychol* 1994 Apr;134(2):175-82

- *“We concluded that the positive atmosphere that humor creates affects the therapeutic alliance between staff and patients but does not affect other social networks because of the regressed nature of schizophrenic social relationships.”*

The Use of Humor with Chronic Schizophrenic Patients

Witztum E. The use of humor with chronic schizophrenic patients. *Journal of Contemporary Psychotherapy*, Volume 29, Number 3, 1999, pp 223-234 (12)

- *“ The use of humorous therapeutic approach combined with drug therapy in the treatment of chronic schizophrenia patients institutionalized for prorated periods of time led to positive changes in their symptoms. The majority of the patients responded well to humorous interpretations. The patients felt that they had the option of adopting the doctors humors manner. This approach appealed to them and raised self-esteem; they likewise gained confidence in their own ability to form judgments. They cooperated better with the doctor in issues pertaining to treatment. The fact that humor made an impact on the patients cognition was evaluated according to the BPRS scale, before the treatment, on a monthly basis during the treatment, and three months upon the completion of the experiment. In the course of the experiment, pharmacological treatment remained unchanged. On average, a perceptible reduction in the BPRS value ($p<.05$) was detected as a result of humor therapy. Amusing representations of affective external stimuli were incorporated into the patients cognition and, along with a newly gained awareness of the possibility of relating to them with humor, were retained long after the termination of the project.”*

Progressive Muscle Relaxation for Schizophrenia

Chen WC . Efficiency of progressive muscle relaxation training in reducing anxiety in patients with acute schizophrenia. J Clin Nurs 2009 Aug;18(15):2187-96

- *“This study demonstrated that progressive muscle relaxation can effectively alleviate anxiety in patients with schizophrenia”*

Vancampfort D. Effects of progressive muscle relaxation on state anxiety and subjective well-being in people with schizophrenia. Clin Rehabil 2011 Jun;25(6):587-75

- *“Progressive muscle relaxation is highly effective in reducing acute feelings of stress and anxiety in patients with schizophrenia.”*

Dance Movement Therapy for Schizophrenia

Xia J. Dance therapy for schizophrenia. Cochrane Database Syst Rev 2009 Jan 21;(1):CD006868

- *“At the end of treatment significantly more people in dance therapy group had a greater than 20% reduction in PANSS negative symptom score, and overall average endpoint scores were lower. There is no evidence to support-or refute-the use of dance therapy in this group of people”*

Application of the Primitive Expression Form of Dance Therapy in Psychotic Patients

Margariti A. An application of the Primitive Expression form of dance therapy in a psychiatric population. The Arts in Psychotherapy 39 (2012) 95-101

- *“In this paper we present preliminary results of PE-based protocol with a small group of psychiatric patients (psychotic and depressive disorders). It is shown that a relatively short duration of PE treatment led to observable changes in psychological state, behavior, and brain physiology. It was found that the patients (1) experienced an increase in their happiness level, (2) expressed a positive attitude to the PE process by utilizing appropriate word associations, and (3) exhibited (a patient subset) an increase in EEG activity related to relaxed awake state. The study presents encouraging results related to the application of PE therapy with psychiatric patients. PE can be added to other dance therapy methodologies which have been shown to be promising therapeutic approaches in psychiatric populations.”*

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Tai-Chi for Movement Coordination and Interpersonal Functioning in Schizophrenia

Rainbow TH. Ho. Tai-Chi for residential patients with schizophrenia on movement coordination, negative symptoms, and functioning: A pilot randomized controlled trial. Evidence-Based Complementary and Alternative Medicine, Volume 2012

- *“Tai-Chi buffered from deteriorations in movement coordination and interpersonal functioning, the latter with sustained effectiveness 6 weeks after the class was ended. Controls showed marked deteriorations in those areas, The Tai-chi group also experienced fewer disruptions to life activities at the 6-week maintenance. There was no significant improvement in negative symptoms after Tai-chi. The study demonstrated encouraging benefits of Tai-chi in preventing deteriorations in movement coordination and interpersonal functioning for residential patients with schizophrenia. The ease of implementation facilitates promotion at institutional psychiatric services.”*

Qigong as a Mindful Exercise for Schizophrenia

Lloyd C. Qigong as a mindful exercise intervention for people living with mental ill health. International Journal of Therapy and Rehabilitation, 16 (7), 393-399

- *“It is suggested that mindful exercise may be used as an intervention to assist people living with mental ill health to improve their community functioning and hence their recovery.”*

Exercise Therapy for Schizophrenia

Gorczyński P. Exercise therapy for schizophrenia. Cochrane Database Syst Rev 2010 May 12;(5):CD004412

- *“.....results indicated that regular exercise programs are possible in this population, and that they can have healthful effects on both the physical and mental health and well-being of individuals with schizophrenia”*

Sports in the Treatment of Schizophrenic Patients

Langle G. Role of sports in the treatment and rehabilitation of schizophrenic patients. *Rehabilitation (Stuttg)*. 2000 Oct;39(5):276-82

- *“Sports activities as part of the care of chronically ill psychiatric patients are effective as well as cost-effective and should receive more attention in both practice and research.”*

Takahashi H. Effects of sports participation on psychiatric symptoms and brain activations during sports observation in schizophrenia. *Translational Psychiatry* (2012) 2, e96

- *“Compared with baseline, activation of the body-selective extrastriate body area (EBA) in the posterior temporal-occipital cortex during observation of sports related actions was increased in the program group. In this group, increase in EBA activation was associated with improvement in general psychopathology scale of PANSS. Sports participation had a positive effect not only on weight gain but also on psychiatric symptoms in schizophrenia. EBA might mediate these beneficial effects of sports participation. Our findings merit further investigation of neurobiological mechanisms underlying the therapeutic effect of sports for schizophrenia.”*

Audio Hallucinations Treated with Radio Headphones

Feder R. Auditory hallucinations treated by radio headphones. *Am J Psychiatry* 1982 Sep;139(9):1188-90

- *“Listening to a radio through stereo headphones in conditions of low auditory stimulation eliminated the patients hallucinations.”*

Auditory Hallucinations Treated with Personal Stereo

Johnston O. The efficacy of using a personal stereo to treat auditory hallucinations. *Behav Modif* 2002 Sep;26(4):537-49

- *“The personal stereo led to a decrease in severity of O.C.’s auditory hallucinations. A slight decrease in other psychopathology also occurred during personal stereo stages.”*

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Radio in the Treatment of Auditory Hallucinations

Mallya AR. Radio in the treatment of auditory hallucinations. *Am J Psychiatry* 1983 Sep;140(9):1264-5

- *“From 1976 to 1981 he did well receiving 40mg/day of fluphenazine hydrochloride and 6 mg/day of trihexyphenityl. In 1981 his disability benefit was terminated and the financial stress increased his hallucinations, but the neurologist warned against the increase of neuroleptics for fear of worsening his parkinsonism. The patient was advised to buy a pair of headphones to control his hallucinations. The relief was so dramatic that the patient bought a Sony Walkman. However, when he takes off the headphones, auditory hallucinations recur immediately.”*

Audiotape Therapy for Persistent Auditory Hallucinations

McInnis M. Audiotape therapy for persistent auditory hallucinations. *Br J Psychiatry* 1990 Dec; 157:913-4

- *“We report a case of a man with recurrent depression and persistent second-person auditory hallucinations telling him to kill himself. Using an audiotape cassette and headphones the duration of the hallucinations decreased significantly. Helpfulness of the audiotape continued at 15 months follow-up.”*

Animal-assisted Therapy for Schizophrenia

Nathans-Barel I. Animal-assisted therapy ameliorates anhedonia in schizophrenia patients. A controlled pilot study. *Psychother Psychosom* 2005;74(1):31-5

- *“The AAT group showed a significant improvement in the hedonic tone compared to controls. They also showed an improvement in the use of leisure time and a trend towards improvement in motivation.. AAT may contribute to the psychosocial rehabilitation and quality of life of chronic schizophrenia patients.”*

Kovacs Z. An exploratory study of the effect of animal-assisted therapy on nonverbal communication in three schizophrenic patients. *A Multidisciplinary Journal of the Interactions of People & Animals*, 1 December 2006, vol.19, no.4, pp353-364(12)

- *“The therapy was oriented toward improving non-specific (i.e., general well being) and specific (i.e., communication patterns) areas of the patient’s daily activities. The outcome measure was the change in the patient’s nonverbal communication, as measured by analysis of standardized, video-recorded scenarios registered at the beginning of the therapy, and six months later, and the end of it. Because two patients completed less than half of the sessions, we analyzed the data of only three parameters. All three patients improved in the usage of space during communication, while partial improvement in other domains of nonverbal communication (anatomy of movements, dynamics of gestures, regulator gestures) was also observed. Animal-assisted therapy can improve certain aspects of nonverbal communication in schizophrenic patients.”*

Barak Y. Animal-assisted therapy for elderly schizophrenic patents: a one-year controlled trial. *Am J Geriatr Psychiatry* 2001 Fall;9(4):439-42

- *“The authors evaluated, in a blinded, controlled manner, the effects of AAT in a closed psychogeriatric ward over 12 months. Subjects were 10 elderly schizophrenic patients and 10 matched patients (mean age: 79.1 +/-6.7 years). The outcome measure was the Scale for Social Adaptive Functioning Evaluation (SAFE). AAT was conducted in weekly 4-hour sessions. Treatment encouraged mobility, interpersonal contact, and communication and reinforced activities of daily living (ADLs), including personal hygiene and independent self-care, through the use of cats and dogs as “modeling companions.” The SAFE scores at termination showed significant improvement compared with baseline scores and on the Social Functions subscale. AAT proved a successful tool for enhancing socialization, ADLs, and general well-being.”*

Animal-assisted Therapy with Farm Animals for Persons with Schizophrenia

Berget B. Animal-assisted therapy with farm animals for persons with psychiatric disorders: effects on self-efficiency, coping ability and quality of life, a randomized controlled trial. *Clinical Practice and Epidemiology in Mental Health* 2008, 4:9

- *“AAT with farm animals may have positive influences on self-efficiency and coping ability among psychiatric patients with long lasting psychiatric symptoms.”*

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Alternative and Complementary Treatments for Bipolar Disorder

Successful Treatment of Bipolar Disorder with Micronutrient Formula

Ruckidge JJ. Successful treatment of bipolar disorder II and ADHD with a micronutrient formula: a case study. *CNS Specs* 2010 May;15(5):289-95

- *“After 8 weeks on the formula she showed significant improvements in mood, anxiety, and hyperactivity/impulsivity. She then chose to come off the formula; after 8 weeks her depression scores returned to baseline, and anxiety and ADHD symptoms worsened.”*

Frazier EA. Micronutrient supplement as treatment: literature review and case report of a 12-year-old boy with bipolar disorder. *J Child Adolesc Psychopharmacol* 2009 Aug;19(4):453-60

- *“EMP+ [Empower Plus] resulted in outcome superior to conventional treatment.”*

Frazier EA. Nutritional and safety outcomes from an open-label micronutrient intervention for pediatric bipolar spectrum disorders. *J Clin Adolesc Psychopharmacol* 2013 Oct;23(8):558-67

- *“In this open prospective study. Short-term use of EMP+ in children with BPSD appeared safe and well-tolerated, with a side effect profile preferable to first line psychotropic drugs for pediatric bipolar spectrum disorders.”*

Bonnie K. Effective mood stabilization with chelated mineral supplement: An open-label trial in bipolar disorder. *J Clin Psychiatry* 2001;62:936-944

- *“Some cases of bipolar illness may be ameliorated by nutritional supplementation.”*

Dermot G. Database analysis of adults with bipolar disorder consuming a micronutrient formula. *Clinical Medicine Psychiatry* 2009;4 3-16

- *“Mean symptom severity was 41% lower than baseline after 3 months (effect size =0.78), and 45% lower after 6 months (effect size= 0.76) (both paired t-tests significant. P< 0.001) In terms of responder status, 53% experienced >50% improvement at 6 months .”*

Omega-3 for the Treatment of Bipolar Disorder

Sarris J. Omega-3 for bipolar disorder: meta-analyses of use in mania and bipolar depression. *J Clin Psychiatry* 2012 Jan;73(1):81-6

- *“The meta-analytic findings provide strong evidence that bipolar depressive symptoms may be improved by adjunctive use of omega-3. The evidence, however, does not support its adjunctive use in attenuating mania.”*

Omega-3 Fatty Acids Decrease Irritability in Bipolar Disorder

Sagduyu K. Omega-3 fatty acids decreased irritability of patients with bipolar disorder in add-on, open label study. *Nutrition Journal* 2005 4:6

- *“Omega-3 Fatty Acid intake helped with irritability component of patients suffering from bipolar disorder with significant presenting sign of irritability. Low dose (to 2 grams per day), add-on O-3FA may also help with the irritability component of different clinical conditions, such as schizophrenia, borderline personality disorder and other psychiatric conditions with a common presenting sign of irritability. “*

Flax Oil in the Treatment of Bipolar Disorder

Barbra GL. Randomized, placebo-controlled trial of flax oil in pediatric bipolar disorder. *Bipolar Disord* 2010 March; 12(2):142-154

- *“Although flax oil may decrease severity of illness in children and adolescents with bipolar disorder who have meaningful increases in serum EPA percent levels and/or decreased AA and DPA-n6 levels, individual variations in conversion of α -LNA to EPA and DHA as well as dosing burden favor the use of fish oil both for clinical trials and clinical practice.”*

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Inositol for Treatment of Bipolar Depression

Chengappa KN. Inositol as add-on treatment for bipolar depression. *Bipolar Disord* 2000 Mar;2(1):47-55

- *“Among 22 subjects who completed the trial, six (50%) of the inositol-treated subjects responded with a 50% of greater decrease in baseline Hamilton Depression Rating Scale (HAM-D) score and a Clinical Global Improvement (CGI) scale score change of much or very much improved, as compared to three subjects assigned to placebo, a statistically nonsignificant difference.”*

N-acetyl cysteine Add-on Treatment for Bipolar Disorder

Magalhaes PV. N-acetyl cysteine add-on treatment for bipolar II disorder: a subgroup analysis of randomized placebo-controlled trial.

- *“Fourteen individuals were available for this report, seven in each group. Six people achieved full remission of both depressive and manic symptoms in the NAC group; this was true for only two people in the placebo group.”*

Xiao Yao San Jia Wei for Improvement of Bipolar Disorder

Zhang LD. Traditional Chinese medicine typing of affective disorders and treatment. *Am J Chin Med* 1994;22(3-4):321-7

- *“The results are 26 patients with marked improvement, 17 patients with improvement, 7 patients with no improvement.”*

Adjunctive Folic Acid for Treatment of Mania in Bipolar Disorder

Behzadi AH. Folic acid efficacy as an alternative drug added to sodium valproate in treatment of acute phase of mania in bipolar disorder: a double-blind randomized controlled trial. *Acta Psychiatrica Scand* 2009 Dec;120(6):441-5

- *“Based on our findings, folic acid seems to be an effective adjunctive to sodium valproate in the treatment of the acute phase of mania in patients with bipolar disorder.”*

Curcumin in the Treatment of Bipolar Disorder

Brietzke E. Is there a role for curcumin in the treatment of bipolar disorder? Medical Hypotheses 80 (2013) 606-612

- *“Curcumin putative targets, known based on studies of diverse central nervous system disorders other than bipolar disorders (BD) include several proteins currently implicated in the pathophysiology of BD. These targets include, but are not limited to, transcription factors activated by environmental stressors and pro-inflammatory cytokines, protein kinases (PKA, PKC), enzymes, growth factors, inflammatory mediators, and anti-apoptotic proteins (Bcl-XL). Herein, we review previous studies on the anti-inflammatory and antioxidant properties of curcumin and discuss its therapeutic potential in BD.”*

Adjunctive Free and Easy Wanderer Plus for the Treatment of Bipolar Disorder

Zhang ZJ. Adjunctive herbal medicine with carbamazepine for bipolar disorders: A double-blind, randomized, placebo-controlled study. J Psychiatr Res 2007 Apr-Jun;41(3-4):360-9

- *“Compared to CBZ monotherapy, adjunctive FEWP with CBZ resulted in significantly greater improvement on depressed subjects (84.8% vs. 63.8%, $p=0.032$), but failed to produce significantly greater improvement on manic measures and the response rate in manic subjects.”*

Zhang ZJ. The beneficial effects of the herbal medicine Free and Easy Wanderer Plus (FEWP) for mood disorders: double-blind, placebo-controlled studies. J Psychiatry Res 2007 Nov;41(10):826-36

- *“Both unipolar and bipolar patients assigned to FEWP displayed significantly greater improvement on the three efficiency indices and significantly higher clinical response rate (74%) than those treated with placebo (42%) at endpoint.”*

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Melatonin for Treatment of Mania and Insomnia

Robertson JM. Case study: the use of melatonin in a boy with refractory bipolar disorder. *J Am Acad Child Adolesc Psychiatry* 1997 Jun;36(6):822-5

- *“A trial of melatonin led to rapid relief of insomnia and aborted a manic episode. He continued to take melatonin and adjunctive alprazolam for 15 months without reoccurrence of insomnia or mania.”*

Attenuation of Mania with Lecithin

Cohen BM. Lecithin in mania: A preliminary report. *Am J Psychiatry* 137:2 February 1980

- *“The design of this preliminary study does not permit definite conclusions as to the efficiency of lecithin in mania. However, the results are consistent with a beneficial effect. All subjects who received Phospholipon 100 improved rapidly, and three of four showed some worsening following withdrawal of lecithin.”*

Choline in the Treatment of Rapid-Cycling Bipolar Disorder

Stoll AL. Choline in the treatment of rapid-cycling bipolar disorder: clinical and neurochemical findings in lithium-treated patients. *Biol Psychiatry* 1996 Sep 1;40(5):382-8

- *“The study examined choline augmentation of lithium for rapid cycling bipolar disorder. Choline bitartrate was given openly to 6 consecutive lithium-treated outpatients with rapid-cycling bipolar disorder. Five patients also underwent brain proton magnetic resonance spectroscopy. Five of 6 rapid-cycling patients had a substantial reduction in manic symptoms, and 4 patients had marked reduction in all mood symptoms during choline therapy.”...“Choline, in the presence of lithium, was a safe and effective treatment for 4 of the 6 rapid-cycling patients in our series.”*

L-tryptophan for Acute Mania

Chouinard G. A controlled trial of L-tryptophan in acute mania. *Biol Psychiatry* 1985 May;20(5):546-57

- *“In a 2 week study, 24 newly admitted manic patients were treated for 1 week with L-tryptophan (12g/day); during the second week, half the patients, chosen at random, continued to receive tryptophan, while placebo was substituted in the other half under double-blind conditions. In the open phase of the study, there was a clinically and statistically (p less than 0.001) significant reduction in manic symptom scores, with little need for haloperidol prn. Patients who continued to be treated with tryptophan showed no significant change in mean scores during the second week, but those who were switched to placebo tended (p less than 0.10) to show an increase in mean scores for manic symptoms.”...“These results suggest that increasing the synthesis of 5-hydroxytryptamine has some therapeutic effect in mania.”*

Magnesium Augmentation in Mania

Giannini AJ. Magnesium oxide augmentation of verapamil maintenance therapy in mania. *Psychiatry Res* 2000 Feb 14;93(1):83-7

- *“The authors compared the antimanic effects of verapamil-magnesium (V-M) combination with verapamil-placebo combination (V-P) in patients pretreated with verapamil. BPRS scores and serum magnesium levels were compared. The V-M combination was found to be significantly more effective than V-P in reducing manic symptoms ($P=0,015$). Serum magnesium levels were significantly higher in V-M group ($P<0.04$). These data suggest that magnesium may increase antimanic efficacy of verapamil by mechanisms which may operate at the intercellular level.”*

Magnesiocard as a Mood Stabilizer for Rapid Cycling Bipolar Disorder

Chouinard G. Pilot study of magnesium aspartate hydrochloride (Magnesiocard) as a mood stabilizer for rapid cycling bipolar affective disorder patients. *Prog Neuropsychopharmacol Biol Psychiatry* 1990;14(2):171-80

- *“Nine severe rapid cycling manic-depressive patients were treated with magnesium preparation, Magnesiocard 40mEq/day in an open label study for a period up to 32 weeks.. Magnesiocard was found to have clinical results at least equivalent to those of*

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lithium in about 50% of these patients. These results were obtained in an exploratory study and should be interpreted with caution."

Treatment of Severe Manic Agitation with Intravenous Magnesium Sulphate

Heiden A. Treatment of severe mania with intravenous magnesium sulphate as supplemental therapy. *Psychiatry Res* 1999 Dec 27;89(3):239-46

- *"Ten patients with severe, therapy-resistant manic agitation received magnesium sulphate infusions with continuous magnesium (Mg) flow of approximately 200mg/h (4353+/-836mg/day;daily monitored Mg plasma level: 2.44+/-0.34 mmol/l) for periods ranging from 7 to 23 days." "Seven patients showed a marked improvement in the Clinical Global Impression Scale. In case of bradycardia detected by the ECG monitor (n=5), mg flow was reduced and bradycardia disappeared promptly. Mg i.v. may be a useful supplemental therapy for the clinical management of severe manic agitation."*

N-acetylcystein as Adjunctive Treatment in Bipolar Depression

Berk M. The efficacy of N-acetylcysteine as and adjunctive treatment in bipolar depression: an open label trial. *J Affect Disord* 2011 Dec;135(1-3):389-94

- *"In this trial, the estimated mean baseline Bipolar Depression Rating Scale (BDRS) score was 19.7 (SE=0.8), and the mean BDRS score at the end of the 8 week open label treatment phase was 11.1 (SE=0.8). This reduction was statistically significant (p<0.001). Improvements in functioning and quality of life were similarly evident. These open label data demonstrate a robust decrement in depression scores with NAC treatment."*

Berk M. N-Acetyl Cysteine for Depressive Symptoms in Bipolar Disorder—A Double-Blind Randomized Placebo-Controlled Trial. *Biol Psychiatry* 2008;64:468-475

- *"NAC appears a safe and effective augmentation strategy for depressive symptoms in bipolar disorder."*

L-Tryptophan in the Maintenance Treatment of Bipolar II Disorder

Beitman BD. L-tryptophan in the maintenance treatment of bipolar II manic-depressive illness. *Am J Psychiatry* 139:11, November 1982

- *“Although tryptophan is quite expensive and may require concomitant ascorbic acid and/or nicotinamide, it appears safe and may be considered an alternative maintenance treatment in bipolar patients who are unresponsive to or unable to take lithium. The effective dose range appears to be quite wide (2-12 g/day), which may indicate the absence of a therapeutic window.”*

Tryptophan for Treatment of Rapid-Cycling Bipolar Disorder Comorbid with Fibromyalgia

Sharma V. Tryptophan for the treatment of rapid-cycling bipolar disorder comorbid with fibromyalgia. *Can J Psychiatry* 2001 Jun;46(5):452-3

- *“Ms A is a 40-year-old lady who has presented with a history of recurrent episodes of depression since her mid-teens. She questioned the effectiveness of various treatment interventions and became increasingly frustrated with her ongoing mood instability, chronic pain condition, and poor psychosocial functioning. At this time, it was decided to prescribe a trial of tryptophan. The dosage was gradually increased over a couple of weeks to 4 g daily. She remained on lorazepam 1mg and oxazepam 25mg daily, which she had taken for years. Within 2 weeks of reaching the 4 g dosage, she developed a mixed state characterized by symptoms of feeling “revved up, “irritable, agitated, with racing thoughts, preoccupation with thoughts of suicide, and dysphroia. The tryptophan dosage was gradually lowered to 2 g, and her mood has been quite stable for a least 18 months. She continues to experience symptoms of fibromyalgia, but these are not as intense or disabling as before. She has been gainfully employed for more than 1 year and remains on the drug regimen of tryptophan 2g, lorazepam 1mg, and oxazepam 25mg daily.”*

Tryptophan for Refractory Bipolar Disorder and Sleep Phase Delay

Cooke RG. Tryptophan for refractory bipolar spectrum disorder and sleep phase delay. *J Psychiatry Neurosci* 2010;35(2)

- *“A trial of L-tryptophan, starting at a dose of 1 g in the evening was begun in June 2007, and within 3 weeks she began to report an improvement in her ability to get to sleep and*

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wake in time on the morning. Over a few more weeks, the dosage was increased to 3.5g daily combined with over -the-counter pyridoxine to limit the toxic metabolites of tryptophan. After about 10 weeks of treatment, she began to consistently arrive at work at 9 am, and her depressive symptoms cleared. Two years after L-tryptophan was initiated, she continued to show a normal sleep-wake pattern and remained free of depressive and hypomanic symptoms. She was taking no prescribed medications except L-tryptophan and pyridoxine."

Siberian Ginseng as Adjunctive Therapy for Lithium in Pediatric Bipolar Disorder

Shenhong W. Comparison of the addition of Siberian Ginseng (*acanthopanax senticosus*) versus Fluoxetine to Lithium for the treatment of bipolar disorder in adolescents: A randomized, double-blind trial. *Current Therapeutic Research*, Vol. 68 No. 4, July/August 2007

- *Our study found no significant differences in these adolescents with BD treated with lithium plus adjunctive A senticosus or fluoxetine. All treatments were generally well tolerated.*

Chromium for Treatment Resistant Rapid-Cycling Bipolar Disorder

Amann BL. A 2-year, open-label pilot study of adjunctive chromium in patients with treatment-resistant rapid-cycling bipolar disorder. *Journal of Clinical Psychopharmacology* Volume 27, Number 1 February 2007

- *"Six of 7 patients showed a reduction in the numbers of affective episodes within 1 year. The mean number of affective episodes in 7 patients before entry decreased from 6 (SD, 4.0; range, 4]5) to 2.6 (SD, 2.0; range, 0]6) after 1 year having received add-on CC. This reduction in 6 of 7 patients was also evident in the analysis of the CGI-BP. The mean overall CGI changed from 3.9 (SD, 1.4; range . 1]6) to 3.2 (SD, 1.8; range 1]6)...In general, chromium in doses up to 800 Ag/d was very well tolerated by all patients. However, some patients reported side effects, which were in general mild and did not lead to any dropout during the study."*

Citicoline Add-on Therapy for Improvement with Declarative Memory and Cocaine Use in Bipolar Disorder

Brown ES. A randomized, placebo-controlled trial of citicoline add-on therapy in outpatients with bipolar disorder and cocaine dependence. *J Clin Psychopharmacol* 2007 Oct;27(5):498-502

- *“The use of citicoline was associated with improvement relative to placebo in some aspects of declarative memory and cocaine use, but not for mood. The findings are promising and suggest that larger trials of citicoline are warranted.”*

Natural Treatment of Cognitive Impairment in Bipolar Disorder

Schrauwen E. Galantamine treatment of cognitive impairment in bipolar disorder: four cases. *Bipolar Disord* 2006 Apr;8(2):196-9

- *“This pilot case series suggests that galantamine may have some utility in improving chronic cognitive impairment in bipolar disorder.”*

Use of Branched Amino Acid Drink in Mania

Scarna A. Effects of branched-chain amino acid drink in mania. *Br J Psychiatry* 2003 Mar;182:210-3

- *“A nutritional intervention that decreases tyrosine availability to the brain acutely ameliorating’s manic symptoms.”*

Dietary Tyrosine Depletion Attenuates Symptoms of Mania

McTavish SFB. Antidopaminergic effects of dietary tyrosine depletion in healthy subjects and patients with manic illness. *Br J Psychiatry* 2001, 179:356-360

- *“We also obtained preliminary evidence that the TYR-free mixture is capable of attenuating the symptoms of acute mania. As is common in the in-patient treatment of manic illness, our subjects were receiving treatment with antipsychotic drugs at doses likely to produce a high degree of dopamine D2 receptor occupancy. Despite this, they continued to experience clinically significant manic symptomology that was diminished by tyrosine depletion.”*

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Dietary Tryptophan Depletion as Treatment for Acute Mania

Applebaum J. Rapid tryptophan depletion as a treatment for acute mania: a double blind, pilot-controlled study. *Bipolar Disord* 2007 Dec;9(8):884-7

- *“Rapid tryptophan depletion may have an antimanic effect.”*

Letter to the editor. Rapid tryptophan depletion as a treatment for acute mania: safety and mechanism of the therapeutic effect. *Bipolar Disorder* 2008 10: 850-851

- N/A

Zepf FD. Dietary tryptophan depletion according to body weight—anew treatment option in acute mania. *Med Hypotheses* 2009 Jan;72(1):47-8

- N/A

Ketogenic Diet May Have Mood Stabilizing Properties

El-Mallakh RS. The ketogenic diet may have mood stabilizing properties. *Med Hypotheses* 2001 Dec; 57(6):724-6

- N/A

Phelps JR. The ketogenic diet for type II bipolar disorder. *Neurocase* 2012 Oct 3

- *“Two womwn with type II bipolar disorder were able to maintain ketosis for prolonged peroids of time (2 and 3 years, respectively). Both experienced mood stabilization that exceeded that acheieved with medication; experienced a significant subjective improvement that was directly related to ketosis and tolerated diet well. There was no significant adverse effects in either case. These cases demonstrate that the ketogenic diet is potentially sustainable option for mood stabilization in type II bipolar illness.”*

Antidepressant Properties of the Ketogenic Diet

Murphy P. The antidepressant properties of the ketogenic diet. *Biol Psychiatry* 2004 Dec 15;56(12):981-3

- *“The rats on the ketogenic diet spent less time immobile, suggesting that the rats on a ketogenic diet, like rats treated with antidepressants are less likely to exhibit “behavioral despair”. It is concluded that the ketogenic diet has antidepressant properties.”*

Folic Acid Enhances Lithium Prophylaxis

Coppen A. Folic acid enhances lithium prophylaxis. *J Affect Disord* 1986 Jan-Feb;10(1):9-13

- *“A double-blind trial was carried out to investigate the effect the effect on affective morbidity of a daily supplement of 200 micrograms folic acid or a matched placebo in a group of 75 patients on lithium therapy. During the trial the patients with the highest plasma folate concentrations showed a significant reduction in their affective morbidity. Patients who had their plasma folate increased to 13 ng/ml or above had a 40% reduction in their affective morbidity. It is suggested that a daily supplement of 300-400 micrograms folic acid would be useful in long term lithium prophylaxis.*

Magnesium Sulfate Blocks Methylphenidate-induced Hyperlocomotion

Barbosa FJ. Magnesium sulfate and sodium valproate block methylphenidate-induced hyperlocomotion, and animal model of mania. *Pharmacol Rep* 2011;63(1):64-70

- *“The present study evaluated the effects of MgSO₄ and sodium valproate (as a positive control) on hyperlocomotion induced by methylphenidate in mice. Acute MgSO₄ (300-400mg/kg), but not sodium valproate (100-300mg/kg), prevented the increased in locomotor activity induced by methylphenidate (5.0mg/kg). “*

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Antidepressant Potentiation by 5-hydroxytryptophan

Mendlewicz J. Antidepressant potentiation of 5-hydroxytryptophan by L-deprenil in affective illness. *J affect Disord* 1980 Jun;2(2):137-46

- *“In an open label study, L-Deprenil, an irreversible selective MAO-B inhibitor without ‘cheese effect’ was given to 14 patients with unipolar and bipolar depression receiving L-5-Hydroxytryptophan (L-5-HTP) and benzerazide. Ten out of 14 patients showed a good response to the combination of drugs and correlation was found between the degree of platelet MAO inhibition and clinical response. In a double-blind controlled study, 18 affectively ill patients were randomly allocated to L-Deprenil plus L-5-HTP and benzerazide, 21 patients were treated with L-5-HTP and benzerazide and 19 patients placebo only. Patients treated with combination of L-Deprenil and L-5-HTP showed a significantly greater clinical improvement than placebo patients but this was not the case with 5-HTP alone. “*

Potentiation of Lithium by L-Tryptophan in Bipolar Disorder

Chouinard G. Potentiation of Lithium by tryptophan in patient with bipolar illness. *Am J Psychiatry* 136:5, May 1979

- *“It was decided to add L-tryptophan, 3 g p.o. b.i.d., and nicotinamide, 750mg p.o. b.i.d., to her treatment regimen...”*
- *“In this case described here, the patient had been treated with tricyclics, lithium alone, and subsequently with lithium in combination with a neuroleptic. These treatment regimens had not adequately controlled her manic or depressive symptoms or altered her cycles length. However, the addition of tryptophan-nicotinamide to lithium resulted in an almost complete remission of symptoms. The first effect was seen 7 weeks after addition of tryptophan-nicotinamide, with a reduction in the severity of the depressed phase. After 10 weeks the patient entered her first extended period of normality since the illness began 4 years ago.”*

Kampo Medicine for Manic-Depressive Psychosis

Matsuhasi T. The treatment with Kampo medicine for manic-depressive psychosis. Nihon Rinsho 1994 May;52(5):1221-5

- N/A

Non-Invasive Therapies and Treatments for Bipolar Disorder

Treatment of Bipolar Disorder with a Radioelectric Asymmetric Conveyor

Mannu P. Long-term treatment of bipolar disorder with a radioelectric asymmetric conveyor. Neuropsychiatric Disease and Treatment 2011;7 373-379

- *“REAC showed good efficacy in treating both the manic and depressive phases of bipolar disorder, and the prevention of recurrences/relapses.”*

Mindfulness for Bipolar Disorder

Weber B. Mindfulness-based cognitive therapy for bipolar disorder: a feasibility trial. Eur Psychiatry 2010)ct;25(6):334-7

- *“Most participants reported having durably, moderately to very much benefited from the program, although mindfulness practice decreased over time.change of mindfulness skills was significantly associated with change in depressive symptoms between pre- and post-MBCT assessments.”*

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Acupuncture in the Treatment of Manic Psychosis

Hu J. Acupuncture in the treatment of manic psychosis. J Tradit Chin Med 1996 Sep; 16(3):238-40

- N/A

Vestibular Stimulation for Mania

Dodson MJ. Vestibular stimulation in mania: a case report. J Neurol Neurosurg Psychiatry 2004;75:163-171

- *“This case describes an impressive and relatively sustained improvement in manic symptoms following left caloric vestibular stimulation. Caloric vestibular stimulation represents a novel approach to the treatment of mania.”*

Treatment of Mania with Ambient Air Anionization

Giannini AJ. Treatment of acute mania with ambient air anionization: variants of climatic heat stress and serotonin syndrome. Psychol Rep 2007 Feb;100(1):157-63

- *“High concentrations of ambient anions (O₂⁻) were used to augment treatment for 20 acutely manic male patients. Anions were produced by anion generator in sealed room. A double-blind crossover design was used and responses were evaluated with Brief Psychiatric Rating Scale by 2 blinded raters. This produced significant antimanic effect: total rating scores declined with anion treatment. Presham and postsham total scores for these 5 were 31.3 and 31.6, respectively. Pretreatment and posttreatment total scores were 31.6 and 26.3, respectively.”*

Effect of Negative Air Ions on Manic Patients

Misiaszek J. The calming effects of negative air ions on manic patients: a pilot study. *Biol Psychiatry* 1987 Jan;22(1):107-10

- *“The unexpected finding in this two-phase study is that seven of eight manic patients fell asleep during negative ion exposure and that six of them had to be awakened after the session was over. The short-lived calm behavior and sense of well-being following awakening may have been as much a function of sleep as of any direct effect benefit of negative ions. It is unlikely that medications accounted for the decrease in agitation.”*

Bright Light Therapy for Bipolar Disorder

Papatheodorou G. The effect of adjunctive light therapy on ameliorating breakthrough depressive symptoms in adolescent-onset bipolar disorder.

- *“These preliminary results indicate that some bipolar adolescents with breakthrough depressive symptoms could benefit from light therapy as an adjunct to their continued thymoleptic treatment.”*

Forced Bed Rest for Treatment of Rapid Cycling Bipolar Disorder

Wehr TA. Treatment of rapidly cycling bipolar patient by using extended bed rest and darkness to stabilize the timing and duration of sleep.

- *“Fostering sleep and stabilizing its timing by scheduling regular nightly periods of enforced bed rest in the dark may help prevent mania and rapid cycling in bipolar patients.”*

Dark Therapy for Mania

Barbini B. Dark Therapy for mania: a pilot study. *Bipolar Disord* 2005 Feb;7(1):98-101

- *“Adding DT to TAU [therapy as usual] resulted in a significantly faster decrease of YMRS scores when patients were treated within 2 weeks from onset of the current manic episode.”*

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Dark Therapy for Rapid Cycling Bipolar Disorder

Phelps J. Dark therapy for bipolar disorder using amber lenses for blue light blockade. *Med Hypotheses* 2008;70(2):224-9

- *“If amber lenses can effectively simulate darkness, a broad range of conditions might respond to this inexpensive therapeutic tool: common forms of insomnia; sleep deprivation in nursing mothers; circadian rhythm disruption in shift workers; and perhaps even rapid cycling bipolar disorder, a difficult-to-treat variation of common illness.”*

Long Nights, Bedrest, Light Therapy for Rapid Cycling Bipolar Disorder

Wirz-Justice A. A rapid-cycling bipolar patient treated with long nights, bedrest, and light. *Biol Psychiatry* 1999;45: 1075-1077

- *A previous study using morning light therapy in rapid-cycling bipolar patients worsened clinical state (Leibenluft et al 1995), but was not, as here, administered in combination with long nights and extended sleep. Our independent replication of dark/rest treatment strategy (Wehr et al 1998) indicates that chronobiologic protocols may be used as valuable adjunctive treatments to psychopharmacology, in particular, to interrupt rapid cycling.”*