Uses of non-conventional approaches in mental health care: *research update*

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View Bibliography

Assessment

- Emerging approaches may enhance diagnostic accuracy or specificity permitting improved treatment planning
- Assessment in mental health care is often over-looked or minimized
- Emerging assessment approaches include QEEG, serologic studies, VR testing environments and others

Emerging assessment methods

- Depression
- Mania and cyclic mood changes
- Anxiety
- psychosis

Assessment: depression

- Low serum folate levels predict more severe depressed mood and non-response to fluoxetine, other conventional antidepressants, lithium augmentation and thyroid hormone (Fava et al. 1997; Papakostas 2004a)
- A significant percentage of severely depressed patients have low serum folate levels.
- Many treatment refractory depressed patients respond to conventional or non-conventional treatments when folate in the form of folinic acid is added to their existing regimen (Papakostas 2004a).

Assessment: depression

- **QEEG is helpful in differentiating Unipolar and Bipolar depressed mood**
- Abnormal EEG findings occur in up to 40% of depressed patients (Small 1993). EEG changes described as “small sharp spikes” are often present in severely depressed suicidal patients (Small 1993).

Assessment: depression

- QEEG analysis of Unipolar depressed patients typically reveals increased alpha or theta power, and decreased inter-hemispheric coherence (Nieber 1992; Princhep 1990).
- In contrast, Bipolar depressed patients often have reduced alpha activity and increased beta power (John 1988).
- Bipolar patients often come to treatment after experiencing a single major depressive episode, but have not had a manic episode. In such cases a QEEG brain map provides valuable diagnostic information that can inform the most appropriate treatment.

Assessment: depression

- **Abnormal high auditory evoked response (AER) and decreased pre-frontal cordance predict enhanced antidepressant response rates**
- Response rates to conventional antidepressants can be predicted on the basis of differences in brain electrical activity evoked by sounds of various intensities.
- Relatively greater auditory evoked potentials (AER) correspond to lower brain serotonin levels, and predict improved response of Unipolar depressed patients (Gallinat, et al., 2000) to serotonin reuptake inhibitors (SSRIs).
- Cordance is a measure of localized electrical brain activity relative to averaged brain EEG patterns. Prospective studies show a relationship between *cordance* and response to anti-depressants that increase brain serotonin levels (Suffin 1997).

Assessment: depression

- Over half of patients with severe depressed mood who subsequently had the highest response rates to SSRIs showed significant decreases in pre-frontal cordance during the first 48 hours of therapy, suggesting that improvement was due to normalization of low brain serotonin levels (Demott, 2002; Cook, et al., 2002).
- Non-responders to SSRIs or placebo did not show negative pre-frontal cordance following treatment, suggesting that low serotonin was not the primary cause of depressed mood in these cases.
- Differences in prefrontal EEG cordance also predict response differences of depressed patients to homeopathic remedies (Bell 2004).

Assessment: depression

- **Low RBC membrane fatty acids may be correlated with increased severity of depressed mood**
- Red blood cell membrane levels and serum levels of DHA, an Omega-3 fatty acid, are consistently lower in depressed individuals (Peet et al. 1998; Tiemeier 2003).
- Preliminary findings suggest that the average dietary ratio of Omega-6 to Omega-3 EFAs is correlated with incidence of depression. Lower dietary intake of foods rich in Omega-3 fatty acids resulted in relatively higher ratios of AA (an Omega-6) to EPA (an Omega-3) in red blood cells, which in turn were positively correlated with greater severity of depressed mood (Adams et al, 1996; Edwards et al 1998).

Assessment: depression

- **Low serum cholesterol levels are correlated with severity of depressed mood and suicide risk**
- Depressed patients who attempt suicide have abnormal low serum total cholesterol and triglyceride levels, which may provide future clinical markers for suicide risk (Bocchetta 2001).
- Low serum lipid levels are associated with persistently low platelet serotonin levels in depressed suicidal patients (Steegmans 1996; Alvarez 1999).
- Low cholesterol levels indirectly lead to reduced brain serotonin because of the requirement of adequate cholesterol in nerve cell membranes in order to maintain the functional integrity of serotonin receptors (Sarchiapone 2001; Steegmans 1996).

Assessment: depression

- Total serum cholesterol and triglyceride levels are significantly decreased in patients who are considering suicide or who have recently attempted suicide (Yong-Ku 2003).
- Individuals afflicted with a rare genetic syndrome that causes an enzyme deficiency resulting in abnormal low serum cholesterol have a high rate of severe depression and suicide (Lalovic 2004).
- Non-suicidal depressives tend to have cholesterol levels in the range of 180mg/dl, and severely depressed suicidal patients tend to have serum total cholesterol levels in the range of 150mg/dl (Kim 2004)

Mania and cyclic mood changes

- **Low red blood cell (RBC) folic acid levels but normal serum levels are common in Bipolar patients**
- Folic acid deficiency may be a common nutritional factor in manic patients diagnosed with Bipolar disorder (Coppen 1986).
- Chronic folate deficiency is believed to interfere with normal synthesis of serotonin. Manic patients often have abnormal low red blood cell folic acid levels but normal serum folic acid levels (Lee 1992; Hasanah 1997).
- Chronic folate deficiency is associated with both phases of Bipolar illness however
- Bipolar patients who are taking lithium often have normal red blood cell folate levels (McKeon 1991).

Assessment: mania

- **Left-sided QEEG abnormalities may predict improved response to conventional treatments of mania**
- Abnormal EEG findings are more common in mania than depressed mood (Hughes 1999).
- Depressed mood, psychosis and acute mania are associated with distinctive patterns of brain electrical activity on QEEG mapping.
- Global disturbances in EEG synchronization are similar in schizophrenia and Bipolar Disorder. However, in contrast to schizophrenics, Bipolar patients do not show disorganization in the superior temporal lobes.
- Non-medicated manic patients have lower EEG amplitudes in the left anterior and temporal brain regions (Small 1998). QEEG findings may predict differential response rates to conventional treatments (Small 1999).

Assessment: mania

- Non-responders to conventional medications are more likely to have diffuse theta activity at baseline, and higher amplitudes in the left temporo-parietal regions during treatment (Small 1998; 1999).
- Acutely manic inpatients who responded to subsequent conventional treatments were more likely to have left sided abnormalities. The significance of these findings is limited by the low rate of cooperation of acutely manic inpatients in studies completed to date.

Assessment: mania

- **Elevated serum GABA levels predict improved response of mania to divalproex**
- High serum GABA levels may predict improved response of manic symptoms to divalproex (Depakote™) however, pre-treatment GABA levels do not predict improved response to lithium.
- In a large placebo-controlled double-blind trial, acutely manic patients who had abnormal high serum GABA levels responded differentially to divalproex (Petty 1996). GABA levels normalized with clinical response to treatment.

Assessment: mania

- **Children with low brain N-acetylaspartate levels may be at increased risk of developing Bipolar Disorder**
- Findings from a functional brain imaging study using proton magnetic resonance spectroscopy suggest that children at risk of developing Bipolar Disorder have abnormally low brain levels of N-acetylaspartate (Chang 2003).
- Children with low brain levels of this amino acid may be at increased risk of developing Bipolar disorder at an early age
- ***More studies needed***

Assessment: anxiety

- **EEG changes may correlate with specific anxiety symptoms and QEEG findings may predict differential response to conventional treatments**
- Anxiety symptoms frequently correlate with abnormal EEG or electro-cardiogram findings.
- EEG changes typically associated with anxiety include decreased alpha activity in generalized anxiety, increased theta activity in obsessive-compulsive patients, and paroxysmal activity in patients who experience panic attacks (Hughes 1999).
- EKG findings in anxious patients typically reveal increased sympathetic activity and decreased parasympathetic activity.

Assessment: anxiety

- QEEG findings may predict differential response rates of OCD patients to conventional medications. In one series, approximately 80% of OCD patients who exhibited increased alpha power responded to SSRIs, compared to 80% of OCD patients with increased theta activity who did not respond to SSRIs (Princhep 1993).
- Abnormal QEEG findings associated with other anxiety symptoms are highly inconsistent, and the future role of QEEG in the assessment of other anxiety symptom patterns remains unclear.

Assessment: anxiety

- **Elevated serum cholesterol may be a marker for many anxiety symptoms**
- Elevated serum cholesterol may be a biological marker for different anxiety syndromes including generalized anxiety, panic attacks and possibly also obsessive-compulsive disorder (Peter 2000).
- In contrast to high cholesterol levels in chronically anxious patients, many chronically depressed individuals have low serum cholesterol levels.

Assessment: anxiety

- Patients diagnosed with Obsessive-compulsive Disorder (OCD) have higher serum cholesterol levels compared to individuals diagnosed with Panic Disorder (Peter 1997).
- Successful response of anxiety symptoms to conventional medications is associated with a reduction of total serum cholesterol to normal levels.

Assessment: anxiety

- **Chronically anxious patients are often deficient in magnesium, selenium or phosphorous**
- Chronically anxious patients are often deficient in magnesium, selenium or phosphorous (Durlach 1994; Webb 1981; McCleane 1990).
- Mineral deficiencies often occur in patients who are malnourished in general.
- Always check serum chemistries of chronically anxious patients, and especially those who may be malnourished and who do not take quality vitamin and mineral supplements.

Assessment: anxiety

- **Electrodermal skin testing (EDST) may help determine whether Healing Touch is helpful for stress reduction**
- Electrodermal skin testing (EDST) may prove to be a useful assessment approach when determining whether conventional or subtle energy treatments of anxiety will be effective for a particular patient (Forbes 2004).
- Healing Touch (HT) practitioners conducted six trials comparing the anxiety reducing efficacy of conventional relaxation with Healing Touch. They concluded that electrodermal skin testing (EDST) reliably measured changes in “bioenergy” in meridians (according to Chinese medical theory) following both conventional and subtle energy treatments of anxiety (Stouffer in press).

Assessment: psychosis

- Consistently reduced red blood cell membrane levels of two fatty acids: arachidonic acid (AA) and decosahexanoic acid (DHA) have been reported in non-medicated schizophrenics compared to medicated schizophrenics and normal controls (Horrobin 1998; Arvindakshan 2003; Assies 2001).

Assessment: psychosis

- An open study compared serum lipid levels in 16 patients diagnosed with Dissociative Disorder according to DSM-IV criteria with 16 normal controls.
- Patients diagnosed with dissociative disorder had consistently lower total serum cholesterol, triglycerides, LDL and VLDL levels compared to matched controls.
- The relationship between red blood cell (RBC) levels of Omega-3 fatty acids is confounded by the high rate of smoking in schizophrenics and patients with other chronic psychotic syndromes. Smoking is correlated with reduced consumption of foods rich in Omega-3s and also with abnormally low RBC Omega-3s levels (Leng 1994; Hibbeln 2003).

Assessment: psychosis serum DHEA level

- Abnormal low serum DHEA level may be a marker for vulnerability to depression, anxiety, and schizophrenia.
- Serum DHEA (but *not* cortisol) levels increased significantly in chronically psychotic patients who improved when treated with DHEA.
- Lower serum DHEA may correlate with increased severity of psychotic symptoms on standardized scales (Harris 2001).
- Increases in serum DHEA correlated with reductions in negative psychotic symptoms (Strous 2003).

Assessment: psychosis DHEA and estrogen level

- In a prospective study of 26 active duty military personnel, higher serum DHEA levels correlated with fewer symptoms of dissociation and overall improved performance during periods of extreme stress (Morgan 2004).
- Women diagnosed with schizophrenia or other chronic psychotic syndromes frequently have abnormal low serum estradiol levels, and it has been suggested that women may be more susceptible to developing a psychotic syndrome when estrogen levels are low, including the premenstrual, post-partum periods, and following discontinuation of oral contraceptives (Huber 2001).

Assessment: psychosis niacin challenge test

- Emerging evidence suggests that the flushing response to niacin (and associated elevation in skin temperature) is attenuated in schizophrenia and other chronic psychotic syndromes.
- The mechanism of action probably involves dysregulation of phospholipid-dependent signal transduction and increased phospholipase A2 activity (Messamore 2003; Tavares 2003).
- Approximately 80% of schizophrenics do not flush when challenged with niacin compared to healthy controls. In one series, 43% of schizophrenics experienced abnormal low vasodilation in response to a 200mg challenge dose of niacin, compared to only 6% of individuals diagnosed with Bipolar disorder.

Assessment: psychosis

- Response to niacin is significantly affected by the dose used, age and gender. At low doses healthy men are more likely to be non-responders compared to women, suggesting that these factors should be considered when determining normative responses to a niacin challenge in male versus female schizophrenics.
- Continued refinement of the niacin challenge test may eventually provide a specific and sensitive clinical method for differentiating schizophrenia from other severe psychiatric syndromes (Hudson 1997; Puri 2002).

Assessment: psychosis
QEEG brain mapping

- QEEG may prove a useful adjunct to conventional assessment methods when the underlying causes of psychotic symptoms are not clearly established, or when a psychotic patient fails to respond to conventional treatment.
- Decreased alpha power in the frontal lobes is a typical finding in chronically psychotic schizophrenic patients who exhibit positive symptoms (Merrin 1992) and conventional antipsychotic medications are known to increase alpha power (Galderisi 1994).
- Conversely, negative psychotic symptoms are more often associated with changes in slow wave (delta) activity in the temporal lobes (Gattaz 1992).

Assessment: psychosis
QEEG brain mapping

- However, research findings are inconsistent suggesting that there are no simple correlations between EEG changes and psychosis (Lifshitz 1974).
- The range of findings suggests wide variation in the neurophysiological correlates of disparate psychotic symptom patterns (John 1994).
- This model is consistent with differential response rates to conventional antipsychotic drugs in psychotic patients exhibiting different QEEG findings (Czobor 1991, 1993).
- Differences in inter-hemispheric EEG coherence may prove useful in differentiating depressed or Bipolar patients who are psychotic from patients who are schizophrenic (Pockberger 1989).

Assessment: psychosis
serum phospholipase A2

- **High serum phospholipase A2 levels may be correlated with increased risk of developing schizophrenia or other severe psychiatric syndromes**
- Preliminary evidence suggests that serum levels of phosophlipase A2 are abnormally high in patients diagnosed with schizophrenia. In normal individuals this enzyme is involved in the turn-over of phospholipids in nerve cell membranes.
- schizophrenia and other severe psychiatric syndromes may be caused by abnormal high levels of this enzyme in the brain, resulting in a general deficiency of phosophlipids in nerve cell membranes, and associated abnormalities in neurotransmission Horrobin 1996; 1998).

Assessment: psychosis serum HVA level

- **Abnormal high serum homovanillic acid (HVA) levels may correspond to lower effective doses of first generation antipsychotics**
- Pretreatment serum homovanillic acid (HVA) levels may predict response to certain conventional antipsychotic medications in the treatment of acutely manic or psychotic inpatients.
- Abnormal high serum HVA levels may reflect an increased turnover rate of brain dopamine, and correspond to lower effective doses of dopamine blocking antipsychotics in the management of psychotic symptoms.

Assessment: psychosis serum HVA level

- Higher serum HVA levels predicted an improved response rate to lower doses of first generation antipsychotics including haloperidol (eg, 5mg/day).
- In contrast, lower pre-treatment HVA levels correlated with a need for higher dosing strategies of typical antipsychotics (eg, up to 25mg/day) (Chou 2000).
- It is unclear whether these findings generalize to treatment strategies using atypical antipsychotics or other conventional medications.

Treatment

- Non-conventional and integrative treatments may improve outcomes, enhance compliance, reduce adverse effects, and improve cost-effectiveness
- Emerging treatments include Omega-3 EFAs, DHEA, 5-HTP, glycine, acetyl-L-carnitine, L-theanine, EEG biofeedback, spiritually oriented support groups, acupuncture, VR exposure therapy, high density negative ions, qigong and others

Emerging treatment approaches

- Depression
- Mania and cyclic mood changes
- Anxiety
- psychosis

Treatment: depression
Omega-3 fatty acids

- **Omega-3 Fatty acids are an effective adjunctive treatment when combined with conventional antidepressants**
- Research findings suggest that several mechanisms of action may underlie the putative antidepressant effects of Omega-3 fatty acids, including increased CNS serotonin activity (Hibbeln 1998), anti-inflammatory effects (Calder 1997), suppression of phosphatidyl-inositol second messenger activity (Kinsella 1990), and possibly increased heart rate variability (Villa 2002).

Treatment: depression
Omega-3 fatty acids

- The mechanism of action may be similar to that of conventional antidepressants including tri-cyclics (TCA) and SSRIs, which are known to suppress release of many pro-inflammatory cytokines by immune cells, possibly causing beneficial changes in the brain that manifest as improved mood (Maes 1998).
- Increased production of pro-inflammatory cytokines takes place in the initial or “acute phase” of severe depressed mood (Maes 1996).

Treatment: depression
Omega-3 EFAs

- one small double-blind study has evaluated the efficacy of DHA alone as a treatment of severe depressed mood (Marangell 2003). Patients treated with DHA 2g/day or placebo improved at the same rate.

Treatment: depression
Omega-3 fatty acids

- Three small double-blind controlled studies have evaluated Omega-3s in combination with conventional anti-depressant medications (Peet 2001; Nemets 2002; Su 2003).
- In two studies EPA (1g/day or 2g/day) was added to the on-going conventional treatment. In the third study patients were treated with a mixture of EPA and DHA (9.6g/day) in addition to their conventional medication.
- In all three studies treatment response was significantly greater in the combined Omega-3/antidepressant groups compared to groups treated with antidepressants only.

Treatment: depression
Omega-3 fatty acids

- Some patients who had previously been refractory to conventional antidepressants improved significantly when Omega-3s were added to their conventional treatments.
- Patients in the combined Omega-3/antidepressant groups reported significant improvements in insomnia, and reduced feelings of guilt and worthlessness.
- Severe side effects were not reported in the combined treatment groups or the conventional treatment groups.

Treatment: depression exercise

- **Regular exercise is as effective as most conventional and non-conventional treatments**
- Case reports, randomized controlled trials and two meta-analyses confirm that regular exercise has beneficial effects on depressed mood (Lawlor 2001; Tkachuk 1999).
- Increased brain levels of mood-elevating endorphins, dopamine, norepinephrine and serotonin following sustained exercise have been proposed as possible antidepressant mechanisms.
- Regular exercise enhances self-sufficiency and ensures positive social interactions with other people.

Treatment: depression exercise

- It is difficult to separate beneficial effects of exercise from other life style factors, and it is possible that exercise contributes to overall feelings of wellness while not having specific mood elevating effects.
- The optimum duration or frequency of exercise in depressed mood has not yet been determined but probably varies with age and conditioning.
- Both aerobic exercise and non-aerobic strengthening exercises are equally efficacious.

Treatment: depression exercise

- Exercise is probably comparable to individual cognitive therapy and group therapy for depressed mood (Tkachuk 1999).
- The therapeutic benefits of regular exercise are also comparable to validated non-conventional treatments of depressed mood including St. John's Wort (Ernst 1998).
- Running 45 minutes twice each week, regular relaxation, meditation or group psychotherapy probably have equivalent antidepressant effects (Int J Ment Health, 1986, 13:148-177).

Treatment: depression exercise

- Depressed patients who exercise in a brightly lit (2500 to 4000 lux) indoor environment experience more significant improvements in mood and greater feelings of vitality compared to depressed individuals who exercise indoors in ordinary room light (400 to 600 lux) (Partonen 1998).
- Depressed women patients who combined exercise with bright light exposure while taking a daily vitamin regimen reported significant improvements in mood (Brown 2001).

Treatment: depression exercise

- In a 16 week study one hundred fifty six depressed patients over the age of 50 were randomized to aerobic exercise three times a week, medications (sertraline (Zoloft™) up to 200mg), or exercise and medications (Blumenthal 1999).
- All groups had improved significantly by the end of the study, and there were no significant differences in response rates using standardized symptom rating scales assessing mood, self-esteem, negative thoughts, etc.

Treatment: depression exercise

- Patients taking sertraline only improved faster initially than the other two groups, but patients who exercised only had a lower 6-month relapse rate.
- 60% of patients who exercised only experienced complete remission, versus 65% of patients taking Sertraline and 69% of patients who exercised and took a conventional antidepressant.
- Differences in these outcomes are not significant.

Treatment: depression dietary modification

- **Foods rich in B vitamins are beneficial in depressed mood**
- Observational trials show consistent relationships between good nutrition and improved mood.
- Reducing or eliminating consumption of refined sugar and caffeine significantly improves mood in some depressed patients, but research findings are inconsistent (Christensen 1991).

Treatment: depression dietary modification

- Foods rich in B-vitamins, especially folate, pyridoxine (B-6), and methyl-cobalamin (B-12) are especially beneficial. These vitamins work as enzyme co-factors, and facilitate the production of endogenous neurotransmitters including serotonin, dopamine and nor-epinephrine, whose deficiencies are hypothesized to be associated with depressed mood.
- Foods rich in B-vitamins include whole grains and dark green leafy vegetables.

Treatment: depression dietary modification

- **Diets high in Omega-3 fatty acids are associated with lower prevalence rates of depression**
- Food preferences influencing fatty acid consumption may be directly related to different rates of depressed mood when industrialized countries are compared to more traditional cultures.
- Epidemiological surveys have demonstrated an inverse correlation between risk of depressed mood and fish oil consumption. Countries where fish is an important part of the average diet are characterized by significantly lower rates of depressed mood and suicidality (Hibbeln, 1998; Tanskanen 2001; Silvers 2002).

Treatment: depression dietary modification

- **Negative findings from recent studies continue to obscure the relationship between a high-fish diet and the risk of depressed mood.**
- 452 men with histories of cardiovascular disease and angina were randomized to a diet high in fatty fish (or fish oil supplements) or “no fish advice” over a six month period (Ness 2003).
- At the end of the study period there were no significant group differences in new cases of anxious or depressed mood, and in fact more patients in the high-fish group reported depressed mood or anxiety.
- Principle sources of omega-3s include Salmon, Halibut, other deep sea fish, and flaxseed oil.

On-going research: depression
Omega-3 EFAs

- **Omega-3 fatty acids may accelerate response to conventional antidepressants**
- A NCCAM-sponsored double-blind controlled trial will evaluate a possible synergistic anti-depressant role of the Omega-3 fatty acid EPA when combined with a conventional antidepressant.
- All patients will take a conventional antidepressant (Citalopram), half will take EPA while half will take a placebo

Treatment: depression
5-HTP

- **5-hydroxytryptophan (5-HTP) in combination with conventional antidepressants is probably an effective treatment in some cases of refractory depressed mood**
- 5-HTP and L-tryoptophan are amino acid precursors of serotonin. Both have been evaluated for their antidepressant efficacy.
- 5-HTP is generally preferred over L-tryptophan because it crosses the blood-brain barrier at a higher rate, is converted converted into serotonin more efficiently than L-tryptophan, and has a more marked antidepressant effect.
- 5-HTP begins to have an antidepressant effect at doses between 100mg and 300mg/day.

Treatment: depression
5-HTP

- More than 15 controlled studies have demonstrated consistent positive effects of 5-HTP in moderate depressed mood (Birdsall 1998). However, most studies on 5-HTP in depressed mood are small and study design problems preclude definitive conclusions at present.
- A Cochrane review of 5-HTP and L-tryptophan in depressed mood identified 108 studies but analysis of findings was limited to only two studies involving 64 patients that met strict inclusion criteria (Shaw 2004). On the basis of those limited findings the Cochrane reviewers concluded that 5-HTP is *probably more effective* than placebo in depressed mood.

Treatment: depression
5-HTP

- 63 depressed patients randomized to fluvoxamine 150mg or 5-HTP 300mg experienced similar improvements in mood (Poldinger et al. 1991).
- Case reports show that treatment-refractory patients sometimes improve when 5-HTP 300mg is combined with Carbidopa, tricyclic antidepressants, MAOIs or SSRIs (van Hiele 1980; Nardini 1983; van Praag 1984; Sargent et al. 1998; Kline & Sacks 1980; Mendlewicz & Youdim, 1980).

Treatment: depression
5-HTP

- In an open study almost half of 100 patients who had been refractory to conventional antidepressants responded to 5-HTP (up to 600mg/day) in combination with carbidopa 150mg/day over a period of weeks to months (van Hiele 1980).
- Findings from another open trial suggest that 5-HTP 300mg/d is more effective against Bipolar depression than unipolar depressed mood (Fujiwara 1974).
- Rapid clinical improvement in depressed mood has been reported in patients treated by intravenous 5-HTP 25 to 50mg who are already taking oral MAOIs (Kline and Sacks 1980).
- 5-HTP is moderately sedating, and doses greater than 100mg are typically taken at bedtime.

Treatment: depression
Acetyl-L-carnitine

- **Acetyl-L-Carnitine is probably beneficial when depression occurs with cognitive impairment**
- Acetyl-L-carnitine (ALC) has been studied in placebo-controlled double-blind trials in severely depressed patients, elderly depressed patients, and depressed demented patients (Garzya 1990; Bella 1990).
- ALC has general neuroprotective effects, and mediates improved mood and possibly also reduction in the severity of cognitive impairments in normal aging, dementia or traumatic brain injury by enhancing mitochondrial energy production and partially compensating for deficits in CNS cholinergic activity.

Treatment: depression
Acetyl-L-carnitine

- Most studies conducted to date have evaluated ALC in elderly depressed patients, and have demonstrated a consistent antidepressant effect after about one month of treatment (Pettegrew 2000).
- In a two month placebo controlled study demented depressed patients treated with ALC 3g/day in divided doses experienced significantly greater improvements in mood and global functioning compared to patients taking a placebo (Bella 1990).

Treatment: depression
Acetyl-L-carnitine

- In a double-blind placebo controlled study almost half of elderly severely depressed patients (N=28) treated with ALC 500mg QID experienced full remission, and previously elevated serum cortisol levels normalized (Gecele 1991).
- In a small double-blind cross-over study hospitalized elderly depressed patients ALC had superior antidepressant efficacy compared to placebo, but comorbid anxiety symptoms did not improve (Tempesta 1987).

Treatment: depression
DHEA

- **Dihydroepiandosterone (DHEA) may be an effective monotherapy of moderate depressed mood, and should be considered when depression occurs together with psychosis, anxiety or cognitive impairment**
- The putative antidepressant mechanism of DHEA remains unclear, but may involve androgen receptors, estrogen receptors, or well defined neurotransmitter systems including serotonin, GABA, NMDA and norepinephrine.

Treatment: depression
DHEA

- Physiological replacement doses of DHEA (ie, 30 to 90mg/day, a dose range corresponding to DHEA serum levels that are normal in people younger than age 40) probably improve mood in middle-aged or elderly depressed patients (Wolkowitz et al. 1997).
- In a small 6-week study (N=22) DHEA administered in an escalating dose (30mg/day for two weeks followed by 30mg twice a day for two weeks and 30mg three times daily for two weeks) resulted in significant improvements in mood compared to placebo (Wolkowitz et al. 1999).
- Two thirds of patients in both groups continued on their conventional antidepressants, however 3 patients in the DHEA group and 4 patients in the placebo group did not take medications during the study.
- Depressed mood scores in half of patients in the DHEA group improved by 50% or more using standardized rating scales.

Treatment: depression
DHEA

- A larger follow-up study suggests that higher doses are probably more effective when DHEA is used as a monotherapy. In a six-week double-blind randomized placebo-controlled controlled, cross-over study (N=46) moderately depressed adults were randomized to DHEA 90mg/day for three weeks followed by DHEA 450mg/day (150mg TID) for three weeks versus placebo (Schmidt 2005).

Treatment: depression
DHEA

- None of the patients used conventional antidepressants concurrently with DHEA.
- A 50% or greater reduction in depressive symptoms was observed in the majority of patients in the DHEA group, which also reported improvements in baseline sexual functioning.
- Significantly, most patients who responded to DHEA remained asymptomatic at 12 months follow-up.
- Further research is needed to replicate these findings, evaluate DHEA for severe depressed mood, and clarify the mechanism for a synergistic or independent antidepressant effect of DHEA.

Treatment: depression

Yoga

- **Yoga is probably beneficial in both moderate and severe depressed mood**
- Of the various mind-body disciplines used to obtain relief from psychiatric symptoms, more studies have been done on Yoga than any other discipline (Shannahoff-Khalsa 2004).
- The mechanism of action of yogic breathing might be similar to vagal nerve stimulation (VNS) in that both approaches involve modulation of the balance of parasympathetic and sympathetic autonomic tone.
- Yogic breathing achieves desirable changes through a variety of specific breathing exercises that differentially affect the brain stem and limbic system while VNS relies on a weak electrical current to achieve desirable changes in brain autonomic activity that mediate improved mood or reduced anxiety.

Treatment: depression high-density negative ions

- **Regular exposure to high-density negative ions is beneficial in seasonal depressed mood**
- Research findings from double-blind controlled trials suggest that regular daily exposure to high-density negative ions is an effective treatment of depressed mood when there is a seasonal pattern of occurrence, and probably has comparable efficacy to bright light exposure for this condition.
- 25 depressed patients with seasonal depressed mood were randomized to high-density negative ions (2.7 X 10(6) ions/cm3) versus low-density negative ions (1 X 10(4) ions/cm3) using in-home ion generators 30 minutes daily for three weeks (Terman 1995).
- 58% of patients exposed to high-density negative ions experienced significant improvements in mood on standardized rating scales compared to 15% of patients exposed to low-density negative ions.

Treatment: depression acupuncture

- **Evaluating the clinical efficacy of acupuncture in depressed mood poses many methodological problems** (MacPherson 2004)**:**
  - heterogeneity in the severity and comorbidity of mental, emotional or physical symptom patterns
  - concurrent uses of other conventional or non-conventional treatments in patients receiving acupuncture
  - different Chinese medical diagnoses
  - the use of different acupuncture treatment protocols depending on the energetic formulation).

Treatment: depression
acupuncture

- **Acupuncture (including electro-acupuncture and computer-controlled electro-acupuncture) is probably beneficial in moderate and severe depressed mood**
- Controlled studies and case reports suggest that acupuncture has beneficial effects on depressed mood, including conventional needle acupuncture, electro-acupuncture (Hechun 1990), and computer-controlled electro-acupuncture (CCEA) (Hechun 1993).

Treatment: depression acupuncture

- The evidence base for acupuncture treatments of depressed mood has been extensively reviewed (Flaws and Lake 2000; Schnyer 2001).
- Findings of a double-blind sham-controlled study suggest that traditional acupuncture (ie, in the absence of electrical current) is an effective treatment of severely depressed outpatients (Allen 1998).
- By the end of the 8-week study 68% of 33 female outpatients being treated with an acupuncture protocol directed at depressed mood had achieved full remission. Interestingly, depressed women patients who were not receiving any treatment in the “wait-list” group showed equivalent improvement in mood.

Treatment: depression acupuncture

- In a large six week multi-center study 241 depressed inpatients were randomized to receive electro-acupuncture plus placebo or electro-acupuncture plus amitriptyline (Luo 1998).
- Both groups experienced equivalent improvement in depressed mood. Factor analysis using the Hamilton Rating Scale for Depression (HRSD) showed that electro-acupuncture was superior to amitriptyline when there was co-morbid anxiety.

On-going research: depression acupuncture

- An on-going NCCAM-sponsored study is being conducted to further examine the reported efficacy of acupuncture as a treatment of depressed mood.
- 150 patients diagnosed with major depressive disorder will be randomized to acupuncture or a wait-list.
- Patients receiving acupuncture will receive individualized treatment based on energetic imbalances from the perspective of Chinese medical diagnosis.
- Post-treatment follow-up will last 18 months during which the investigators will study relationships between beneficial energetic changes associated with acupuncture and clinical measures of improved mood used in conventional biomedicine.

Treatment: depression high-density negative ions

- In a randomized controlled trial 158 patients with seasonal depressed mood were randomly assigned to bright light exposure (10,000 lux) at different times of day versus high-density or low-density negative ions for two weeks (Terman 1998).
- Patients exposed to high-density negative ions or bright light experienced significant and equivalent improvements in mood. There was a differential beneficial effect of morning versus evening bright light exposure.

Treatment: depression
Yoga

- Like Yogic breathing techniques, the regular practice of various Yoga postures (asanas) probably results in beneficial changes in the autonomic nervous system resulting in improved cardiorespiratory performance and increased feelings of psychological well-being (Harinath 2004).
- Many styles of Yoga are probably beneficial in depressed mood. A particular style of yogic breathing called Sudarshan Kriya (SK) yoga has been extensively evaluated as a potential treatment of depressed mood and other mental or emotional symptoms (Shannahoff-Khalsa 1999).
- Moderately depressed patients improved significantly by the end of a 5-week yoga class (Woolery 2004).

Treatment: mania

- **EMPowerPlus ™, a unique nutrient formula, is probably an effective adjunctive or stand-alone treatment of both depressive and manic symptoms in Bipolar disorder**
- The findings of two case series suggest that EMPowerPlus ™, a nutrient formula containing 36 separate constituents including chelated minerals, vitamins, and trace elements may significantly reduce symptoms of mania, depressed mood and psychosis in Bipolar patients when taken together with conventional mood stabilizing medications (Popper 2001; Kaplan 2001).

Treatment: mania
EMPowerPlus™

- Bipolar patients are genetically predisposed to develop manic or depressive mood symptoms related to different micronutrient deficiencies. The mechanism of action may involve correction of in-born metabolic errors that predispose some individuals to become symptomatic when certain micronutrients are deficient in the diet (Kaplan 2001).
- Findings to date suggest that EMPowerPlus™ is probably beneficial alone or in combination with conventional mood stabilizers.
- Patients in the first series took 32 capsules of EMPowerPlus™ daily in four divided doses. 11 patients who completed the 6-month protocol were able to reduce their conventional mood stabilizing medications by half while improving clinically according to standardized symptom rating scales.

Treatment: mania EMPowerPlus™

- In another case series, 13 out of 19 Bipolar patients who continued to take EMPowerPlus™ reportedly remained stable after discontinuing conventional mood stabilizing medications (Simmons 2003).
- Four patients stopped taking the nutrient formula because of gastrointestinal side effects including nausea and diarrhea. Three other patients resumed conventional mood stabilizers because of recurring manic symptoms while taking EMPowerPlus ™.
- 11 of the 19 patients in the case series who elected to discontinue conventional mood stabilizers while continuing EMPowerPlus™ have remained stable for more than one year.

Treatment: mania
EMPowerPlus™

- Two randomized placebo-controlled double-blind studies are on-going at this time, one in Canada and one in the U.S. Bipolar patients enrolled in those studies will initially take 6 capsules three times a day, and further reduce the dose to a maintenance regimen of 3 capsules three times a day after two months on the initial protocol.
- On-going trials will identify specific nutrients in the complex EMPowerPlus ™ formula that have the most beneficial effects in Bipolar patients in order to simplify future treatment regimens and reduce adverse effects.
- More studies are needed to clarify whether a micronutrient formula alone is sufficient to stabilize Bipolar patients, and to determine possibly differing micronutrient treatments that address different symptom severities.

Treatment: mania
EMPowerPlus™ safety issues

- Significant micronutrient-medication interactions have been reported in patients taking EMPowerPlus™ with conventional mood stabilizers (Popper 2001).
- Interactions with micronutrients reportedly potentiate the effects of mood stabilizers and necessitate gradual reductions in doses as the nutrient formula is started.
- Researchers caution clinicians who are considering recommending EMPowerPlus™ to proceed gradually while carefully monitoring for adverse effects when transitioning Bipolar patients to the micronutrient formula in order to minimize the risk of toxicity.
- Lowering the doses of conventional mood stabilizing medications too rapidly after starting a patient on EMPowerPlus™ (or another nutrient formula) entails the risk of worsening symptoms, while maintaining conventional medications at their usual doses may result in significant toxicity.

Treatment: mania
branched-chain amino acids

- **A branched-chain amino acid drink resulting in acute depletion of tyrosine and phenylalanine may reduce symptoms of acute mania**
- Oral administration of certain branch-chain amino acids may rapidly improve acute manic symptoms by interfering with the synthesis of the catecholamine neurotransmitters norepinephrine and dopamine (Barrett 2004).
- A mixture of bioavailable amino acids excluding tyrosine and phenylalanine (the precursor of tyrosine) is believed to reduce brain dopamine in Bipolar patients, resulting in diminished manic symptoms and improved overall cognitive functioning (Gijsman 2002).

Treatment: mania
branched chain amino acids

- Twenty adult inpatients diagnosed with mania were randomized to receive the tyrosine-free mixture or placebo four hours before methamphetamine (which stimulates dopamine release) (McTavish 2001).
- Significant improvements in objective and subjective indicators of mania were noted in patients taking the tyrosine-free mixture of amino acids.
- The researchers speculated that restricting tyrosine in manic patients would result in diminished brain dopamine and attenuation of non-stimulant-induced manic symptoms.

Treatments: anxiety
L-theanine

- **L-theanine (gamma-ethylamino-L-glutamic acid) is an effective treatment of moderate and severe anxiety and does not cause drowsiness**
- Green tea is used as a restorative in traditional Chinese medicine and contains many bioactive constituents including the amino acid L-theanine.
- In recent years L-theanine has been extracted from Green tea, and is now widely used to treat anxiety symptoms and depressed mood in China, Japan and other Asian countries.
- The calming effects of L-theanine are believed to compensate for the stimulating effects of caffeine in Green tea (Kakuda 2000).
- The anti-anxiety effect of L-theanine is achieved through enhanced alpha brain wave activity and increased synthesis of GABA (Juneja 1999; Kakuda 2000).

Treatments: anxiety
L-theanine

- Increased GABA, in turn, increases brain levels of dopamine and reduces serotonin, resulting in general feelings of calm and well-being (Mason 2001).
- Changes in brain electrical activity measured by EEG are dose-dependent, and are similar to beneficial EEG changes observed in meditation, including increased alpha waves in the occipital and parietal regions (Ito 1998).
- A calming effect is usually noted within 30 to 40 minutes after L-theanine is taken at a dose of 50 to 200mg, and typically lasts 8 to 10 hours.
- Moderate anxiety symptoms often improve with a regimen of 200mg once or twice daily. More severe anxiety symptoms may require doses up to 600mg to 800mg daily taken in increments of 100mg to 200mg spaced over the day.
- Unlike benzodiazepines and other conventional anti-anxiety treatments, L-theanine does not result in increased drowsiness, slowed reflexes or impaired concentration. There is no risk of developing tolerance or dependence, and there have been no reports of serious adverse side effects or interactions with other natural products or synthetic drugs.

Treatment: anxiety

VR graded exposure therapy

- VRGET is an effective treatment of many anxiety symptom patterns including specific phobias, generalized anxiety, panic disorder with agoraphobia (Vincelli 2000) and post-traumatic stress disorder (Riva 2001).
- In a controlled study VRGET and conventional cognitive-behavioral therapy were equally effective in the treatment of panic disorder with agoraphobia, however patients who underwent VRGET required 33% fewer sessions (Vincelli 2003).

Treatment: anxiety
VR exposure therapy

- Case reports and controlled studies have demonstrated the effectiveness of VRGET in many specific phobias including fear of flying (Rothbaum 2000; Wiederhold 2002), fear of heights, fear of small animals, fear of driving, and others (Rothbaum 1999; Glantz 1996).
- In one controlled study 65% of anxious adults (N=45) diagnosed with a specific anxiety disorder according to DSM-IV criteria reported significant reductions in 4 of 5 anxiety measures (Maltby 2002).

Treatment: anxiety
VR exposure therapy

- VRGET is as effective as conventional exposure therapy for fear of flying, and is more cost-effective because both patient and therapist avoid significant time commitments and the need to use airplanes (Rothbaum 1999; Rothbaum 2000).
- In a pilot study individuals who overcame fear of flying using VRGET combined with biofeedback (including respirations, GSR and heart rate) were able to fly without the use of conventional medications or alcohol 3 months after treatment ended (Wiederhold 2002).

Treatment: anxiety
VR exposure therapy

- VRGET is also beneficial for traumatized patients who have been diagnosed with PTSD. A virtual environment that simulates the devastation that took place following the September 11, 2001 attacks of the World Trade Towers has been successfully used to treat individuals who suffered from severe PTSD following the attacks (Difede 2002).

Treatment: anxiety
VR exposure therapy—safety issues

- Fewer than 4% of individuals experience transient symptoms of disorientation, nausea, dizziness, headache and blurred vision when in a virtual environment.
- “Simulator sleepiness” is a feeling of generalized fatigue that occurs infrequently. Intense sensory stimulation during VRGET can trigger migraine headaches, seizures, or gait abnormalities in individuals who have these medical problems.
- VRGET is therefore contra-indicated in these populations. Anxious patients who are actively abusing alcohol or narcotics should not use VRGET.

Treatment: anxiety
VR exposure therapy—safety

- Patients who have disorders of the vestibular system should be advised to not use VRGET.
- Psychotic patients should not use VRGET because immersion in a virtual environment can exacerbate delusions and potentially worsen reality-testing (Wiederhold 2005).

Treatment: anxiety
EEG biofeedback

- **EMG, GSR and EEG biofeedback training reduces symptoms of generalized anxiety**
- Biofeedback has non-specific beneficial effects on many anxiety symptoms. EMG, thermal and EEG biofeedback training are efficacious treatments of generalized anxiety (Hurley 1992; Wenck 1996; Vanathy 1998).
- Biofeedback is probably equivalent to relaxation techniques (Scandrett 1986; Roome 1985) for the management of generalized anxiety in both adults and children.
- Chronically anxious patients trained in EEG or EMG biofeedback achieve symptom reduction similar to those taking conventional anti-anxiety medications (Rice 1993; Sarkar 1999).

Treatment: anxiety biofeedback

- GSR biofeedback in combination with a relaxation technique improves anxiety more than relaxation alone (Fehring 1983).
- The residual benefits of EEG biofeedback for anxious patients have not been clearly established. One study evaluated two EEG biofeedback machines on patients complaining of anxiety and “burnout” in an addiction treatment center (Ossebaard 2000).
- Although patients experienced immediate reductions in state anxiety during biofeedback training, long-term effects on “burnout” were not maintained following discontinuation of treatment.

Treatment: anxiety
5-HTP

- **5-HTP may be as effective as conventional medications for generalized anxiety**
- L-tryptophan and 5-HTP are widely used non-conventional treatments of generalized anxiety, but to date few rigorously conducted studies have examined their efficacy.
- Both amino acids are essential precursors for serotonin synthesis, a neurotransmitter that has a central role in the regulation of mood and anxiety.
- There is a more extensive research literature on 5-HTP for anxiety compared to L-tryptophan.
- In a double-blind study, 58% of generally anxious patients (N=79) randomized to L-tryptophan 3g/day reported significantly greater reductions in baseline anxiety compared to placebo (Zang 1991).
- Animal studies and human clinical trials provide evidence that 5-HTP has consistent anti-anxiety effects (Soderpalm 1990; Kahn et al. 1987).

Treatment: anxiety

5-HTP

- 5-HTP may inhibit panic attacks induced by carbon dioxide (Schruers 2000). Patients randomized to 5-HTP with carbidoba (a drug that inhibits the enzyme that breaks down 5-HTP in the peripheral blood supply, thus increasing the amount of 5-HTP that crosses the blood-brain barrier) reported significant reductions in anxiety that were comparable to clomipramine, a conventional anti-anxiety medication.
- Patients taking a placebo did not improve (Kahn 1987). 5-HTP may be safely combined with conventional anti-anxiety drugs with monitoring for adverse effects related to excessive brain serotonin, including insomnia, agitation and nervousness.

Treatment: anxiety

5-HTP

- The risk of adverse effects is minimized when 5-HTP is started at doses of 25mg/day and gradually increased over several weeks to a daily regimen that is well tolerated and produces beneficial anti-anxiety effects.
- 5-HTP 50mg to 100mg three times a day is well tolerated without excessive daytime sedation, and is effective approach for many chronically anxious patients when used alone or in combination with SSRIs or other conventional anti-anxiety drugs.
- Gradually titrating a bedtime dose of 5-HTP to 200 to 400mg often reduces daytime anxiety and improves the quality of sleep in chronically anxious patients who complain of insomnia.

Treatment: anxiety acupuncture

- **Acupuncture and electro-acupuncture probably reduce symptoms of generalized anxiety**
- Acupuncture and acupressure are widely used to treat anxiety. Extensive case reports from the Chinese medical literature suggest that different acupuncture protocols are beneficial in the management of anxiety symptom pattern that resemble generalized anxiety and panic attacks (Flaws and Lake 2001).
- Only a few small prospective controlled studies support the use of these traditional energy therapies, and most studies on the anxiety-reducing effects of acupuncture examine the general benefits of acupuncture on several mental and emotional symptoms, including anxiety.

Treatment: anxiety acupuncture

- A narrative review of controlled studies, outcomes studies and published case reports on acupuncture as a treatment of anxiety and depressed mood was recently published by the British Acupuncture Council. (British Acupuncture Council 2002). Sham-controlled studies yielded consistent improvements in anxiety using both regular acupuncture and electro-acupuncture.

Treatment: anxiety
Reiki

- **Regular Reiki treatments may reduce symptoms of anxiety associated with chronic pain or depressed mood**
- The findings of two studies suggest that regular Reiki treatments reduce the severity of anxiety symptoms in individuals who are chronically stressed (Heidt 1981; Kramer 1990).
- Patients with mixed anxious depressed mood experienced significant relief following weekly treatments with contact or non-contact Reiki (Shore 2004).
- Reiki treatments may improve state anxiety in chronic pain patients. 120 chronically ill patients were randomized to receive Reiki, sham Reiki, progressive muscle relaxation and no treatment (Dressen 1998).

Treatment: anxiety
Reiki

- Improvements in state anxiety (and pain) in patients receiving Reiki were significantly greater than the other three groups.
- Significance of findings limited by absence of control for possible differences in the use of anxiety reducing medications between the active treatment groups and the control groups.

Treatment: psychosis
Ayurvedic herbal formulas

- **Brahmyadiyoga, an Ayurvedic compound herbal medicine, holds significant promise for the management of psychosis**
- Brahmyadiyoga is a compound herbal formula used in Ayurvedic medicine for the treatment of symptom patterns that resemble schizophrenia. The formula includes six herbs including *Rauwolfia serpentina* from which reserpine was isolated in the early 20th century and shown to have significant antipsychotic efficacy.
- Reserpine is seldom used to treat schizophrenia in Western countries today because of concerns over reports of severe depressed mood.

Treatment: psychosis
Ayurvedic herbal formulas

- In a two-month double-blind placebo controlled study, 108 chronically psychotic patients were randomized to Brahmyadiyoga 8-12g in four divided doses, Valarian 8-12 g in four divided doses, chlorpromazine 200-300mg/day and placebo (Mahal 1976).
- Patients treated with Brahmyadiyoga (but not Valerian) and chlorpromazine reported significant and comparable improvements in symptom severity. No significant adverse effects were reported in the group taking Brahmyadiyoga.
- A subsequent study confirmed the antipsychotic efficacy of Brahmyadiyoga (Ramu 1992).
- Preliminary research findings suggest that another compound herbal formula, Mentat ™, may reduce negative psychotic symptoms (Das 1989).
- Ayurvedic herbal medicines should be used only under the supervision of a qualified Ayurvedic physician.

Treatment: psychosis
Omega-3 fatty acids

- **Supplementation with Omega-3 fatty acids may improve both positive and negative psychotic symptoms**
- Findings from case reports (Puri 2002; Su 2001) suggest that Omega-3 fatty acids improve psychotic symptoms.
- In a small open study (Arvindakshan 2003b) chronically psychotic patients experienced significant clinical improvements when treated with Omega-3s (EPA and DHA) 300mg and antioxidant vitamins twice daily over a four month period. Sustained improvements in psychotic symptoms were reported throughout the trial.
- A small double-blind study (Peet 1997) demonstrated sustained improvement in both positive and negative psychotic symptoms in chronically psychotic patients treated with Omega-3 fatty acids, with or without conventional antipsychotic medications.

Treatment: psychosis
Omega-3 fatty acids

- In a more recent and larger study (Peet 2002) 115 treatment-refractory schizophrenics were randomized to receive 1, 2 or 4g/day of EPA or placebo together with their conventional antipsychotic medications.
- Only patients taking Clozapine (but not other antipsychotics) experienced improvements greater than those observed in the group taking EPA. Clinical improvements were observed in all EPA-treated groups taking Clozapine, but the group receiving 2g/day benefited most.

Treatment: psychosis
Omega-3 fatty acids

- Another double-blind placebo-controlled study revealed no differences in response between an Omega-3 fatty acid, ecosapentanoic acid (EPA) (3gm/day), and placebo over a 4 month period in a group of 87 chronically psychotic patients taking conventional antipsychotics concurrently (Fenton 2001).
- In contrast to earlier studies, patients in the Fenton study were treated for residual psychotic symptoms, but *did not receive Omega-3 fatty acids while in the early acute phase of illness*.
- Significantly, the results of a similar study (Emsley 2002) using ethyl-EPA instead of EPA concluded that EPA was an effective augmentation treatment.

Treatment: psychosis
DHEA

- **DHEA may be an effective adjunctive treatment especially for *negative* psychotic symptoms**
- The sulfated form of DHEA—DHEA-S—is the most abundant steroid in the body. DHEA is an important neuroactive steroid because it acts as an antagonist to the GABA receptor complex, thus modulating neuronal excitability (Howard 1992).
- Possible mechanism of action include increased dopamine release in the frontal cortex and enhanced activity of NMDA and sigma receptors (Majewska 1987; Maurice 2001).
- In a six-week randomized placebo-controlled study thirty schizophrenic inpatients treated with DHEA 100mg/day in addition to their regular antipsychotic medications experienced significant improvements in negative psychotic symptoms including reduced apathy and social withdrawal.

Treatment: psychosis

DHEA

- Patients taking DHEA report marked improvement in depressed mood and anxiety (Strous 2003).
- There were no significant changes in positive psychotic symptoms including auditory hallucinations and delusions.
- Findings of another small double-blind study (N=30) suggest that DHEA augmentation (100mg/day for six weeks) of conventional antipsychotic medications, is well tolerated, significantly reduces negative symptoms, and may be especially effective in women (Strous 2005).

Treatment: psychosis glycine

- **Adding glycine to conventional antipsychotics may improve negative symptoms**
- Some cases of chronic psychosis may be related to abnormal low activity of the excitatory neurotransmitter glutamate or dysregulation of NMDA receptors to which glutamate binds.
- NMDA receptors function best when both glutamate and glycine bind to them, increasing their excitatory activity (Ishimaru 1997).
- Provisional evidence is consistent with the hypothesis that atypical antipsychotics increase brain glutamate.

Treatment: psychosis
glycine

- In one small open series, 11 patients switched from a first-generation antipsychotic to a newer atypical agent were found to have significantly higher brain glutamate concentrations (Goff 2001).
- Increased glutamate correlated with significant improvements in negative psychotic symptoms including reduced social withdrawal and apathy.
- A small open trial resulted in beneficial effects of glycine at doses up to 60g/day (Leiderman 1996).
- In a six week double-blind cross-over study 22 treatment-resistant schizophrenics were randomized to glycine 0.8g/kg versus placebo in addition to their conventional antipsychotic medication (Heresco-Levy 1999).

Treatment: psychosis
glycine

- Negative symptoms and global functioning decreased by 20 to 30% with glycine augmentation (up to 60g/day) compared to conventional treatment alone, and glycine was well tolerated at therapeutic doses.
- Case reports suggest that glycine supplementation may improve mood and overall cognitive functioning in some chronic schizophrenics (Heresco-Levy 1996; Zylberman 1994).
- Glycine has few adverse effects however there are case reports of acute psychosis in some chronically psychotic patients treated with large doses.
- The clinical use of glycine is complicated by the fact that it is impractical for many chronically psychotic patients to take large doses of glycine (or any nutritional supplement) that can potentially ameliorate their symptoms.

On-going research: psychosis--glycine

- **Glycine may improve negative and positive symptoms when combined with Clozapine**
- Previous research has established that high doses of glycine result in significant improvements in negative psychotic symptoms (above).
- D-cycloserine may improve negative psychotic symptoms when used in conjunction with conventional antipsychotics, but may exacerbate psychotic symptoms when used concurrently with Clozapine.
- Glycine and Clozapine may have a shared mechanism of action involving modulation of the NMDA complex.
- This NCCAM-sponsored study will determine whether there is a significant synergistic effect when glycine is taken together with Clozapine.
- Researchers will also evaluate D-cycloserine to determine a possible worsening effect when used with Clozapine.

Treatment: psychosis
spiritual support group and yoga

- **Yogic breathing combined with spiritually oriented group psychotherapy improves overall functioning in chronic schizophrenics**
- Complex relationships exist between religious or spiritual beliefs and practices and psychotic symptoms.
- Individuals who have a history of schizophrenia or another chronic psychotic illness and are stable or have well controlled residual symptoms may benefit from social support that comes with involvement in organized religion.
- A spiritual orientation can provide encouragement, social support and valuable insights to people who struggle daily with schizophrenia (Sullivan 1993).
- Innovative efforts to build support groups for chronic schizophrenics around spiritual themes and mind-body practices have identified important benefits of this approach (Sageman 2004).

Treatment: psychosis
spiritual support group and Yoga

- Individuals who participated in the support group reported significant improvements in general self-esteem and increased hopefulness together with a deeper sense of connection with their peers and communities.
- Group prayer, reading passages from various spiritual traditions, and Yogic breathing practices are valuable components of the group process. Sudarshan Kriya yoga is especially effective in reducing anxiety and improving mental clarity (Brown 2002).

Treatment: psychosis spiritual support groups

- The researchers felt that schizophrenic patients who attended spiritually oriented support groups improved more than patients in more conventional support groups.
- Significant clinical benefits of regular spiritually oriented groups include improved range of affect, enhanced feelings of subjective well-being, improved cognitive functioning during groups, deeper experiences of interpersonal bonding with other group members, and enhanced capacity for empathy.

Treatment: psychosis laser acupuncture

- **Daily laser acupuncture treatments may improve global functioning in schizophrenics**
- The use of laser light to stimulate specific acupuncture points reportedly results in significant clinical improvements in patients diagnosed with schizophrenia based on standardized symptom rating scales.
- Researchers at the Institute of Mental Health, Beijing College of Medicine, have developed a protocol that uses laser light of different wavelengths to stimulate the ermen acupoint in schizophrenics **(Liu 1986).**
- The protocol is based on daily 10 minute sessions , excluding Sundays, and reportedly reduces the severity of auditory hallucinations and other positive psychotic symptoms. In a single-blind study 15 schizophrenic patients with a 5 year or shorter history of active symptoms were randomly assigned to receive laser acupoint therapy with a 25mW versus a 5.9mW laser for a total number of 30 consecutive daily treatments (Jia 1987).

Treatment: psychosis

laser acupuncture

- Patients did not know the specifications of the laser used. Conventional antipsychotic drugs were not taken throughout the 30 day trial.
- Protocols using both lasers reportedly resulted in significant and equivalent clinical improvement by blind physician raters on the Brief Psychiatric Rating Scale (BPRS), the CGI, and other standardized symptom rating instruments. No significant between-group differences were observed.
- Changes in blood chemistries or adverse physical or psychological effects of laser acupoint treatment in this population have not been reported.

Treatment: psychosis laser acupuncture

- A subsequent controlled study on 33 individuals diagnosed with schizophrenia concluded that laser acupuncture following the above protocol and daily chlorpromazine were equally effective as measured by standardized rating scales of positive and negative psychotic symptoms (Zhang 1991).
- Larger studies including a sham-laser treatment arm, a sham acupuncture protocol, and double-blinding are needed to confirm the significance of these findings.

Closing remarks

- Many non-conventional assessment and treatment approaches are supported by strong research evidence
- Emerging assessment approaches may improve the diagnostic accuracy or specificity
- Emerging treatments used alone or in combination with conventional approaches may improve outcomes, cost-effectiveness, and safety

Forthcoming publications

- ***A Clinical Manual of Complementary and Alternative Treatments in Mental Health***, eds. Lake and Spiegel, American Psychiatric Press, Inc., expected publication date March, 2006.
- ***A Textbook of Integrative Mental Health Care: Foundations and Clinical Methods,*** Lake, Thieme Medical Publishers, expected publication date March 2006

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